THE PROPAGANDA FOR REFORM IN PROPRIETARY MEDICINES

THE PROPAGANDA FOR REFORM

— IN —

Proprietary Medicines

FIFTH EDITION

REVISED TO SEPTEMBER 12, 1908.

PREFACE

In February, 1905, the Council on Pharmacy and Chemistry of the American Medical Association was organized to investigate the proprietary medicine question and to pass on those which should be up to the standard required of ethical proprietary medicines. From time to time reports of this Council have appeared in the columns of THE JOURNAL of the American Medical Association, and THE JOURNAL has also contained other matter relating to the question of nostrums and proprietary medicines not directly connected with the work of the Council. Requests have been received repeatedly for this or that number of THE JOURNAL containing an article on the subject, and as it has been impossible to furnish many of the copies asked for, it has been thought best to collect some of the matter and issue it in this reprint form. The matter is reprinted from THE JOURNAL, and following each article is given the date on which it appeared.

THE PROPAGANDA FOR REFORM IN PROPRIETARY MEDICINES.

PART I.
COUNCIL REPORTS.

ACETANILID MIXTURES.

Official Report of Council on Pharmacy and Chemistry.

(*From The Journal A. M. A., June 3, 1905.*)

The following report has been approved by the council:

To the Council on Pharmacy and Chemistry of the American Medical Association:

In response to the request of your chairman we have investigated the below-mentioned preparations and report as follows:

Specimens of the articles were bought in different cities in the open market, and in original, sealed packages, and were analyzed by some of us or under our direction. Each article was examined by at least two chemists, and some were subjected to several analyses. While certain of the preparations are represented as being chemical compounds, the specimens examined were all found to be mixtures; the principal ingredient being acetanilid. The percentage proportions of acetanilid given below are the minimum obtained by any of the analysts.

Soda and ammonia, combined with carbonic acid, are calculated and reported as sodium bicarbonate and as ammonium carbonate (U. S. P.) respectively. Salicylic acid is calculated and reported as sodium salicylate. Diluents and other constituents than those reported were not determined.

AMMONOL.

According to the analyses of the contents of the original sealed packages as purchased, this was found to be a mixture, and to contain the following ingredients approximately in the proportions given:

Acetanilid.	Sodium Bicarb.	Ammonium Carb.
50.	25.	20.

ANTIKAMNIA.

According to the analyses of the contents of the original sealed packages as purchased, this was found to be a mixture,

and to contain the following ingredients approximately in the proportions given:

Acetanilid	Caffein	Citric Acid	Sodium Bicarb.
68.	5.	5.	20.

KOEHLER'S HEADACHE POWDERS.

According to the analyses of the contents of the original sealed packages as purchased, this was found to be a mixture, and to contain the following ingredients approximately in the proportions given:

Acetanilid	Caffein
76.	22

ORANGEINE.

According to the analyses of the contents of the original sealed packages as purchased, this was found to be a mixture, and to contain the following ingredients approximately in the proportions given:

Acetanilid	Sodium Bicarb.	Caffein
43.	18.	10.

Other constituents said to be present were not determined.

PHENALGIN.

According to the analyses of the contents of the original sealed packages as purchased, this was found to be a mixture, and to contain the following ingredients approximately in the proportions given:

Acetanilid	Sodium Bicarb.	Ammonium Carb.
57.	29.	10.

Certain packages of phenalgin were purchased which on analysis did not show ammonium carbonate.

SALACETIN.

According to the analyses of the contents of the original sealed packages as purchased, this was found to be a mixture, and to contain the following ingredients approximately in the proportions given:

Acetanilid	Sodium Bicarb.	Ammonium Carb.
43.	21.	20.

We recommend that this report be printed in THE JOURNAL of the American Medical Association.

Respectfully submitted

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ANASARCIN AND ANEDEMIN.

Reports of the Council on Pharmacy and Chemistry and Comments Thereon.

(From The Journal A. M. A., May 4 and 11, 1907, pp. 1535, and 1641.)

The following reports were submitted to the Council by the subcommittee to which these articles were assigned:

ANASARCIN.

To the Council on Pharmacy and Chemistry:—Your subcommittee to whom Anasarcin (Anasarcin Chemical Co., Winchester, Tenn.) was assigned, herewith submits its report:

This remedy is offered in two forms: "Anasarcin Tablets," a pretended combination of the active principles of oxydendron arboreum, sambucus canadensis, and urginea scilla; and "Anasarcin Elixir," said to contain the active principles of oxydendron, sambucus, hepatica and potassium nitrate. The advertisements of these articles conflict with the rules of the Council as follows:

With Rules 1 and 2: The composition of these articles is kept secret, in that the proportion of the ingredients is not furnished. The statement that it contains the "active principles" is misleading, since these are for the most part unknown.

With Rule 6: The description of the pharmacologic action of Anasarcin agrees practically with that of squill. No material part of its effects can be attributed to the other ingredients. Nevertheless, the advertisement studiously cultivates the impression that Anasarcin has no relation whatever to the digitalis group in which scilla is commonly placed. The claims are therefore misleading. The claim of its infinite superiority to digitalis, the claims that it cures neurasthenia, eliminates uric acid in rheumatism, and is useful in obesity, cystitis, lumbago and eclampsia, dyspepsia and asthma, and that it works wonders in exophthalmic goiter, appear exaggerated or false.

The recommendation of its indiscriminate use in nephritis, for lowering the blood pressure and the statement (contradicted in the firm's own literature) that it is not depressing are actually dangerous.

It is recommended that the articles be refused recognition, and that the report, with explanations, be published.

ANEDEMIN.

To the Council:—Your subcommittee to whom Anedemin (Anedemin Chemical Co., Winchester, Tenn.) was assigned herewith submits its report:

Anedemin is an evident imitation of Anasarcin. It is marketed as tablets, said to contain the isolated active principles of strophanthus, apocynum, squill and sambucus—chemically combined. The quantities are not stated. The therapeutic claims are copied almost literally from the Anasarcin circulars and are equally false. Anedemin, therefore, conflicts with Rules 1, 5, 6 and 7.

It is recommended that this report be published, with comments.

The reports were adopted by the Council and are herewith published.

W. A. PUCKNER, Secretary.

REMARKS ON ANASARCIN AND ANEDEMIN.

ANASARCIN.

This wonderful remedy, Anasarcin, has already been exposed in these columns (vol. xlvi, p. 288), but it deserves additional mention, as it teaches several important lessons of general application. It is a typical example of the revival, under a new name and a thin disguise, of an old, time-worn article, squill, presumably because experience has demonstrated its general inferiority to other drugs. Anasarcin further illustrates the dangers involved in the use of semi-secret nostrums. It also shows how a short experience with a widely advertised but little understood drug is apt to lead to conclusions which more extensive experience demonstrates to be entirely fallacious.

The first lesson is, that formulas are not always what they seem. A hasty glance at the formula of Anasarcin tablets, the basis of the Anasarcin dropsy cure, creates the impression that it is a non-secret remedy; for it is said to represent a combination of the active principles of oxydendron, sambucus and scilla. As a matter of fact, it is a secret nostrum of the insidious kind. A formula which omits the quantities of its potent ingredients means very little. Further than this, we do not hesitate to charge that the claimed composition is a deliberate deception. The circulars emphasize the claim that Anasarcin consists of the *isolated principles*, and not of the crude drugs. Now, the isolated active principles of sambucus and oxydendron are not on the market, for the good and sufficient reason that no active principles have ever been isolated. Are we to believe that the Anasarcin Company has surpassed the accredited chemists and has discovered such principles and is isolating them? We shall have more to say on this subject presently; but any one in the least familiar with the difficulties attending the isolation of organic principles knows such

an idea to be preposterous. Indeed, it is absolutely incompatible with the exhibition of ignorance of the elementary facts of pharmaceutical chemistry which is given by these people when they call the active principles of digitalis and squill "alkaloids."

It is an axiom that the effects of a mixture can only be understood if the action of its components are known. So far as we know, the physiologic effects of oxydendron and sambucus have never been scientifically investigated, for the simple reason that they are too slight and indefinite to promise results. Both are credited with some slight, obscure diuretic action. Oxydendron, the sour wood or sorrel tree, is a small tree of the heath family, the acid leaves of which are said to be chewed by hunters for their pleasant taste and for the relief of thirst. Sambucus is the common elder. It is most unlikely that these two innocuous substances should play any part in the claimed powerful effect of Anasarcin; they are evidently put in the formula, we do not say in the preparation, to obscure the fact that Anasarcin is composed principally of squill. That this is so can be gathered unmistakably from a study of the pharmacologic action of Anasarcin as described by its promoters:

> Acting primarily on the heart and arterial systems through the nerve ganglia, a natural physiologic balance is established between the arterial and venous systems, whereby effusions . . . are eliminated . . . . Coincident with this action there is a noteworthy *slowing* of the pulse. . . . If the remedy is pushed, can be brought down to 20 or 30 beats per minute. . . . Its physiological action is to stimulate the cardiac motor-ganglia through the cardiac plexus of the sympathetic system and at the same time exert an inhibitory influence upon the cardiac fibers of the pneumogastric, thereby dilating the arterioles, slowing the heart's action, and increasing the force of the systole. . . . The prolonged diastole allows the ventricle time to completely fill, and the more forcible contraction causes the mitral valve to close more thoroughly and at the same time increases pressure in the coronary arteries, serving thereby the double purpose of relieving pulmonary engorgement and increasing heart nutrition.
>
> Anasarcin will nauseate some persons.

To appreciate fully the meaning of this description of the actions of Anasarcin, it should be compared with the effects of the digitalis group, to which squill belongs. The following account is quoted literally from a recent Text-Book of Pharmacology (Sollmann):

The phenomena of the therapeutic stage of digitalis action are said to be:

1. Slowing of the heart, with systole and diastole both lengthened.
2. Increased strength of beat, leading to greater efficiency of the individual contractions, and to an increase in the total efficiency.
3. A tendency to the systolic phase.
4. A rise of blood pressure, due mainly to the increased action of the heart, but partly also to a vaso-constriction.

The therapeutic action may be explained, in part, as follows:

A larger amount of blood will be thrown into the aorta and coronary circulation. The first effect will be an improved nutrition of the heart. . . . The tonic action . . . narrows the ring of the valves, brings them together, narrows the orifice. . . . The venous congestion will tend to be relieved. This relief . . . will fall in the first place upon the lungs. . . . The lowering of the venous pressure will tend to cause absorption of the effusions.

The nauseant action of squill, which is alluded to in connection with Anasarcin, is too well known to require more than a mention.

In brief, then, it appears from the statements of the Anasarcin Company that the action of the remedy is that of squill and that the other ingredients are a mere blind. It is, of course, well known that squill can be used as a substitute for digitalis in cardiac dropsy, although it is generally considered very inferior to the latter drug. Rose Bradford, for instance, states: "Squill is not used to any extent in the treatment of cardiac disease and cardiac dropsy, digitalis being a far more efficient and less toxic substance." However, it has been frequently observed that digitalis occasionally fails, and it may then be replaced successfully by another member of the group. At all events, it is very likely that squill is a fairly efficient substitute for digitalis, especially when it is supplemented by a very free course of Epsom salts and by potassium nitrate (the active ingredient of Anasarcin Elixir), both of which are stated to be essential adjuvants to the Anasarcin (or squill) tablets. There can be no objection to the use of squill when it is indicated; but any one who wishes to use it should do so with his eyes open, knowing what substance he is using and how much (which he does not in Anasarcin); knowing also that it has the same indications and limitations as digitalis. He should not be misled by such statements as the following:

"Does what dropsy medicaments have hitherto failed to accomplish."

"Superior to digitalis, strophanthus, scoparius, squills, acetate of potash and the hydragogue cathartics all put together."

"The only known relief" (how modest!) "and permanent cure of dropsies."

"Unrivaled heart tonic." "The most powerful agent known."

Any one wishing to use squill should take the trouble to acquaint himself with the results obtained by competent and independent observers, and not rely on it in eclampsia, septicemia, "vices of civilization," all forms of neurasthenia, as "an active eliminator of uric acid in rheumatism," in hepatic cirrhosis, dyspepsia, asthma, obesity, cystitis (!), lumbago, exophthalmic goiter, etc.

He should also learn the contraindications to the use of squill, deducible from the fact that it causes vasoconstriction and raises the blood pressure (prohibiting its use in Bright's disease and arteriosclerosis), and that it produces marked gastric irritation, consequently nausea and depression, that it is a very toxic agent, and that the dangers of cumulative action must be borne in mind. In respect to these the advertisements of the Anasarcin people are little short of criminal, for these state:

"Safe in administration." "Non-toxic as ordinarily administered." "Will nauseate some persons," but "the reaction from the temporary depression is prompt." "In Bright's disease, both the interstitial and parenchymatous forms of nephritis, acute or chronic, no remedy . . . to equal it in efficacy." "Without increasing the debility of the patient or interfering with nutrition by producing loss of appetite." "This treatment is to be continued without cessation until all symptoms of dropsy have disappeared."

Physicians who are inclined to disregard this warning, and who follow the advice of the Anasarcin people, should remember that their patients—or their friends—will put the blame for the results, which are bound to follow sooner or later, on the prescribers, and not on the deceptive advertisements of the Anasarcin Chemical Company.

There is another little matter which throws an illuminating side-light on the Anasarcin Company. They take every occasion to say that Anasarcin is "not offered to the laity," "never sold to the laity," etc.; but witness the following, which was found in the *Retail Druggist* of May, 1906, p. 179. The italics are ours:

CURE FOR DROPSY.

As every druggist knows, dropsy has been one of the incurable diseases when caused either from heart, liver or kidney trouble. A *pharmacist* in Winchester, Tenn., *has worked out a remedy* called Anasarcin, which he is exploiting to the physicians, and his remedy is showing itself as possessing great merit. Several hopeless cases have been treated as a last resort by Anasarcin and in a very short time the patient has shown marked improvement and has effected permanent cures.

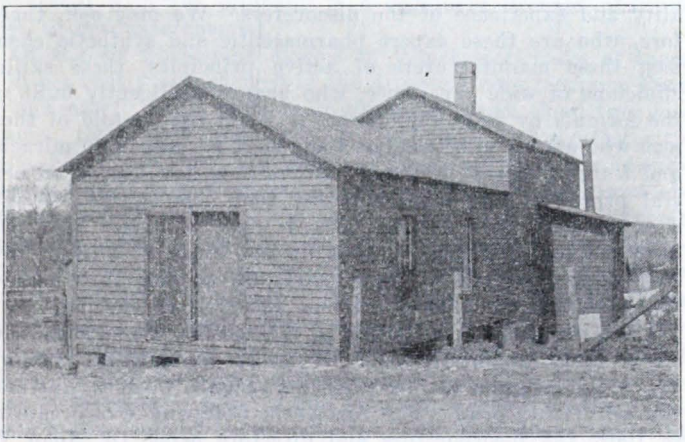
The result of the cases as handled by the physician with the aid of Anasarcin has been so easily and quickly cured that physicians of Tennessee and the southern states are high in their praises of the remedy. The company which now manufactures and sells it is known as the Anasarcin Chemical Co., of Winchester, Tenn. *Any druggist who knows of a case of dropsy would be conferring a favor on the patient and mankind in general by telling the party* or his physician *of the southern pharmacist*, and we have no doubt but what a prompt relief and permanent cure would be affected [Probably means effected.—ED.]

ANEDEMIN.

If we are disposed to doubt the vaunted scientific ability of the Anasarcin Company, we are forced to admire their business methods, at least, if there is any truth in the saying that imitation is the seal of success. Anasarcin has had this rather undesirable compliment paid to it, for its native town of Winchester has given birth to another remedy, Anedemin, which looks like a fair-haired twin brother. The Anedemin Company has adopted Anasarcin almost bodily. The name—"opposed to edema"—is about as close as the copyright laws permit. The pharmacologic and therapeutic claims agree almost literally with those of Anasarcin and contain the same exaggerations and dangerous mis-statements. There is the same emphasis on free purgation with Epsom salts. The dose is the same. Both are marketed at two dollars for a box of 100—only the Anedemin people have adopted the prize package device of throwing in 20 or 30 tablets extra, for good measure, and give a discount of 75 cents or so.

In short, the Anedemin Company has appropriated all of Anasarcin which they considered of any value. It is, therefore, rather suggestive that they drew the line at the formula. Anasarcin is said to contain squill, sambucus and oxydendron; Anedemin discards the oxydendron and reinforces the squill with strophanthus and apocynum. Notwithstanding this material change in composition, the actions are described as identical; this is again rather suggestive.

The Anedemin Company, like the Anasarcin Company, scorns crude drugs and claims to use only the isolated principles. It was saved the trouble of discovering active principles for strophanthus and apocynum, for these are known; but it managed to find some scope for its inventive genius, "both drugs being so chemically treated and disposed as to absolutely eliminate all objectionable and disagreeable properties and effects" so as to convert a vasoconstrictor action into a dilator action; so as to render them non-toxic and non-cumulative; so as to deprive apocynum of its characteristic nauseant effect. Who can say that the days of miracles are past? Even this is not the limit of Anedemin alchemy; if we are to believe their claims, they have succeeded in forcing strophanthin, apocynum,



Labaroratory and Warehouse of the Anasarcin Chemical Company, Winchester, Tenn.

scillain, etc., to combine with each other: "It is a *definite chemical compound* of the active principles" of these drugs! This makes the achievements of Emil Fischer in synthesizing sugars and proteids appear as mere child's play.

Since the formulas were completed, however, clinical reports have been numerous enough—almost too numerous, if we are to believe them. Anedemin has been on the market for less than three years; the circulars emphasize that testimonials and endorsements are not solicited. Nevertheless, we are told that it is "endorsed by over fifty thousand clinicians throughout the United States." Since the total number of physicians in the United States and Canada is only about 128,000, this means that nearly every second physician has endorsed Ane-

demin. The Anasarcin Company solicits endorsements and they seem to do the larger business. Hence the majority of physicians of the United States must have written an endorsement of either Anedemin or Anasarcin, or both. Or is this statement another "invention?" It is a little peculiar that nearly all the endorsements come from small towns in sparsely settled districts; practically none from the centers of population. Does this mean that dropsy is more common in the rural communities than in the cities?

THE INVENTORS OF ANASARCIN AND ANEDEMIN.

Even the newspapers, when they tax our credulity with pretended scientific "discoveries," feel the moral obligation of justifying themselves by telling us something of the personality and experience of the discoverers. We may ask, therefore, who are these expert pharmaceutic and synthetic chemists, these manufacturers of active principles, these skilled clinicians of wide experience, who have "intelligently built up the formula by wide application"? What are we told of these men who ask us to believe, on their mere assurance, in miracles and feats of magic; who tell us that they have converted neutral principles into alkaloids, that they have effected definite chemical compounds between these neutral principles, that they have discovered principles that do not exist, that they have changed the actions of these principles to suit their wishes, that, in short, they have reversed the laws of Nature?

These companies are located in Winchester, Tenn., a town of about 1,500 inhabitants, situated in an agricultural country. The town boasts of neither scientific schools, colleges, universities nor laboratories. The Anasarcin Company was organized in 1902, the incorporators and directors being Dr. John W. Grisard and his sons, Dr. John P. Grisard, B. A. Grisard, and A. F. Grisard, and Will W. Walker, all of Winchester. Dr. John W. Grisard seems to be the originator and promoter of Anasarcin. W. E. Walker is an insurance solicitor of Winchester and is not actively identified with the business. We are informed that he owns but a single share of stock having a face value of $100, and that he was added to the company in order to comply with the laws of Tennessee, which require five directors for any corporation. Dr. John W. Grisard, the father, has practically retired, but still has a general supervising interest in the business. There is no regularly licensed pharmacist or chemist connected with the company. The office is in the rear of a jewelry store in the business part of Winchester and on the second floor above. According to our reporter, an office force of about ten stenographers and clerks handles the correspondence and labels and sends out the preparation which

is made in a crude frame building located on a side street and without laboratory equipment. According to our reporter, the work is done by the Grisards and a colored man.

The Anedemin Chemical Company was organized in 1905 with a capital of $20,000, the incorporators and directors being Dr. T. B. Anderton, Floyd Estill, J. J. Lynch, J. M. Littleton and I. G. Phillips, all residents of Winchester, and all lawyers with the exception of Dr. T. B. Anderton. A Mr. Gordon, a clerical employé of the company, is reported to have active charge of the business, to prepare the medicine and conduct the correspondence. The office headquarters, laboratory and complete outfit of the Anedemin Company comprises two rooms over the law office of Estill and Littleton. No one connected with the company is a regularly licensed pharmacist or graduate chemist.

Of the six physicians located in Winchester, three of them (50 per cent.) are engaged in the dropsical cure business. Poor Winchester! Aside from their connection with these two nostrums, these physicians may be estimable and worthy citizens, but where, pray, did they find the extensive clinical facilities and pharmaceutical knowledge necessary for their wonderful and epoch-making discovery? Were they aided in their scientific work by the four lawyers connected with the Anedemin Company or by the insurance solicitor who is a director of the Anasarcin Company? Did the 1,500 inhabitants of the town furnish the vast clinical material necessary for discovering and working out the formulas of these two preparations? If so, we fear that dropsical affections are much more prevalent in Winchester than in any other known spot on the globe. This matter should be investigated. Without doubt the vital statistics of Franklin County would be most interesting and we commend them to the special attention of the medical profession in Tennessee.

CAMPHO-PHENIQUE.

Report of the Council on Pharmacy and Chemistry and Some Comments Thereon.

(From The Journal A. M. A., April 20, 1907, 1365.)

The following report was submitted to the Council on Pharmacy and Chemistry by the subcommittee to which Campho-Phenique had been assigned:

> *To the Council on Pharmacy and Chemistry:*—Campho-Phenique, sold by the Campho-Phenique Co., St. Louis, Mo., is claimed to be composed of phenol 49 per cent., and camphor 51 per cent.

Examination of specimens, purchased in the open market, made under our direction, demonstrate that the statements made in regard to the composition are not true. Instead of containing 49 per cent. of phenol (carbolic acid), the analysis showed that it contains not more than 20 per cent. Instead of containing 51 per cent. of camphor, the analysis demonstrates that the amount of camphor is not more than 38 per cent. Besides phenol and camphor, a third substance was found which proved to be liquid petrolatum and to be present to the extent of 38 per cent. or more.

Since the statements made in regard to the composition of Campho-Phenique are deliberate misrepresentations of the facts, it is recommended that the article be not approved.

Besides Campho-Phenique, the above-mentioned firm also sells a preparation labeled Campho-Phenique Powder. While no statement in regard to the composition of this product is made on the label or in the literature, such expressions as "Campho-Phenique in a powdered form" and "Powdered Campho-Phenique" lead to the inference that it has essentially the same composition as that stated for the liquid preparation. An examination of a specimen of Campho-Phenique Powder purchased in the open market showed that 92 per cent. of it was a talcum-like inorganic substance. The remaining 8 per cent. consisted chiefly of camphor with a small amount of phenol.

In view of the fact that Campho-Phenique Powder contains very little phenol, but instead consists chiefly of an inorganic talcum-like substance, its name is misleading and deceptive. It having been shown that Campho-Phenique Powder corresponds to a camphorated talcum powder, the claims that it "has no equal as a dry dressing," that it is "absolutely superior to iodoform," and that it has "all the excellent properties of aristol and iodoform," are unwarranted. It is recommended that the article be not approved, and that this report be published.

The recommendations of the subcommittee were adopted by the Council, and in accordance therewith the above report is published. W. A. PUCKNER, Secretary.

The above report on a much advertised "ethical" proprietary medicine is worthy of the thoughtful consideration of the members of the medical profession, as it illustrates admirably some of the conditions connected with this proprietary medicine business.

THE FORMULA A FAKE.

First, it illustrates the fact that the published formulas of the "ethical" proprietaries are not always reliable. The

Campho-Phenique Company has been very willing to give out a formula, purporting their product to be 51 per cent. camphor and 49 per cent. phenol (carbolic acid). Now, these two drugs will make a liquid mixture, and any druggist can make it, and the mixture will have about the same consistency and appearance as Campho-Phenique. But its effect differs decidedly from that of Campho-Phenique. Some months ago a very intelligent physician, in discussing the proprietary medicine business, said that in some cases physicians could not get druggists to make preparations which were as satisfactory as those which could be bought ready made. He cited Campho-Phenique as an illustration. He said that he had used this preparation for burns, etc., but as he did not like to use preparations put up by companies about which he knew nothing, he asked his druggist to make the mixture in accordance with the published formula. The druggist's preparation was not satisfactory; it had a decidedly different effect from Campho-Phenique, and so he tried another druggist. This druggist also followed the published formula, but his results, too, differed materially from the proprietary article.

The various analyses that have been made show why the preparations put up by the druggists did not resemble that made by the company; since, according to the analyses, Campho-Phenique consists of 40 per cent. liquid petrolatum, which is an inert but soothing diluent, while instead of 49 per cent. of carbolic acid, as claimed, it really contains less than 20 per cent. This is an entirely different proposition. Now, if the physician referred to above will have his druggist make a mixture of 20 per cent. of carbolic acid, 40 per cent. of camphor and 40 per cent. of liquid petrolatum, and will then compare this resulting compound with Campho-Phenique, he will find that there is not much difference. Furthermore, he will realize that there is nothing either new or wonderful about the preparation. Camphorated oil and carbolized oil are both in common use. Campho-Phenique is apparently simply a mixture of the two.

THE POWDER STILL WORSE.

So much for the liquid. The powder seems to be something entirely different, for, according to the chemist's report, over 90 per cent. of it is inert, absorbent, talcum-like material. There is enough camphor and carbolic acid to give the powder an odor and thus mislead physicians, especially those who are in the habit of taking for granted that whatever statements nostrum manufacturers make are true. Perhaps it is a fairly good dressing for wounds—at least it will do no

harm—but its name is misleading and deceptive. For all practical purposes it is essentially a camphorated talcum powder.

THE CAMPHO-PHENIQUE COMPANY A "PATENT-MEDICINE" CONCERN.

The second interesting phase of this "ethical" proprietary is that it illustrates another point, i. e., that many of these articles are supplied to our profession by those who are not legitimate manufacturing pharmacists. The Campho-Phenique Company of St. Louis, according to all reports, is owned and controlled by a gentleman named Ballard. This "company" supplies the medical profession with the preparations under consideration and also with chloro-phenique and scrofonol. We are informed that this same Mr. Ballard is the principal owner, if not the sole owner, of quite a number of "patent-medicine" companies, such as Ballard-Snow Liniment Co., Brown's Iron Bitters Co., Mayfield Medicine Mfg. Co., Smith Bile Beans Co., Swain's Laboratory, and several others. We learn from the wholesale drug trade lists that these various "companies" make and sell, beside the campho-phenique preparations, Ballard-Snow Liniment, Ballard's Herbine, Brown's Iron Bitters, Dr. Herrick's Pills, Richardson's Life-Preserving Bitters, Smith's Bile Beans, Swain's All Healing Ointment, and several other "patent medicines."

It is hardly necessary to make any further comments. The whole business is nauseating to those who know the actual conditions of this nostrum business and how our profession is being deluded. The Campho-Phenique matter is not an exception; it is simply another illustration of these conditions.

The majority of "ethical" proprietaries are foisted on our profession, either without any formula accompanying them, or with a "formula" that is a fake. The majority of the "ethical" proprietaries are manufactured and supplied to physicians, with instructions regarding their use, by men who bear the same relation to legitimate pharmacy that the veriest quack that ever swindled a credulous public bears to scientific medicine.

CELLASIN.

Report of the Council on Pharmacy and Chemistry.

(*From The Journal A. M. A., Sept. 12, 1908.*)

The following report was submitted to the Council by a committee:

To the Council on Pharmacy and Chemistry:—Cellasin, a product of Mead Johnson & Co., was first submitted under the title of "Cellulin," with the claim that it is a

ferment which is absorbed unchanged into the tissues; that it cures diabetes mellitus, and that it cures tuberculosis and establishes immunity against this disease. As these claims were unsupported by reliable evidence, they were considered extravagant and highly improbable, and it was therefore voted that the product be refused recognition. The manufacturers then indicated a willingness to modify the therapeutic claims, and the product was reconsidered and the statements made in regard to its chemical properties were submitted for verification to the committee on chemistry. This committee reported as follows:

Report of the Committee on Chemistry.—We have completed our experiments on Cellasin, prepared by Mead Johnson & Co., and we are obliged to report that the claims made for it are only in part true. Our tests show that it has at best only very weak fat-splitting power, too weak to make it of any real value. After digestion with pepsin and hydrochloric acid the same slight fat-splitting power seems to be present and this part of the claim of the manufacturer is admitted. We find also that the substance resists the action of 2.5 per cent. hydrochloric acid, as submitted in the modified claims of the firm. As the action on fat is very weak we have not been able to make a perfectly satisfactory experiment on the question of the behavior with trypsin mixtures. On receipt of the new advertising circular we have made further extended tests of Cellasin from which we conclude that the claims as published are very greatly exaggerated. The action of the product on cane sugar is so weak that a quantitative change could not be detected in 24 hours, either by the process recommended by the manufacturers or by tests of our own. The action on starch is quite distinct from that described and likewise very faint. Although a faint fat-splitting power is present, as reported above, the claims as a whole are so far from the truth that it is recommended the product be refused recognition.

The committee on pharmacology reported that the firm was still making extravagant claims for the product and endorsed the recommendations of the committee on chemistry. In accordance with the recommendations of the two committees the Council voted that Cellasin be refused recognition on account of exaggerated chemical and therapeutic claims. The above was submitted to Mead Johnson & Co., who in reply strongly insisted on the correctness of their claim that the action of Cellasin on carbohydrates and fats in acid solution is most powerful. In view of the emphatic assertions of the manufacturer the committee again made tests with Cellasin and reported as follows:

Second Report of the Committee on Chemistry:—We must again report regarding Cellasin that our findings are entirely at variance with the claims submitted by the manufacturers. Since Mead Johnson & Co. have advertised widely that their product has been submitted to the Council for inclusion in New and Non-Official Remedies, we suggest that the reasons for its rejection be published. We have given an unusual amount of time to the investigation of Cellasin and every opportunity has been afforded the firm to substantiate its claims. These claims could not be verified in any samples submitted, and the committee now and finally recommends the adoption and publication of the report.

On motion, the report was adopted and its publication directed. W. A. PUCKNER, Secretary.

CHLORAL, ISOPRAL AND BROMURAL.

T. Sollmann, M.D., and R. A. Hatcher, M.D.

(Abstracted from The Journal, Aug. 3, 1908.)

In view of the statements of Impens, an investigation was made of the effects of chloral and isopral on cats. Impens had stated that what he calls the "toxic quotient" for these drugs, i. e., the quotient of minimum fatal dose divided by the minimum "effective" dose, is uniformly greater for isopral than for chloral and that isopral is, therefore, the safer drug. Impens' experiments were too few to make his conclusions acceptable, especially in view of the observations of Hatcher, which did not accord with them. The subject has been discussed also in the pages of THE JOURNAL by Impens and Reid Hunt, but some points remain which seem not yet adequately decided; hence this investigation.

It seemed to Sollmann that an independent study of the subject, besides his own, would be valuable as a control. He, therefore, asked the collaboration of Professor Hatcher and, receiving his results, has, with his permission, incorporated them with his own. He also tested a new product, bromural, by the same methods and gives the results. Cats were used exclusively and the drugs were administered by stomach tube. The series includes 77 experiments with chloral on 57 cats, 50 experiments with isopral on 40 cats and 23 experiments with bromural on 10 cats. Tables and diagrams are given illustrating the effects of different doses on the animals in producing the various gradations from light natural sleep to the fatal dose, maximum and minimum.

Their findings were radically different from those of Impens, and Sollmann points out that the latter's definition of

the toxic dose as the smallest one which ever causes death, is especially objectionable. Accepting it, however, it is clearly wrong, as shown by Sollmann's experiments which make out isopral nearly twice as fatal to cats as chloral. Impens gives the toxic dose of isopral as 0.4, while in Sollmann's experiments 0.25 proved fatal in two out of three animals, and if we count the late deaths against isopral the lowest recorded fatality would be 0.11 gm. Some of the most important differences refer to the rapidity and duration of their action, and these were recorded in each experiment. With therapeutic doses the onset and culmination of the effect and start and completion of recovery are most rapid with isopral, nearly as rapid with bromural and slowest with chloral. Complete recovery from nearly fatal doses is most prompt with bromural and slowest with isopral, which has the most severe after-effects.

All three drugs tend to produce a fall of temperature, bromural causing the least; their effects on the respiratory center so far as could be observed seemed to be quantitatively identical and proportional to their general narcotic effects. Chloral and isopral produce more or less nausea and retching, especially chloral, while these are conspicuously absent with bromural. This is an undesirable effect, since the weakened heart is not equal to the concomitant excitement, and this explains, in Sollmann's opinion, the occasional cases of death from small doses of chloral. On the other hand, the vomiting may save life, and from this standpoint chloral appears to be the safest drug. This is shown in a table of cases which recovered from ordinarily fatal doses, which shows that 73 per cent. of the animals recovered from chloral, most of them after vomiting, while only 35 per cent. of those taking excessive doses of isopral survived.

Instead of isopral being the "safe hypnotic" of the chloral group, it causes death twice as frequently as chloral with doses of corresponding narcotic effect. Both drugs have a decided effect in causing loss of weight, and isopral is the worst in this respect. The loss varies with different animals and does not appear to be proportional to the dose or narcotic effect. This loss, if serious, tends to progress for some time and recovery is slow. The effect of this loss of weight on mortality is rather striking when it is remembered that the doses were calculated according to the weight at the time of administration, emaciated animals receiving much less than those in good condition. The most probable explanation is the diminished general resistance in the emaciated animals.

Sollmann concludes that Impens worked with altogether too small a material and that his conclusions are entirely unjustified. A fair comparison between different hypnotics can be made only on the basis of the averages of a considerable number of experiments or by trying the several drugs on the same animal. The comparison of a few exceptional or artificially selected results is wholly misleading. If the dose of chloral required to produce a given effect is taken as 100, that of isopral would be about 60 (as stated by Hatcher) and that of bromural about 100. The bromural narcosis is, however, less profound. These ratios hold for all doses, small and large. The toxic quotient of the three drugs is about the same, but in practice chloral is only half as dangerous as isopral, as excessive doses are generally expelled by vomiting and since the subsequent very dangerous cachexia is less pronounced. Occasionally, however, relatively small doses of chloral cause sudden death, namely, when there is great excitement. Large doses of bromural are nearly as dangerous as corresponding doses of chloral, so that it can not be called "absolutely harmless." It does not produce perceptible gastric irritation, differing in this respect from the other two drugs. The gastric irritant effect appears to be about six times as great for chloral as for isopral, i. e., with doses producing the same narcotic effect. Age, size and repeated administration do not influence the susceptibility, but emaciation markedly reduces the resistance.

Sollmann ends his article with the following practical conclusions: "The claims for the superior safety of isopral are totally unjustified. It differs from chloral mainly in the lesser dose (½ to ⅔) required to produce a given effect; in the quicker and shorter action, and in producing less gastric disturbance. Bromural also acts more quickly and less persistently than chloral. The action of therapeutic doses is, moreover, less profound. There is no gastric irritation. Larger doses would be equally as dangerous as chloral."

In the discussion following Professor W. A. Puckner remarked that Dr. Sollmann's paper brought out very forcibly the need of controlling all statements made by interested persons and expressed a hope that other pharmacologists would similarly investigate proprietary drugs. There has been too much hesitancy thus far in this matter. Dr. F. E. Stewart, of Philadelphia, made the suggestion that it would be an excellent thing if manufacturers would pass over their products to the Council on Pharmacy and Chemistry before doing any advertising at all, and in that case they would have

facts instead of fancies to give to the public. Dr. Sollmann remarked that such a course would prevent many heart burnings.

DIGESTIVE FERMENTS.

(From The Journal A. M. A., Feb. 2, 1907.)

Medicinal preparations are on the market that are said to contain the digestive ferments pepsin and pancreatin. A combination containing these two digestives, at least in liquid form, is, as some one has expressed it, "a therapeutic absurdity and a chemical monstrosity." The subcommittee of the Council on Pharmacy and Chemistry, to which some of the proprietaries, or "specialties," were referred, has for nearly a year labored with the problem as to what should be done with them. The committee appreciated that some of these preparations were being used by a large number of physicians, and to refuse to recognize any of them might subject the Council to the charge of being too narrow, too particular, or too something or other—at least unless the reason for such refusal was explained in a convincing manner.

In the Pharmacology Department this week[1] will be found the report of the committee as adopted by the Council relative to this class of preparations. In so many words, the Council refuses to approve—and gives reasons for its action—any liquid preparation said to contain both pancreatin and pepsin. The fact that so many of this class of combinations have been used for so long with scarcely a protest is remarkable. It can only be explained on the assumption that many physicians believe the literature sent them by the manufacturers rather than scientific works and recognized text-books. Those who use these preparations have at least forgotten the fundamental physiologic facts relating to digestion and to the digestive ferments. Certainly every medical student knows that pepsin acts only in an acid medium, and the pancreatic juices only in an alkaline medium; and every physician, if he will stop to think, knows that pepsin and pancreatin can not possibly remain in the same solution without one destroying the other, much less be effective as therapeutic agents.

That there are such preparations on the market is a reflection on those who make them as well as on those who use them. In some instances it must be charged to present-day commercialism, in others to indifference, and in still others to ignorance. The manufacturers who know better blame physicians. The chief chemist of one of the largest manufac-

1. The Journal A. M. A., Feb. 2, 1907, 434.

turing pharmaceutical houses, which puts out two or three of these monstrosities, said to us recently that physicians call for these preparations, that the company simply supplies the demand. A representative of another large house openly declared that the firm considers it its business to supply whatever is demanded, and that it is in the business for money, and not to try to curtail a demand, the supplying of which is found profitable. It is a pleasure to record the fact that one firm has already withdrawn its preparation from the market.

Undoubtedly, the real facts are that the desire for a universal digestant always has predisposed to a belief in its possibility, that this belief has been fostered by certain unscrupulous manufacturers, and that other more or less honest pharmaceutical houses, threatened by loss of prestige and tempted by the profits on such preparations, have felt obliged to follow suit. Even the National Formulary includes a formula for such a preparation!

While this condition of affairs is a serious reflection on scientific pharmacy, it must not be forgotten that the medical profession is very seriously to blame. Professor Sollmann has agreed to contribute two or three short articles on the subject, and the first one[2] appears this week. Aside from presenting an exposition of the scientific evidence as to the absurdity of these mongrel compositions, he will also point out some other facts about these ferments that seem to be overlooked by many physicians.

ANTIDYSPEPTICS AND VEHICLES.

Comments on Some of the Official Preparations Available for These Uses.

(From The Journal A. M. A., Feb. 2, 1907.)

The proprietary mixtures which are claimed to supply the system with digestive ferments, and which the Council on Pharmacy and Chemistry has shown to be impossible combinations, have attained wide popularity entirely through persistent advertising. However, since they are largely used, they must serve some purpose. What is it? Simply that they make excellent vehicles and occasionally are effective as antidyspeptics.

AS VEHICLES.

The choice of a proper vehicle for nauseous drugs prescribed in solution has received too little attention in the education

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2. THE JOURNAL A. M. A., Feb. 2, 1907, 415.

of physicians. In consequence, many physicians have accepted eagerly the solution of the problem offered by the proprietary manufacturer and have fallen into the habit of using these preparations simply as vehicles without reference to their value as digestive agents. Apparently physicians forget or do not know that both the Pharmacopeia and the National Formulary furnish us with preparations just as serviceable as vehicles as the proprietary digestives like elixir of lactopeptine, pan-peptic elixir, peptenzyme elixir, etc.

The subject of vehicles, etc., was treated somewhat extensively in one of the series of special articles on the Pharmacopeia and the Physician (THE JOURNAL, June 23, 1906), but it may be worth while again to refer to some of these which should replace the impossible proprietaries.

When the attention of a very intelligent physician was called to the impossibility of a mixture containing the substances which the manufacturers of the Elixir of Lactopeptine claim that their preparation contains, he said that he used it simply as a vehicle, and laughingly acknowledged that its pretty color had something to do with its popularity so far as he was concerned, and undoubtedly he represented many others. The appearance of medicines is well worth the physician's attention, not only from the desire to make himself popular with his patients, but because of the effect produced by psychic impressions.

The addition of some coloring matter is frequently desirable to improve the appearance of medicines, and without doubt much of the popularity of some nostrums is due to their pretty color. An attractive bright red color can be communicated to mixtures by the use of about 1 per cent. (5 minims to the ounce) of tincture of cudbear (tinctura persionis, N. F.). Carmine will produce a red color in alkaline solutions. For brown colors, addition of the compound tincture of cudbear (tinctura persionis co. N. F.), will give the desired result, and for neutral or alkaline solutions glycyrrhizin may be used. For yellow coloring 1 per cent. (5 minims to the ounce) of tincture of hydrastis, U. S. P., may be used.

Medicines should be made as palatable as possible, and the Pharmacopeia and National Formulary contain some excellent vehicles, especially certain elixirs, which may properly supersede the proprietary vehicles. For instance we have elixir aromaticum, U. S. P., elixir adjuvans, U. S. P., elixir eriodictyi aromaticum, N. F., elixir taraxaci compositum, N. F., and the two elixirs of glycyrrhiza. The vehicle should be

chosen to fit the remedy to be administered, so far as practicable, and in this respect a selection from the variety of official preparations has decided advantages over the use of a single proprietary elixir whose exact composition is not known. For salts like potassium bromid the elixir aromaticum, U. S. P., forms an excellent vehicle. Thus we may direct:

℞.	Potassii bromidi	℥iiss	10
	Elixir aromatici	ℨij	60

M.

This mixture contains 10 grains of the bromid to the fluidrachm and is of the same composition as elixir potassi bromidi, N. F.

Sodium salicylate can also be disguised by the use of aromatic elixir. If we wish to secure the effect of color at the same time we can add five drops to the ounce of tincture of cudbear (tinctura persionis, N. F.). Thus:

℞.	Sodii salicylatis	℥iiss	10
	Tincturæ persionis	m. xv	1
	Elixir aromatici, q. s. ad	ℨiv	120

M. Sig.: Each teaspoonful contains approximately 4¾ grains of salicylate of soda.

The taste of potassium iodid can be disguised by aromatic elixir in the same way and this vehicle is not surpassed for this purpose by any proprietary digestives.

The National Formulary contains a number of other elixirs of special salts which may be used by those who wish to prescribe elegant and palatable mixtures. Among these are elixirs of calcium, lithium, and sodium bromids, potassium acetate, salicylic acid and the various salts of iron, for which orange flower water or the syrup of orange flower are acceptable. When prolonged use of a remedy such as syrup of hypophosphites is necessary the flavor should be changed from time to time; for example, tincture of vanilla may be substituted for the syrup of orange or lemon.

For the purpose of disguising the taste of quinin the preparations of licorice are very suitable. Elixir adjuvans, U. S. P., consists of a mixture of 12 parts of fluid extract of glycyrrhiza with 88 parts of aromatic elixir. One may prescribe

℞.	Quininæ sulphatis	℥ss	2
	Elixir adjuvantis	ℨij	60

M.

This is to be triturated in a mortar and directed to be shaken before taken. No acid should be used to dissolve the quinin sulphate, since this would precipitate the glycyrrhizin,

the active principle of licorice. A drachm of this preparation contains 2 grains of quinin sulphate.

Instead of the elixir adjuvans the syrup of glycyrrhiza N. F. may be used and sometimes may be preferable, as it contains no alcohol. Ammonium chlorid is a nauseous salt which is best disguised by syrup of glycyrrhiza.

The bitters used as appetizers and as stomachics owe their therapeutic effects to their bitter taste, so that concealment of this taste tends to defeat the purpose for which the medicine is given. Still if it is thought best to disguise the taste the syrups form appropriate vehicles. Thus we may give nux vomica with syrup of orange, improving the appearance by the use of cudbear if desired.

℞.	Tincturæ nucis vomicæ	ʒiiss	10
	Tincturæ persionis	m. xv	1
	Syrupi aurantii	ʒiv	120

M.

AS ANTIDYSPEPTICS.

All the proprietary antidyspeptic remedies contain alcohol and aromatics, to which, undoubtedly, what therapeutic virtue they really possess, is due. In cases of distress after meals the physician, as well as the patient, naturally seeks something to allay the present discomfort while waiting for the result of investigation into the cause of the symptoms and the slow improvement that is apt to attend strictly rational treatment. And there are many official remedies that will answer the purpose fully as well as the much-vaunted proprietaries.

Alcohol has a stimulating action on the functions of the stomach and especially in the form of wine will often relieve the uncomfortable feelings that come on after eating, and herein lies one of the principal reasons for the popularity of mixtures containing alcohol. The carminatives, such as cardamom, cinnamon, allspice and ginger will give relief in most cases. Peppermint, chamomile, anise, etc., have a well-deserved reputation for relieving flatulence, colic, and similar conditions. Chloroform is both anodyne and antiseptic and is a valuable remedy in the milder forms of gastralgia. Alkalies are often beneficial and especially in hyperacidity, but are frequently given in insufficient doses.

While a physician should attempt to individualize in the use of these remedies, sometimes it may be advisable to give them in combination, and the Pharmacopeia and National Formulary present a number of excellent combinations which may be used in such cases. As a combination of alcohol and aromatic carminatives, the compound tincture of cardamom,

U. S. P., is superior in safety and efficiency to any nostrum on the market. It contains cardamom, cinnamon, caraway, cochineal, glycerin and alcohol. In addition to its therapeutic properties it has a pleasing red color, which may serve the purpose of suggestion. The tinctura aromatica N. F. is a similar preparation. The average dose of the former is one teaspoonful, of the latter 30 minims. Mistura carminativa contains carminatives and alkalies, but it also contains opium, and, therefore, should be used with the presence of that drug in mind, especially when given to infants. For adults the amount of opium is so small that a drachm contains only one and a half minims of laudanum. Pulvis cretæ aromaticus combines carminatives with an alkali and may be used for hyperacidity. The average dose of 2 Gm. (30 grains) contains enough alkali to neutralize the free acid in 250 c.c. (8 ounces) of normal stomach contents, so that probably twice this dose should be used for full effect.

Incidentally it may be said that most proprietary digestive remedies contain acid, while the majority of cases of dyspepsia require an alkali. In cases in which an acid is indicated, however, the dose should be much larger than those afforded by the proprietary mixtures. If it has been ascertained that a digestive agent is really needed the simplest way is to prescribe pepsin with large doses of hydrochloric acid, which should be well diluted in administration, but if a ready-made digestive mixture is desired the liquor pepsini N. F. may be used, although it also contains an insufficient amount of hydrochloric acid. The elixir, essence, and wine of pepsin of the National Formulary are better suited for use as aromatics and stomachics than as digestive agents, but are worthy of consideration as substitutes for the proprietary digestive mixtures.

In conclusion, the use of these remedies should be regarded merely as palliative and should not be allowed to obscure the need of thorough investigation and treatment of the disease which underlies the symptoms.

The chief value of the digestive ferments should be as pharmaceutical or biologic reagents rather than as true therapeutic agents, namely, for the preparation and predigestion of food articles as indicated in the peptonization of milk.

DIASTASE FERMENTS.

Report of an Examination of the Diastase Ferments by the Council on Pharmacy and Chemistry.

(From The Journal A. M. A., July 11, 1908.)

A subcommittee makes the following report to the Council with the recommendation that it be published:

Among medicinal agents which may be classed as legitimate pharmaceutical preparations few are more widely advertised than are the starch-digesting ferments, the diastases. Along with a number of very good preparations there are several for which grossly exaggerated claims are made, and which are advertised to the medical profession in such a manner as to lead to distrust. Those which have merit have not always been marketed by methods which are wholly free from criticism. In several cases the claims made are more than can be substantiated by actual tests.

There has always been some obscurity in the method of reporting the digesting value of these diastases, and just what is meant by starch conversion or sugar formation is not always clear. In other words, the claims of the manufacturers are frequently stated in terms which are too general.

To be of value statements regarding the digesting power of the diastases should be based on standard and uniform methods of testing. But manufacturers have followed different methods of examination, which naturally makes a fair comparison of products difficult, and in some cases impossible, for any one not conversant with the methods of analysis. Recognizing the importance of uniformity in such work the subcommittee has had a large number of comparative tests carried out on the more important products of this class, employing several methods of analysis. In practice the diastatic action may be measured in terms of malt sugar formed from an excess of starch in a given time, or by the conversion of the starch to a point where the test with iodin shows the disappearance of the blue color, or the disappearance of all color. Results by these three methods are not directly comparable, although there must be some relation between them. Our first experiments were directed toward the clearing up of this point. These experiments were carried out largely by Mr. W. A. Johnson and the most important of them are given in detail in a paper which appears in the May number of the *Journal of the American Chemical Society*. From his numerous tests Mr. Johnson concluded that the best practical comparison may be made by carrying each digestion to the colorless end point, and in his paper certain suggestions are made as to the best methods of conducting the tests. These will be referred to below.

The following table contains the results obtained with a number of commercial products, when examined in this way, the digestions being continued through a period of ten minutes, at a thermostat temperature of 40 C. in all cases. All the

products here examined came from the manufacturers, and the results were confirmed by tests on similar products bought in wholesale drug houses. The results are expressed in four ways for comparison as follows:

A.—Parts of 100 % starch digested to colorless endpoint in ten minutes.

B.—Parts of 92 % starch digested to colorless endpoint in ten minutes.

C.—Parts of 85 % starch digested to colorless end point in ten minutes.

D.—Parts of 85 % starch digested to loss of blue iodin reaction in ten minutes.

	A.	B.	C.	D.
Holadin	102.1	111.0	120.0	171.0
Taka Diastase	16.0	17.4	18.82	26.0
Taka Diastase Liquid.	0.38	0.41	0.45	0.61
Panase	113.0	123.0	133.0	203.0
Panase Essence	3.6	3.91	4.23	6.1
Vera Diastase Essence.	4.2	4.55	5.0	6.7
Diazyme Essence.....	6.12	6.66	7.14	10.3
Diazyme Glycerole....	6.12	6.66	7.14	10.3
Maltine, Plain	2.30	2.50	2.71	....
Maltzyme	2.87	3.12	3.37	....
Trommer's Extract of Malt, plain	0.65	0.71	0.77	....
Trommer's Extract with Cod Liver Oil.....	0.38	0.41	0.44	....

The blank spaces in the fourth column of figures indicate that no tests were satisfactorily completed here to show the conversion to loss of blue color. In fact, with highly colored mixtures this test is not as easily made as the other.

A comparison of the results given in the table with the statements which appear in the manufacturers' circulars, etc., show that the digestive values are all lower than claimed, if we base our comparison on the colorless endpoint reaction, and anhydrous starch conversion. If, however, we carry the digestion merely to the loss of blue color, which seems to be the case in some of the tests frequently cited, and employ starch with an average water content of about 15 per cent., a very different status must be reported. In this manner of reporting results five of the preparations show even more than the claimed values, but the method should not be tolerated for obvious reasons. The results actually found should always be calculated to anhydrous starch for reporting.

The discrepancies between the values claimed for Holadin, Diazyme Essence and Diazyme Glycerole and those actually found in our tests are not very great.

While one part of Holadin by the firm's method is stated to digest 135 parts of starch to the practically colorless endpoint, column C shows that by the method employed in these experiments only 120 parts of 85 per cent. starch were digested to the colorless endpoint. Similarly, while for Diazyme Essence and Diazyme Glycerole it is stated that 1 c.c. will digest 8 gm. "dry" starch to the colorless endpoint, the results given in the table above show that one part digested 6.12 parts of 100 per cent. starch to the colorless endpoint. This is equiva-

lent to 7.14 parts 85 per cent. starch, the kind referred to by the manufacturer.

The claims made for Panase are somewhat misleading and conflicting. In a recent circular issued by the manufacturers a statement is made to the effect that one part of Panase "is capable of digesting at least 200 times its weight of starch in 10 minutes," while in another part of the same circular the complete conversion of 200 parts of starch into sugars is claimed as the work of 1 part of Panase. This claim is certainly wrong, as there is a wide difference between the two kinds of reactions. The figures in the table are sufficiently clear on this point, and suggest a proper modification of the claim to agree with the facts.

The widest discrepancy between the values as claimed by the manufacturer and those found by actual tests seems to be shown in the case of Taka Diastase. The liquid preparation has been tested a number of times in different samples and has always been found weak. Some samples, in fact, were quite inert. This ferment appears to lose strength very rapidly in solution, as the manufacturers now concede. The stability of the solid product is also far from satisfactory, and appears to be less than that of the ferment as marketed some years ago. The two samples examined recently were weak.

From a number of experiments made it appears that the stability of the diastase preparations from the pancreas is greater. In two tests of the Holadin, made some months apart, no appreciable change was noticed. The same thing is true of Panase and the earlier product of the same firm, Vera Diastase. But in the liquid form these preparations, like the Taka Diastase, seem to undergo some alteration in converting power, as the figures above, and others, suggest. Of the samples reported here the Vera Diastase essence was obtained fresh and examined at once, while the Panase Essence was on hand some time before the tests were made. According to the statement on the label the latter should be the stronger, but the reverse is the case. The Panase Essence seems to convert less than is claimed for it, while the Vera Diastase Essence converts more, if we consider 85 per cent. starch and digestion to loss of blue color merely, as satisfactory conditions of the test. It is possible that the somewhat greater age of the Panase Essence may have some bearing on the result.

The two Diazyme preparations appear to be stable, as far as practical requirements are concerned. We have examined the contents of the same bottles of these products at periods three months apart, and found no change in the starch-converting power. The claims for the numerical value of the diastatic activity and also for the stability which are made for these liquid preparations seem to be borne out by the facts as observed.

For the other liquid preparations, Maltine, Trommer's Extract, Plain and Trommer's Extract with Cod Liver Oil,

there are no exact claims as to the digestive power. For Maltzyme, it is claimed that 1 gm. has the power to produce from starch, in 30 minutes, at 37.8 degrees C., 6 gm. maltose. They contain large quantities of the products of enzyme digestion, and have relatively low residual digestive value. They should be classed among the so-called medicinal foods, rather than as agents of digestion.

In the experiments carried out by Mr. Johnson, referred to above, sugar determinations were made also, and these showed a close agreement with the starch conversion, carried to the colorless endpoint. In making the tests for the sugar formation advantage was taken of the results of the other tests, and enough ferment was weighed out in each case to effect the hydrolysis of one gram of anhydrous starch to the colorless endpoint in ten minutes. A series of tests was made on each substance with the same weight of ferment and starch paste, and at the end of 10, 30, 60, 120 and 180 minutes a flask containing the mixture was removed from the thermostat, and the amount of sugar formed, calculated as maltose, was determined. On removing each flask from the thermostat further action was always checked by immediate boiling. The amount of sugar formed at the end of ten minutes was essentially the same in all the samples tested, which included the first eight of the table above. For the gram of anhydrous starch, made up to a 2 per cent. paste, the maltose formed varied between 611 and 635 milligrams, which agrees very well with the usual findings for diastase digestion, under like conditions. There are many such results in the scientific literature.

In the longer periods, however, the amount of sugar formed by the Taka Diastase increased somewhat more rapidly than was the case with the other ferments, and the results of the determination after 180 minutes pointed to the evident conversion of some of the maltose into glucose. The mean value of the maltose formed by the other ferments in this time was about 860 milligrams, with variations from 855 to 872 milligrams, while for the Taka Diastase it was over one gram. But to secure these close results it must be remembered that very different amounts of the several ferments had to be taken at the start; that is, for the weaker digestants more, and for the stronger less was weighed out. The amounts taken varied inversely as their starch digesting activity, as shown by the first line of tests.

These relations may be illustrated by the figures in the following table, in which the first column gives the name of the substance, the second the number of milligrams actually required to convert 1 gram of starch to the colorless end-point in 10 minutes, and the third the weight of maltose formed in this time. The ferment substances were suspended in water and the proper volume was measured out to give the calculated weight. The sugar was found by titration with standard Fehling solution, and is calculated as pure maltose, proper allowance being made for the dilution of the titrated solution. The sugar

amounts found under these conditions are essentially the same, but in producing the sugar 8.85 milligrams of Panase go as far as 9.79 milligrams of Holadin, 62.5 milligrams of Taka Diastase, 163.4 milligrams of the Diazyme liquids or 238.1 milligrams of the Vera Diastase Essence. In making comparisons by the table the fact must not be overlooked that the three preparations there last named are in solution, while the others are solids.

TABLE OF SUGAR FORMATION IN 10 MINUTES.

Column A gives the weight of ferment required in each case.
Column B gives the weight of sugar formed in each case.

	A.	B.
Panase	8.85	622 mg.
Holadin	9.79	634 mg.
Taka Diastase	62.5	611 mg.
Diazyme Essence	163.4	633 mg.
Diazyme Glycerole	163.4	635 mg.
Vera Diastase Essence	238.1	630 mg.

These results, which have been obtained many times in repeating the tests, show that the starch conversion to the colorless endpoint, which is more easily and quickly carried out than is the sugar determination, gives a practically useful measure of the ferment activity, and a measure which bears a close relation to that of maltose formation. We, therefore, recommend the process for all the routine examinations of this nature which have to be made in the testing of the diastase ferments. As is explained in the article by Mr. Johnson, the process here employed was first suggested by Roberts for the examination of ferments of animal origin, and was later modified by Junck and by Francis, and applied to the ferments of vegetable origin. In our laboratory it has been submitted to critical revision with the object of securing greater accuracy through a fuller specification of details of manipulation. The most important points of the process are these, which are presented as easily and practically workable:

1. A clean grade of potato starch is thoroughly washed, first by decantation and then on a Buchner funnel. It is carefully dried at a low temperature, and finally at a higher temperature to a moisture content of about 10 per cent., the exact moisture content to be determined in a separate experiment.

2. For the actual tests about 22 grams of the starch is mixed with 100 c.c. of cold distilled water to make a uniform cream and then poured into 800 c.c. of boiling distilled water. The boiling is continued through ten minutes, and then enough water is added to make the actual starch content (anhydrous) exactly 2 per cent. by weight. For each test quantities of exactly 50 grams of the paste are weighed into a series of 250 c.c. flasks, which are clamped in a large water-bath kept at a temperature of 40 degrees.

3. The iodin test solution is made by dissolving 2 grams of iodin and 4 grams of potassium iodid in 250 c.c. of distilled

water; 2 c.c. of this solution is then diluted with pure water to make 1,000 c.c.

4. In making up the diastase solution the operator must be guided by the results of a few preliminary experiments in each case. For liquid malt extracts, for example, 10 c.c. diluted to 100 c.c. will generally be a proper strength, while in the examination of the dry preparations on the market 200 to 500 milligrams, dissolved or suspended in 100 c.c. of distilled water will usually answer.

5. These solutions are used in this way: Small definite volumes of the dilutions are added to the flasks containing the starch paste in the thermostat, and with the least possible loss of time. The mixtures are well shaken. The volumes added may be as follows, but all diluted to that of the largest volume before mixing: 1 c.c., 2 c.c., 3 c.c., 4 c.c., 5 c.c., 6 c.c. In about eight minutes tests are begun by removing volumes of 5 drops from each digesting mixture by a pipette and adding this to 5 c.c. of the dilute iodin solution in a clear white test-tube standing over white paper. It is best to have a row of these tubes mounted to receive the liquids to be tested. If at the end of ten minutes drops from one of the flasks fail to give the iodin reaction we are ready for a second and more accurate test. Weigh out now 100 grams of the paste into each of six flasks, and, assuming that the endpoint in the first test was found between 4 and 5 c.c., add accurately to the six flasks these volumes of the diastase solution: 8 c.c., 8.4 c.c., 8.8 c.c., 9.2 c.c., 9.6 c.c. and 10 c.c. These volumes should all stand ready and all diluted to 10 c.c, so that they may be poured into the starch and shaken up without delay. They should also have the normal thermostat temperature of 40°, which precaution should be observed with the mixtures added in the first test. The tests with the iodin solution are repeated as in the first trial, and new limits are found between which the exact value must lie. For example, at the expiration of ten minutes the paste to which 8.8 c.c. of the diastase solution is added may show a faint yellowish dextrin color, while that with 9.2 is colorless. We may go further and try a series of new dilutions, but practically it is not necessary. In fact, we can not carry our readings to a much finer degree of accuracy, because of the difficulty of distinguishing between the effects of dilutions so near together, in many cases. In a case like the above illustration it is sufficient to take the mean of the last named dilutions, and calculate the results to the basis of one part of ferment and the starch converted by it.

6. We have recommended potato starch because it is possible to obtain it in a satisfactory condition of purity. The commercial corn starch, even after washing, does not appear to be suitable for the purpose. On microscopic examination the potato starch granules must appear clean and sharp.

The working method is seen to be simple, and if all the commercial diastase ferments are tested in this way their

practical value may be easily compared. Until something better is proposed we believe the scheme as outlined may be safely followed, and that it will be perfectly fair to all concerned.

The above report was adopted by the Council, with the recommendation that before publication it should be submitted to the manufacturers whose products had been examined. The replies were reported to the Council by the subcommittee, and the following supplemental report was submitted to the Council and adopted:

This report has been submitted to the manufacturers of all of the articles described and opportunity given them to make any comment or criticism they saw fit to make. As might be expected, each firm was desirous of changing in some respect the wording of the report so far as it refers to the firm's products, but a careful consideration of these replies does not warrant the subcommittee in admitting the justness of any of the claims made.

Parke, Davis & Co. state that in testing their product, Taka Diastase, the reaction should be carried to the loss of blue color only, and claim that to digest to the loss of all color would work to their ferment "a very grave injustice." They say that "'Taka-Diastase is recommended, not for the rapidity with which it converts starch into maltose and dextrose, but rather for its usefulness in carrying cooked starch through the preliminary stages of digestion or hydrolysis with remarkable rapidity." The subcommittee fails to see the force of this argument, since what is desired in a diastase is conversion of starch into sugar. Besides this, Taka Diastase does not appear to be any more rapid in the preliminary stages than are some of the others, and in the advertising literature it is praised for its power of sugar formation, as are all the others.

In the comments offered by Frederick Stearns & Co. objection is made to the passage in the report in which we point out the discrepancy between the digestion of 200 parts by weight of starch in ten minutes and the conversion of 200 parts of starch into sugars. The firm promises to correct this discrepancy, which should have been done long ago.

Fairchild Bros. & Foster object most strenuously to the position given Holadin in the table, and insist that by *their* method of testing, the product has a higher value than we give it. This, no doubt, is true, but the subcommittee is not concerned with the firm's method of testing, and must be allowed to employ its own, for the reasons pointed out in the report. The object is in part comparison, and for this uniformity of methods is necessary. In this connection it should be noted that in the past the firm has strongly favored the adoption of a uniform method of testing diastase products.

The manufacturers of Maltzyme write in a somewhat indefinite way of their disappointment in the findings of the report, but the letter calls for no special comment.

W. A. PUCKNER, Secretary.

LIQUID COMBINATIONS CONTAINING PEPSIN AND PANCREATIN.

Report of the Council on Pharmacy and Chemistry of the American Medical Association.

(From The Journal A. M. A., Feb. 2, 1907, 434.)

The following report was submitted to the Council by a subcommittee:

To the Council on Pharmacy and Chemistry:—The U. S. Pharmacopeia, 8th revision, pages 334-5, states: "Pepsin and pancreatin in solution are incompatible with one another. If the solution be neutral or alkaline the pancreatin gradually destroys the pepsin, and if acid the pepsin destroys the pancreatin." The correctness of this statement has been amply demonstrated by the reports which have been submitted to the Council from time to time on liquid preparations claimed to contain these two ferments.

Thus an elixir was investigated which was by the manufacturers claimed to contain "the five active agents of digestion, pepsin, veg. ptyalin, pancreatin, lactic and hydrochloric acids," and to be "superior to all other remedies in dyspepsia and diseases arising from imperfect digestion," and the committee which investigated the article in question reported that "it was impossible to establish the presence of either the proteolytic or the amylolytic ferment."

Similarly, on another liquid preparation, which was said to contain "pancreatin, pepsin, lactic and muriatic acids, etc." . . . "the combined principles of digestion to aid in digesting animal and vegetable cooked food, fatty and amylaceous substances," the committee reported "this product possessed only very slight proteolytic action and failed to digest 2 per cent. of its own weight of starch."

Again, the report on still another preparation stated: "But while it was said to contain pancreatin, the U. S. P. test for the valuation of pancreatin failed to indicate this ferment."

The report on yet another elixir, claimed to be "the only true digestant, because it contains the enzymes of all the glands which are necessary for digestion," showed that this article did not contain "any appreciable enzyme activity, either amylolytic or proteolytic."

The correctness of these findings of the committee of the Council was generally acknowledged by the manufacturers when their attention was called to the matter. Thus, one manufacturer of digestive ferments writes: "We will ask you to hold this matter up until you hear from us further on the subject. The reason

for this request is that we have been going over our liquid preparations very carefully in order to be sure that after aging they would contain the ferments in that we put into them. The pancreatic ferments in alcoholic liquids seem to lose their strength."

The chemist for a large manufacturing house writes: "There are now on the market a number of preparations in which pepsin and pancreatin are combined in liquid form, and the result is that we have had numberless requisitions from our representatives that we also market such a preparation. As the result of this we have carried out a series of experiments no less than four or five times in order to determine whether pepsin, diastase, and pancreatin would retain their activity in the form of a syrup, wine or elixir. We have proven incontrovertibly that this can not be done. While any two of these substances, or even all three of them, can be dispensed in the form of a liquid by the retail druggist and will retain their normal activity for as long a period as three to six weeks, yet if allowed to stand sufficiently long, they mutually destroy each other; so that in a combination of pancreatin and pepsin the pancreatic enzyme is lost and the pepsin greatly injured, and where diastase is present, both diastase and pepsin (or diastase and pancreatin) mutually destroy each other."

Since it has been demonstrated that pepsin and pancreatin can not exist in one and the same solution for any reasonable length of time, it becomes apparent that liquid preparations said to contain these two ferments are sold under impossible claims. It is therefore recommended:

1. That the Council on Pharmacy and Chemistry refuse to approve liquid preparations that are claimed to contain both pepsin and pancreatin.

2. That the medical profession through The Journal of the American Medical Association, be advised of the fallacy of employing such combinations.

3. That the attention of manufacturers be called to the worthlessness of such incompatible liquid preparations of pepsin and pancreatin, and that they be urged to cease offering such products to the profession.

4. That, since the National Formulary has recognized a preparation of this kind under the title "Elixir Digestivum Compositum," the American Pharmaceutical Association be requested to

INSTRUCT ITS COMMITTEE ON THE NATIONAL FORMULARY TO OMIT THIS PREPARATION FROM THE NEXT EDITION.

The recommendations of the subcommittee were adopted by the Council and publication of the report directed

W. A. PUCKNER, Secretary.

The Fallacy of Combining Pepsin and Pancreatin—Advertisements Measured by Scientific Statements.

(From The Journal A. M. A., Feb. 9, 1907, 533.)

In a previous article we published the official announcement of the Council on Pharmacy and Chemistry relative to the liquid mixtures on the market claimed to contain pepsin and pancreatin. Here we present further evidence in the form of quotations from text-books, a class of evidence which, while not always reliable, must be accepted as reliable in this instance, for the reason that it is capable of proof and has been proved. We inject these quotations into a partial list of the preparations on the market, leaving our readers to draw their own conclusions regarding the manufacture and the use of such impossible combinations.

The manufacturer's excuse, as stated last week, is that physicians demand such preparations, and that they are simply supplying the demand. Why do some physicians demand and use such preparations? The answer is easy: because, repeating again, they have depended on the literature of the manufacturer rather than on scientific literature and on text-books. The "literature" in the form of advertisements of Lactopeptin and Elixir of Lactopeptin probably is more responsible for the demand for these monstrosities than any other one thing. It has been said that more money has been spent in advertising Elixir Lactopeptin than has been spent for any other one proprietary preparation on the market. Probably this is true, if we take into account the liberality of the firm in this regard and the time the preparation has been on the market.

It must be remembered that trypsin—mentioned in some of the quotations—is one of the principal constituents of pancreatin.

NEW YORK PHARMACAL ASSOCIATION.

ELIXIR LACTOPEPTINE. "Contains the five active agents of digestion—pepsin, diastase (veg. ptyalin), pancreatin, lactic acid and hydrochloric acid—combined in the proper proportions to insure the best results."

["Useless Pepsin Compounds.—But let me warn you to place no faith in the pharmaceutic monstrosities which are said to contain pepsin combined with pancreatin, with which it is

positively incompatible, nor those in which it is combined with wines or any preparation of alcohol which, except in the weakest dilutions, interfere with its action. . . . Pancreatin not only can not be combined in the same mixture with pepsin, since they mutually destroy each other, but it can not be prescribed with any benefit so long as pepsin and HCl are being secreted by the stomach." Boardman Reed, Diseases of Stomach and Intestine, page 347.]

SHARPE & DOHME.

PAN-PEPTIC ELIXIR. "An efficient tonic-digestion containing pure pepsin, pure pancreatin, pure caffein, lactic acid and celery, the latter being added chiefly for its flavoring properties."

ELIXIR PEPSIN AND PANCREATIN.

ELIXIR PEPSIN, BISMUTH AND PANCREATIN.

ELIXIR PEPSIN, STRYCHNIN, BISMUTH AND PANCREATIN.

["Pancreatin digests albuminoids and converts starch into sugar and proteids into peptones, also emulsifies fats in presence of an alkaline solution (pepsin requiring an acid one). Prolonged contact with mineral acids renders it inert. It is digested by pepsin, and hence probably never passes into the duodenum in its own character." Potter, Materia Medica and Therapeutics, tenth edition, page 373.]

H. K. MULFORD COMPANY.

ELIXIR LACTATED PEPSIN. "Contains pepsin; pancreatin, lactic acid, maltose, hydrochloric acid, etc."

LIQUOR DIASTOS. "Contains pepsin (isolated), diastase, trypsin, ptyalin, nitro-hydrochloric acid, C. P., nux vomica with aromatics."

["In the presence of an acid it (pancreatin) soon becomes inert." A. A. Stevens, Modern Materia Medica, 1903, page 176.]

["Attention is called to the fact that many ferments—especially trypsin—are destroyed by the pepsin. It is, therefore, very doubtful whether any ferment can be given which will act beyond the stomach." Sollmann, Text-Book of Pharmacology, page 749.]

PARKE, DAVIS & CO.

ELIXIR PEPSIN, BISMUTH AND PANCREATIN. "Designed to cover the indications when both the stomach and the duodenum fail in functional activity—that is when there is both gastric and intestinal indigestion—with symptoms of catarrh in the regions named."

ELIXIR PEPSIN, BISMUTH, STRYCHNIN AND PANCREATIN. "Covers the same indications as the preceding, with the advantage of the tonic influence of strychnin."

ELIXIR PEPSIN AND PANCREATIN.

ELIXIR PEPSIN AND PANCREATIN WITH CAFFEIN.

MALT EXTRACT WITH PEPSIN AND PANCREATIN.

ELIXIR LACTATED PEPSIN. "A combination of pepsin, pancreatin, diastase, lactic acid and hydrochloric acid."

["Trypsin is gradually destroyed by gastric juice, and even by digestive hydrochloric acid." Hammarsten, Physiol. Chemistry, page 327.]

["Pancreatin and peptonized foods.—We must again point out that the value of these preparations depends on their

being predigested foods, and it would be an error to suppose that in administering them we are introducing an active digestive ferment into the small intestine; for the proteolytic action of trypsin is arrested in an acid medium like the gastric juice, and the gastric pepsin aids in the destruction of the ferment." Yeo, Hare's System of Practical Therapeutics, vol. i, page 221.]

FREDERICK STEARNS & CO.

ELIXIR LACTINATED PEPSIN. "Few combinations of digestive ferments have given better satisfaction than this one. It contains pepsin, pancreatin, vera diastase, lactic acid, hydrochloric acid, sodium chlorid, and milk sugar, thus representing the various digestive fluids of the body."

ELIXIR PEPSIN, BISMUTH AND PANCREATIN.

ELIXIR PEPSIN AND PANCREATIN.

["Pepsin and pancreatin are incompatible in solution, for the reason that if the menstruum be of such acid nature as to preserve the pepsin, the pancreatic enzyme will in time be destroyed; while if it is neutral or feebly alkaline, the pepsin will be destroyed." B. T. Fairchild, Reference Handbook of Medical Sciences, vol. vi, page 556.]

ARTHUR PETERS & CO.

PETERS' PEPTIC ESSENCE COMP. "This valuable preparation contains pure pepsin, pure pancreatin, pure diastase, pure lactic acid, pure hydrochloric acid, pure glycerin, and aromatics."

["It (pancreatin) may be given dry, in powder, capsules or compressed pills, or in solution. It should be administered in combination with an alkali, as the activity of pancreatin is destroyed by acids." Butler, Materia Medica and Therapeutics, fifth edition, page 499.]

WM. S. MERRELL CHEMICAL COMPANY.

ELIXIR ATONIC DYSPEPSIA, PHENOLATED. "Contains pepsin, pancreatin, cascara sagrada, ipecac, nux vomica, phenolated elixir."

MALT EXTRACT WITH PEPSIN AND PANCREATIN.

["Kühne made the observation that the activity of trypsin was permanently destroyed by digesting its solution with pepsin and hydrochloric acid. . . . Meltzer finds that hydrochloric acid alone destroys trypsin, but not as rapidly as when pepsin is also present." Schaefer's Text-Book of Physiology, vol. i, page 337.]

WILLIAM R. WARNER & CO.

ELIXIR PEPSIN AND PANCREATIN.

LIQUID PANCREOPEPSIN. "Comprises the natural and assimilative principles of the digestive fluids of the stomach and duodenal tract, viz.: Pepsin, pancreatin, lactic and muriatic acids."

["This ferment (pancreatin) is completely destroyed in the gastric juice. This is why thinking practitioners should not use both pepsin and pancreatin together in the same solution, because the medium in which one must act is opposed to that of the other. In the majority of cases in which pancreatin is

given empirically, HCl is still secreted in the stomach and the ferment is destroyed." Hemmeter, Diseases of the Stomach, pages 345-6.]

SMITH, KLINE & FRENCH.

ELIXIR PEPSIN, BISMUTH AND PANCREATIN.
ELIXIR PEPSIN AND PANCREATIN.

["The value of pancreatin is even more problematical than that of pepsin, for though it would no doubt be valuable where the digestive ferments, particularly those of pancreas, were deficient, this has not been shown to occur. On the other hand, the pancreatic ferments are certainly destroyed in passing through the stomach." Cushny, Pharmacology and Therapeutics, on the Action of Drugs, page 710.]

COLUMBUS PHARMACAL COMPANY.

PEPTIC DIGESTANT. "Composed of pepsin, pancreatin, diastase, hydrochloric and lactic acids, combined with an aromatic vehicle."

["Pancreatin does not act in an acid medium and should not be given with acid." W. Gilman Thomson, Practical Medicine, 1900, page 403.]

LILLY & CO.

ELIXIR PEPSIN AND PANCREATIN.
ELIXIR PEPSIN AND PANCREATIN COMPOUND.
ELIXIR PEPSIN, PANCREATIN AND BISMUTH.
ELIXIR PEPSIN, PANCREATIN, BISMUTH AND STRYCHNIN.
ELIXIR PEPSIN AND PANCREATIN WITH CAFFEIN.

["For action it (pancreatin) requires the presence of an alkali and in the acid gastric juice would not only not act, but would itself in all probability be digested and destroyed as a ferment; and it is of no value except for the preparation of predigested foods." H. C. Wood, Therapeutics, Its Principles and Practice, 1900, page 798.]

THE MALTINE COMPANY.

MALTINE WITH PEPSIN AND PANCREATIN. "Contains the three principal artificial digestants, diastase, pepsin and pancreatin, in such proportions as to be capable of converting all foods required by the human organism into the soluble condition necessary for proper assimilation."

["Hence it is obvious that pancreatic extracts or ferments given by the mouth can be of no value whatever, since the proteolytic ferment at least will undoubtedly be destroyed in the stomach before reaching its normal sphere of action." Chittenden, quoted by Yeo in Hare's System of Practical Therapeutics, vol. i, page 221.]

REED AND CARNRICK.

PEPTENZYME ELIXIR. Formula: "Enzymes of the peptic glands. . . . Enzymes of the pancreas. . . . Enzymes of the salivary glands. . . . Zymogens from the spleen. . . . Enzymes of the intestinal glands."

["Pancreatin, a mixture of the enzymes of the pancreas . . . does not act in an acid medium and is rapidly de-

stroyed by the action of hydrochloric acid in the stomach." Croftan, Clinical Therapeutics, page 365.]

["Pepsin is incompatible with pancreatin, this in neutral or alkaline solution destroying pepsin, while in acid media being destroyed by the pepsin." Culbreth, Materia Medica and Pharmacology, 1906, page 655.]

The above is respectfully referred to the thoughtful consideration of the medical profession of the United States.

FORMALDEHYD DERIVATIVES.

Torald Sollmann, M.D.

(Abstracted from The Journal A. M. A., Sept. 5, 1908.)

In view of the conflict of the claims of the manufacturers and the findings of outside investigators in regard to certain proprietary "internal antiseptics," Sollmann undertook a direct experimental investigation of the questions involved.

I. In the determination of the antiseptic value, he has departed from the customary methods and aimed to reproduce as far as possible the conditions under which the drugs are actually used.

II. The antiseptic qualities of most of these drugs are based on the assumption that they are decomposed in the body with regeneration of the formaldehyd or other active radicles. Before investigating whether these decompositions occur in the body he studied them in simple solutions under the influence of reagents slightly more powerful than those acting in the body.

The Jorissen test for formaldehyd was used throughout and the results are summarized as follows:

1. Glutol contains considerable free formaldehyd and an additional amount is liberated by boiling, especially in an alkaline media.

2. Citarin and novasperin develop formaldehyd promptly in all media, even in the cold. The citarin liberates formaldehyd somewhat most readily. The reaction is greatest in the alkaline, least in the acid medium.

3. Hexamethylenamin and tannopin develop formaldehyd in all media, most in acid and least in alkaline. The reaction, slow at room temperature, is prompt on boiling.

4. With iodomuth, tannoform and tannopin the lower temperatures could not be used well on account of discoloration. On distillation they all liberate formaldehyd. Iodomuth: Most with alkali, doubtful trace with acid, none with water. Tannoform: Most with alkali, some with acid and water. Tannopin: Most with acid, less with water, least with alkali.

Tannipin contains no free formaldehyd while tannoform apparently does.

5. Formidin, guaialin, sodi-forma-sal and ur-a-sol do not liberate formaldehyd in any reaction. The postive reaction claimed by the manufacturers with the salicylic acid test as evidence of decomposition of the molecule can not be accepted as such as it was also given by the undecomposed products. Formidin and iodomuth contain iodin in the molecule, but the iodin test can not be utilized to demonstrate a decomposition of these products.

III. In the medicinal use of these drugs their decomposition would occur mostly in the intestines through the agency of the pancreatic juice, as shown by Nencki and Lesnik. This would be the only possibility for insoluble drugs; with soluble ones the possibility of decomposition elsewhere in the body must be accepted. Sollmann preferred the method of digestion outside of the body to that of introducing the drug into a ligatured loop of the duodenum of living animals. His results are given in tabulated form; they indicate that pancreatic digestion does not decompose these drugs more readily than does water; the only exceptions being the saponification of salol, and to a slight extent of urasol.

IV. Urinary examinations were made to test the decomposition of these drugs in the body, all on one person. The methods of testing are described in detail. The urine furnished evidence that hexamethylenamin renders the urine strongly antiseptic; it was made feebly antiseptic by novaspirin, salol and sodium salicylate. The urine did not furnish any definite evidence of the decomposition of tannopin, formidin, urasol, sodiformasal, citarin, novaspirin or tannoform; iodomuth was only slightly decomposed.

V. To test the efficiency as intestinal and wound antiseptics, Sollmann used the retardation of pancreatic and blood putrefaction. The transference of the results of the clinical conditions require some judgment. Side actions must be considered and the observations reported are confined to putrefactive organisms. The most effective drugs which prevented putrefaction were benzoate and salicylate of sodium, creosote, bismuth subnitrate, novaspirin, urasol and hexamethylenamin. Others retarded putrefaction more or less, but citarin was as ineffective as water.

VI. The individual products are discussed separately and the general conclusions are summarized as folows: "1. The methylene radicle is transformed very readily into formaldehyd with some compounds; much more difficult or not at all with others. 2. The formaldehyd thus liberated is completely oxi-

dized in the human organism and does not exert any antiseptic action on the urine. 3. Formidin is neither decomposed nor absorbed to any appreciable extent in the intestine. 4. Hexamethylenamin is the only reliable urinary antiseptic (by mouth) of the various substances tried. The salicylates (sodium salicylate, salol, novaspirin) have a distinct but much inferior, preservative effect. The following are practically useless: Boric acid, citarin, formidin, iodomuth, sodi-forma-sal, sodium benzoate and sodium phenolsulphate, tannoform, tannopin and ur-a-sol. 5. As intestinal antiseptics, the most efficient drugs appear to be bismuth subnitrate and creosote (also novaspirin and ur-a-sol). These are closely approached by tannoform and iodomuth. Distinctly inferior are formidin, salol, guaiacol carbonate, tannopin and glutol. Guaialin appears to be nearly useless. 6. As relatively insoluble wound powders, the greatest antiseptic power appears to be possessed by beta-naphthol, boric acid, iodoform, quinin sulphate and xeroform. These are closely approached by acetanilid, bismuth subnitrate and orphol. Somewhat inferior are chloretone, formidin, iodoform and ur-a-sol. Distinctly inferior are glutol, guaiacol carbonate, tannoform, tannopin, tannin and salol. Non-antiseptic are cerium oxalate, charcoal, chalk and zinc oxid. 7. Of all the products examined for antiseptic value, hexamethylenamin is the only one which offers undoubted advantages over the older antiseptics. This statement is not intended to reflect on the antirheumatic value of the salicylic products, or on the astringent value of the tannin products."

INGLUVIN.

Report of the Council on Pharmacy and Chemistry.

(From The Journal A. M. A., July 11, 1908.)

A subcommittee of the Council reported that unwarranted claims and misrepresentation were made for Ingluvin by its manufacturers, William R. Warner & Co. recommended that the preparation be refused recognition and that the report be submitted to Warner & Co. for action.

The report was submitted to the firm, and after waiting one month and no acknowledgment or reply having been received, the Council directed its publication. It is as follows:

REPORT ON INGLUVIN.

Ingluvin is manufactured by W. R. Warner & Co., chemists, Philadelphia, Pa. The printed matter contains numerous claims and representations of which the following are specimens:

"A positive specific for indigestion, dyspepsia and the most effective remedy in obstinate cases of vomiting of gestation. . . . A specific for vomiting in pregnancy in doses of from 10 to 20 grains, and a potent and reliable remedy for the cure of marasmus, cholera infantum, indigestion, dyspepsia, and sick stomach caused from debility of that organ. It is superior to the pepsin preparations since it acts with more certainty, and effects cures where they fail. . . . The natural glycocholic acid in Ingluvin is the active principle and the most efficient agent in the treatment of all stomachic and enteric disorders."

Two samples were purchased at different times in the open market and on examination found to consist essentially of powdered meat fiber mixed with what appeared to be a membranous tissue resembling the lining of a gizzard. Both samples on being tested by the method prescribed by the U. S. Pharmacopeia for estimating the strength of pepsin were found to possess little, if any, proteolytic activity. In order to determine whether or not the lining of a fowl's gizzard possesses proteolytic action, a fresh gizzard was secured, the lining washed slightly with water, then removed and on using one-half of same in place of pepsin as prescribed by the Pharmacopeial method, it was found to digest 10 grams of albumin within the time limit. Pepsin, when properly kept, does not lose its strength to any material extent.

A careful examination was made for the presence of glycocholic acid, claimed to be the active principle of ingluvin, but its presence could not be established. Furthermore, the anatomic relations of the fowl are such as to preclude its presence.

The above shows that ingluvin does not possess nearly as much proteolytic activity as ordinary saccharated pepsin recognized by the 1880 Pharmacopeia and which was prepared on the basis of digesting 300 times its weight of egg albumin. Inasmuch as no glycocholic acid is present in ingluvin it would seem that saccharated pepsin would be far more efficacious in treating the abnormal conditions for which ingluvin is recommended in the advertising circulars. Furthermore, the claims made for the preparation are grossly extravagant.

A communication from Warner & Co. has been received since the above report was adopted in which it is stated: "The reason that previous letter was not replied to was because we were desirous of securing all the information possible on the subject. Since that time we have made considerable research and also made laboratory investigation, and are enclosing the accumulated data with diagram of a part of the alimentary canal showing the esophagus, crop and gizzard."

Much of the other matter submitted is immaterial. The following, so far as it means anything seems to confirm the correctness of the report of the Council's referee that ingluvin is practically devoid of proteolytic activity: " . . . the

therapeutic activity must be due to the bitter property, rather than any proteolytic activity, and it probably increases, thereby, the functional activity of the stomach, by which the normal digestive process is increased. Ingluvin in a 0.4 per cent. hydrochloric acid solution at 37 to 40 C. or if mixed with an aqueous solution of pepsin under the same conditions possesses an acrid bitter taste and increases the secretion of the saliva and as this is practically the same condition as when in the stomach, it no doubt stimulates the depressed mucosa peptic glands and increases gastric secretion."

W. A. PUCKNER, Secretary.

COMMENT.

The fallacies attending the use of digestive ferments in most stomach diseases have been previously noted in THE JOURNAL.[1] In most digestive disorders a deficiency of the digestive ferment has not been proved. In cases in which pepsin is lacking, its administration is valueless unless it is combined with large doses of hydrochloric acid, and it is doubtful whether this combination is either necessary or conspicuously useful. There is, however, something so alluring about medication by digestive ferments which are assumed to supply a physiologic need, that since their discovery they have formed a fertile field for the activity of the manufacturer of proprietaries. As by scientific laboratory tests, it is possible to determine whether a given preparation has digestive power, the manufacturers of ingluvin avoid this point by claiming that the remedy acts, not on the food, but on the stomach itself. That remedies may exist which act as stimulants to the digestive secretions can not be denied, although at the present time this power has not been satisfactorily demonstrated. The proprietors of ingluvin finding that proteolytic activity is not to be attributed to this preparation of chickens' gizzards, announce a new therapeutic fact in the claim that "the natural glycocholic acid in ingluvin is the active principle and the most efficient agent in the treatment of all stomachic and enteric disorders." According to the report made to the Council there is no glycocholic acid in this preparation, nor is it possible, from the anatomic arrangements of the fowl's digestive apparatus, for it to get there. By all the tests which can be applied to determine its value this preparation is of much less value in digestive disorders than saccharated pepsin which was discontinued in the pharmacopeia because of its inferiority to the other forms of the ferment.

The repudiation, by the manufacturers, of the more absurd claims made for ingluvin, shows the need of maintaining an

1. Feb. 2, 1907, 415 and Feb. 9, 1907, 521.

attitude of healthy skepticism toward the advertised therapeutic virtues of proprietary preparations. If a physician is disposed to use digestive ferments, he should give preference to the official preparations and ferments from other sources should be required to stand the exact tests which demonstrate the worthlessness of so many preparations on the market.

LABORDINE.

A Report by the Council and Some Pertinent Comments Added Thereto.

(*From The Journal A. M. A., March 30, 1907, 1121.*)

The following report was submitted to the Council on Pharmacy and Chemistry by the subcommittee which examined Labordine:

To the Council on Pharmacy and Chemistry:—Your subcommittee presents the following report on Labordine, sold by the Labordine Pharmacal Co., St. Louis.

Labordine is advertised to physicians as having the following composition:

	Per cent.
Apium Graveolens (true active principle) "Process-Laborde"	35⅜
Gaultheria Fragrantissima (true active principle) "Process-Laborde"	25⅛
Acete Amide-Phenyle	15⅛
Quinina	1⅛
Benzoyl-Sulphyonic-Imide	23¼

It is stated to be a "vegetable antipyretic;" that it "reduces temperature without heart depression," and physicians are warned to "avoid acetanilid poisoning and danger from other coal-tar antipyretics."

While the "formula" and the statement just quoted are sufficient evidence of the fraudulent character of the product, yet an abstract of the reports of the chemists who analyzed it is given to further demonstrate its character.

Taking the average of the reports of analyses, Labordine contains:

	Per cent.
Acetanilid	37.9
Free salicylic acid	6.9
Quinin	present
Saccharin	not found
Corn starch	present
Milk sugar	34.7

The report of analysis only makes apparent that Labordine is not what it is claimed to be. While it is claimed to contain 23¼ per cent. saccharin, this substance was not present, or mere traces only. While, in a disguised way, it is stated to contain 15⅛ per cent. acetanilid, it contained nearly 40 per cent.

It is recommended that Labordine be not approved and that this report be published.

The recommendation of the subcommittee was adopted by the Council, and in accordance therewith the above report is published. W. A. PUCKNER, Secretary.

COMMENTS.

A concrete illustration of some general principles previously laid down is furnished by a nostrum too unimportant to be of any value, save to "point a moral and adorn a tale."

About thirteen years ago Labordine was advertised under the name of Analgine-Labordine, "A purely vegetable product," "a combination of the active principles of *Camellia Thea*, *Apium Graveolens*, saccharin and carbohydrates," "Superior to Antipyrine, Phenacetine, Antifebrine, Acetanilid"—note the use of two names for the same thing—"or any of their imitations," and "unexcelled by any coal-tar product or their compounds." In 1894 the name was changed to Labordine, in order, as its owner stated, to prevent it being mistaken for a coal-tar product of similar name.

What its composition was at this time we do not know, since there is no guarantee of the permanence nor stability of nostrum formulas except "the honor and reputation of the manufacturers," which, as investigation has shown, is not always unimpeachable. There has been nothing to prevent alteration of the formula, if the proprietors desired, with every change in the moon. But the name and the general tone of the advertising has been the same. The claim of superiority over coal-tar products has been constantly made.

As to the present conditions, a circular enclosed with a sample of Labordine, recently sent from the St. Louis office, contains the formula given in the above report of the Council. In the same circular are also found these illuminating statements: "The medical profession has long appreciated the dangers involved in the administration of various mineral remedies now so commonly employed, and the value of a safe, effective and reliable vegetable antipyretic is universally recognized. Such a remedy is Labordine. It is purely vegetable in its composition and produces none of the evil after-effects of the coal-tar derivatives. . . . Labordine . . . is a purely vegetable cardiac stimulant. . . . There is nothing mysterious about Labordine or its constituents. . . . The 'Process-Laborde' gives the true active principles of the Celery and Indian Wintergreen, something heretofore difficult to obtain. To this is added the fact that absolutely chemically

pure Acet-Amide-Phenyle is used. The latter is the most valuable and, in fact, the only vegetable antipyretic known."

The above report of the Council shows the following facts:

1. *Apium Graveolens* (true active principle), "Process-Laborde" is probably powdered celery seed. One chemist says: "The powder has the characteristic odor of celery, while a microscopic examination shows the presence of a substance having the characteristic structure of seeds in general." If celery seed has any "active principle" it has never been isolated. As to its therapeutic value, nothing whatever is known. It is, we understand, highly beneficial in the case of singing canaries, but authorities in scientific therapeutics have never discovered that it possessed any remarkable medicinal qualities.

2. *Gaultheria Fragrantissima* (true active principle), "Process-Laborde," is probably ordinary everyday salicylic acid. One analysis showed salicylic acid to be present to the amount of about 7 per cent. The question of whether or not salicylic acid could in any way be considered the "true active principle" of *Gaultheria Fragrantissima*, was submitted to Prof. John Uri Lloyd of Cincinnati, the eminent authority on the chemistry of the proximate principles of plants, who replies:

> The advertisement is evidently so worded that, although the name of the Indian plant *Gaultheria Fragrantissima* is employed, its true and active principle being wintergreen oil, the concocter can mystify his patrons and at the same time use the well-known wintergreen oil, made in America, which in my opinion, so far as any chemical test might be concerned, could not be distinguished from the methyl salicylic acid (wintergreen oil) derived from the Indian plant. Concerning whether salicylic acid is a proximate constituent of *Gaultheria Fragrantissima*, in my opinion, it would be a misnomer to make such an announcement. Salicylic acid, *per se*, does not exist, in my opinion, in the plants mentioned, being made by chemistry.

3. The third and most important ingredient in this "purely vegetable antipyretic" is brazenly announced as "Acete-Amide-Phenyle," but it is only necessary to say that this imposing designation is an attempt to "Frenchify" a scientific name for acetanilid.

Analysis shows that this coal-tar product is present to the amount of 37.9 per cent., or 1.89 grs. in a 5-grain tablet.[1] In other words, this imposing Labordine, made by a mysterious and elsewhere unheard of "Process-Laborde," is simply one

1. Since this article was prepared we find that the national Food and Drugs Act has forced the proprietors of Labordine to put on the label the amount of acetanilid it contains, viz., 40 per cent., or 2 grains in a 5 grain tablet.

more of the herd of acetanilid powders that have been foisted on our profession and that have filled our journals for years past. The only thing in it that is of practical therapeutic value is 2 grains of acetanilid to a 5-grain tablet. The statement that Labordine is a purely vegetable preparation is probably intended by the proprietors as a good joke on the medical profession. Acetanilid is not usually regarded as a vegetable product, at least it is not ordinarily found in market gardens. The only vegetable source from which acetanilid can be obtained is the beautiful flowering coal-tar bush, from which so many other nostrum vendors obtain their "perfectly harmless, purely vegetable antipyretics," all composed of acetanilid and something to hide it. If the statements made by one of the company's employés and quoted below are true, Labordine is not "manufactured and made chemically pure in the laboratories of the Labordine Pharmacal Company," and this company has no laboratory, as its product is manufactured for it.

4. Our readers will be interested to know that the important ingredient entered under the imposing name of Benzoyl-Sulphyonic-Imide is simply a highly scientific name for saccharin. Even on this point, however, the formula is misleading, since it claims 23¼ per cent. of this substance, whereas the analysis shows that the presence of saccharin could not be proved. If it is present at all it is in quantities much less than stated, and so small as to be difficult of recognition. Instead it appears that the product contains common starch and about 35 per cent. of milk sugar.

THE COMPANY ITSELF.

One of the humiliating phases of the proprietary medicine business is that, in many instances, these preparations are foisted on our profession by men who know nothing of medicine, pharmacy or chemistry, yet not only presume to concoct our medicines for us, but also assume to instruct us how to use them.

Gould's Commercial Register for 1907 gives the officers of the Labordine Pharmacal Company as H. M. Coudrey, president; M. Crawley, vice-president, and D. E. Gamble, Jr., secretary and treasurer. The place of business is given as 420 Market street, St. Louis. We are informed that Harry M. Coudrey is an insurance agent and the present member of Congress from the Twelfth Missouri District; that Mark Crawley is a clerk in the insurance office of H. M. Coudrey; and that Mr. Gamble is cashier in the same office. A recent visit of a representative of THE JOURNAL to 420 Market street, St. Louis, showed that the office of the Labordine Pharmacal Company is in Room 12 on the third floor of an old

This advertisement is reproduced from the *Therapeutic Gazette* of November. For brazen effrontery and shameless mendacity the caution "AVOID ACETANILID POISONING AND DANGER FROM OTHER COAL-TAR ANTIPYRETICS" is hard to beat, when the stuff contains nearly 40 per cent. of acetanilid. And yet this is but a fair sample of nostrum advertising that intelligent physicians tolerate in medical journals they help to support. For how much longer ? ? ?

dilapidated building. There was no sign on the door of the office, but on the wall next to an old elevator was a very small sign which read "Labordine Chemical Company, Room 12." The office at the time of the visit was apparently in charge of a young woman about 20 years old. Careful scrutiny of the furniture and fixtures showed that the room contained an old oak roll-top desk in one corner and a kitchen table, on which were piled about half a dozen packages of Labordine. The floor of the room was bare and very dirty. In an adjoining room, the door of which was open, was piled a lot of broken furniture. No laboratories nor chemical apparatus were visible. The young woman in charge stated that Labordine was made by the Mallinckrodt Chemical Works, at No. 3600 North Second street, St. Louis.

This is a fair sample of the nostrums and of the methods of exploiting them. The bitterly humiliating fact about the whole business is that a preparation, advertised under such palpably misleading claims, could actually be advertised in medical journals, even in journals of a supposedly high scientific standard, and could be bought and prescribed for years by supposedly intelligent and conscientious physicians. It is not supposed that every physician should be enough of a chemist to detect the ridiculous discrepancies between the published formula and the therapeutic claims made for such a mixture. But that members of a supposedly learned profession should fail to have enough interest in the preparations they prescribe for their confiding patients to find out that acetanilid is being masked under an obsolete and little used name, that only saccharin is hidden under an imposing polysyllabic designation; that the so-called "active principles Process-Laborde" (whatever that may be), is only equivalent to ⅓ grain of salicylic acid in a 5-grain tablet, and that the advertising matter sent out for years by this company contained absolute falsehoods regarding the composition and therapeutic benefits of its preparation, is certainly just cause for shame and humiliation. If a physician, knowing the composition of Labordine, wishes to prescribe it and prescribes it intelligently, he has a perfect right to do so. If he wishes his patient to have 2 grains of acetanilid, 1/20 of a grain of quinin, and 1/3 of a grain of salicylic acid, and considers a mixture of ground celery seed, starch and milk sugar as a proper vehicle for this medication, no one will question his right to administer it. No physician, however, has any right, either moral or professional, to prescribe a preparation, concerning the ingredients of which he knows absolutely nothing.

Is it possible that such carelessness may be one of the causes of waning public confidence in our profession? We leave it to our readers to determine whether such a moral can be drawn from this typical nostrum story.

LACTOPEPTINE.

Report of the Council on Pharmacy and Chemistry—with Some Comments Thereon.

(From The Journal A. M. A., March 16, 1907, 959, and March 23, 1907, 1047.)

The following report was submitted to the Council by a subcommittee:

We have devoted considerable time to the investigation of Lactopeptine (powder) and report as follows:

The label on the package contains this statement: "Lactopeptine contains the five active agents of digestion —pepsin, diastase (veg. ptyalin), pancreatin, lactic acid and hydrochloric acid—combined in the proper proportion to insure the best results."

Examinations demonstrated that more than 90 per cent. of Lactopeptine is milk sugar.

The amount of pepsin contained in Lactopeptine is somewhat less than 10 per cent. of official pepsin.

Careful examination failed to show the presence of either diastase or pancreatin.

Examination demonstrated a minute trace of chlorid only, therefore the preparation does not contain any appreciable amount of hydrochloric acid. The amount of lactic acid, calculated from the quantity of potassium hydroxid required for neutralization, was found to be 3 per cent.

From the above, it is evident that Lactopeptine (powder) is at least no more efficient as a digestive agent than the ordinary Saccharated Pepsin, official in the 1890 U. S. Pharmacopeia, but replaced in the present Pharmacopeia by the more active and dependable Pepsin.

These findings were submitted to the manufacturers of Lactopeptine, the New York Pharmacal Association, who, in their reply, stated: "Regarding the assertion that Lactopeptine does not contain pancreatin and diastase, we herewith confirm and reassert our statement that Lactopeptine is and has always been manufactured in accordance with the published formula and that the ferments referred to exist in the preparation as stated in the formula."

In view of these reasserted claims regarding the composition of Lactopeptine, another specimen was purchased in the open market. Its examination showed that it was of even poorer quality than the first specimen examined.

The tests not only failed to show the presence of diastase or pancreatin, but also failed to show the presence of any appreciable amount of pepsin.

From these experiments your subcommittee must conclude that Lactopeptine contains but small amounts of pepsin, that it contains no hydrochloric acid or mere traces only, and that it contains neither diastase nor pancreatin. Hence, the statements made by the manufacturers in regard to the composition of Lactopeptine are incorrect. Since the composition of Lactopeptine is not given by the manufacturers, but, instead, corresponds to a weak saccharated pepsin, it is evident that the claims made as to its therapeutic value are unwarranted, exaggerated and misleading. It is, therefore, recommended that Lactopeptine be not approved. In view of the wide publicity given to the claimed composition and therapeutic value of the article, it is further recommended that this report be published.

The recommendations of the subcommittee were adopted by the Council, and in accordance therewith the report is published. W. A. PUCKNER, Secretary.

Reduced to a few words, the above report shows that—whatever the manufacturer may have put into it—Lactopeptine as it exists on the market was found by the subcommittee to be only equal to a weak saccharated pepsin, which has but one-tenth the digestive power of the official pepsin and that Lactopeptine at times is inert.

That the subcommittee which examined Lactopeptine could find neither diastase nor pancreatin was to be expected, since it has been demonstrated repeatedly that those ferments are destroyed by pepsin in the presence of acid. The examination shows that in the absence of solvents the presence of lactic acid still enables the destruction of pancreatin and diastase. That the manufacturers should have attempted to manufacture such an impossible product, and that the medical profession should have accepted it, is not creditable to either party concerned.

That the subcommittee should fail to find the hydrochloric acid claimed to be contained in the product was a foregone conclusion. If it is remembered that ordinary hydrochloric acid is a solution of hydrogen chlorid in water and that hydrogen chlorid itself is a gas, the absurdity of the claim that it is contained in a dry powder is apparent.

It is astonishing that physicians should so long have used a product about whose therapeutic value extravagant claims have been made, when the very statements in regard to its composition should have condemned it.

A Further Report on the Digestive Power of Lactopeptine.

Dr. Charles H. Miller, assistant professor of pharmacology, Northwestern University Medical School, has voluntarily conducted some experiments for the purpose of learning whether or not Lactopeptine Powder is effective either as an amylolytic or a proteolytic ferment. The following is Professor Miller's report of his experiments, which should be read in connection with the report of the Council on Pharmacy and Chemistry, published last week:

Herewith I send report of tests made by myself relative to the digestive powers of Lactopeptine Powder—obtained from an original sealed package. Being interested in the examination of digestive ferments, I was prompted to take up Lactopeptine Powder because it is a preparation widely advertised. The observations are in accord with the report of your Council, published in THE JOURNAL, March 16.

A. AMYLOLYTIC POWER: ACTION OF PANCREATIN AND DIASTASE.

1. Gelatinized starch paste. Subjected to action of Lactopeptine in amount equal to 50 per cent. by weight of starch (before cooking) at 100 degrees F. for a total of twelve hours. Tested hourly for disappearance or modification of starch reaction.

No change was observed in mucilaginous consistence of the starch paste or purity of the starch reaction with iodin.

Control: The same quantity (30 c.c.) of the same starch paste was practically instantaneously changed to a thin liquid, in which the starch reaction was completely lost within five minutes, after the addition of 2 c.c. of saliva; in other words, 2 c.c. of saliva within five minutes converted 1.5 gms. of starch into dextrin and sugar, while 0.66 gm. Lactopeptine was without action on the same quantity after twelve hours.

2. A second test was made in the same way, except that an alkaline reaction was given with $NaHCO_3$.

The result was identical. No action could be detected.

Control: A similar mixture plus 2 cc. of saliva was converted within five minutes, with disappearance of the starch reaction.

B. PROTEOLYTIC POWER: ACTION OF PEPSIN.

Coagulated egg albumin in glass tubes of 2 cm. in length and 5 mm. diameter, open at either end and completely filled, was subjected to digestion for a total of twenty-four hours, at a temperature of 100 F., as follows:

Digestant	Quantity	Medium	Results 12 hours	24 hours
Lactopeptine	0.33 Gm.	0.2% HCl	1/20 digested	1/10 digested
Lactopeptine	0.33 Gm.	H_2O	inactive	inactive
Lactopeptine	0.33 Gm.	Alk. H_2O	inactive	inactive
Blank	Blank	0.2% HCl	inactive	inactive
Scale pepsin	0·3 Gm.	0.2% HCl	1/2 digested	All digested
Pancreatin yr. old specimen	0.3 Gm.	Alk. H_2O	1/8 digested	1/4 digested
Wampole's papain digestant*	4 Cc.	H_2O	inactive	inactive

* Said to contain pepsin, pancreatin, papain and diastase.

Conclusion: Lactopeptine is apparently equivalent in proteolytic power to the Pepsinum Saccharatum of the U. S. P., 1890, which was a 10 per cent. preparation and like it, Lactopeptine is only active in acid media. It is devoid of active enzymes other than the pepsin, and while the powder is feebly acid in reaction, no activity could be shown when water was the medium employed.

CHARLES H. MILLER,

Lactopeptine Exposed Thirty Years Ago.

(*From The Journal A. M. A., April 6, 1907, 1198.*)

SOUTH BEND, IND., March 23, 1907.

To the Editor:—The report on Lactopeptine in THE JOURNAL of March 23 is very interesting and it is hoped that it will prove equally instructive to your readers. While it is interesting to us pharmacists, I can not say it is especially instructive, for the facts contained therein have been surmised if not actually known to pharmacists for many years. The surprising thing, however, is that the members of the medical profession should go along blindly prescribing such preparations year after year, often against our protest, as was more especially the case with the acetanilid mixtures. For years the pharmaceutical journals had pointed out the deception concerned in the exploitation of the medical profession (and eventually of the public) by nostrums of this character without avail, until the Council, through THE JOURNAL, began some two years ago, to show up the true character of these nostrums. Lactopeptine and especially its elixir have been used in enormous quantities by the medical profession, although in 1876, soon after its introduction, Prof. Emil Scheffer of Louisville, Ky., contributed a paper to the American Pharmaceutical Association, in which he reported some experiments he made on Lactopeptine, and proved that it had no greater digestive value than the saccharated pepsin then in vogue. This paper appeared in the Transactions of the American Pharmaceutical Association for 1876. Although Scheffer

was an authority on the subject, he being the author of the first process for obtaining pepsin in a pure state, it is not apparent that any attention was paid to this article by the medical profession; in fact, it was entirely ignored by medical journals, and extensive advertising soon made Lactopeptine the most extensively employed proprietary article. This leads to the observation how helpless we pharmacists have been in the past because of the lack of cooperation of the medical profession. We have had to supply such articles as were in demand, and when such articles as the Compound Powder of Acetanilid and the Compound Powder of Pepsin and its elixir in the Pharmacopeia and National Formulary are criticised, such criticism should be directed against the members of the medical profession because of their lack of interest and co-operation in the preparation of these standard works. Now that their attention has been so forcibly directed to this anomalous condition, it is hoped that physicians will participate actively in the revision of these joint authoritative standards.

LEO ELIEL,
President, American Pharmaceutical Association.

MEDICINAL FOODS.

(*Abstracted from The Journal A. M. A., May 11, 1907, 1612.*)

A report, of which the following is an abstract, was submitted to the Council on Pharmacy and Chemistry by the subcommittee which examined the medicinal foods:

In order to determine the food value of any food product it is necessary to consider the following points: Chemical composition; available potential energy; absorbability and cost. No attempt is made in this article to discuss each of these features separately, but they are utilized as required.

The ingredients on which the food value of any article of food depends are the proteid substances, carbohydrates, fats, certain inorganic bodies and—under certain conditions—alcohol. The amount of each of these present in a preparation must be established by chemical analysis. From the results thus obtained it is possible to calculate the potential energy represented by a given food product. In this report the potential or food value is expressed in the large or kilocalorie, that is, the amount of heat required to raise the temperature of one kilogram of water one degree centigrade.

The factors employed in this report for expressing in calories the actual amount of energy utilized by the system are 4.8 for proteid substances, 4.1 for carbohydrates, and 9.2 for fats.

The accompanying table embodies the results obtained by submitting all the well-known so-called "predigested foods" to chemical examination. The table as published in THE JOURNAL included columns on: Price per bottle, number of cubic centimeters in a bottle, cost per 500 cubic centimeters, reaction, specific gravity, percentage of non-volatile residue, ash, percentage of nitrogen, calories as proteids in 500 grams, carbohydrates before inversion, alcohol by volume, average recommended adult dose per diem in cubic centimeters, cost per diem to supply 1,430 calories. These columns were eliminated from this abstract, as they were unessential, so far as the practical value of the article is concerned. In most cases two samples of the same brand were purchased at an interval of about six months. All the analyses were made before Jan. 1, 1907. Some of the preparations contain much glycerin which does not, so far as known at present, possess any recognized food value, although there are a number of experiments on record to indicate that it influences metabolism.

The percentage of nitrogen accredited to each of these products represents the total amount of nitrogen, irrespective of the nature of the nitrogenous substances, although some of this nitrogen has no nutritive value.

By multiplying the percentage of nitrogen found by the factor 6.25 we obtain the percentage of nitrogenous matter (proteids) contained in the various preparations. By multiplying the number of grams of nitrogenous matter present in 500 grams of material by the factor 4.8 it is found that the potential energy available by the nitrogenous matter varies from 10.3 calories to 153.1 calories. Five hundred grams of the material is made the basis of calculation, because it approximates a pint, the amount usually believed to be present in the various trade packages, and because it affords a ready basis of calculation.

The carbohydrates are represented by cane sugar, maltose, dextrin and invert sugar. Lactose is probably also present in some, but it is impossible to establish this. By multiplying the number of grams of carbohydrates present in 500 grams of the foods by the factor 4.1 we obtain the potential energy represented by the carbohydrate, which varies from 11.3 to 319.2 calories. The total calorific value of both the proteids and carbohydrates ranges from 54.7 to 397.5 calories. The total food value of an equal quantity of milk, including fat, approximates 360 calories.

The value of alcohol as a food product pure and simple in disease is, however, an open question. There is no doubt whatever but that it acts to a certain

TABULATED RESULTS OF EXAMINATIONS OF MEDICINAL FOODS.

Name of Preparation and Manufacturer.	Glycerine and undetermined matter.	Per cent nitrogenous matter (6.25).	Calories as proteids in 500 grams.	Carbohydrates after inversion.	Calories as carbohydrates in 500 grams.	Calories as proteids and carbohydrates in 500 grams.	Alcohol, by weight.	Calories as alcohol in 500 grams.	Calories as proteids and carbohydrates per diem dose.	*Total calories in per diem dose.	No. Cc. required per diem to supply 1430 calories.
Carpanutrine—John Wyeth & Brother	28.45	4.28	102.7	5.34	109.5	212.2	12.5	437.5	25.5	78.0	1100.7
Carpanutrine—John Wyeth & Brother	21.29	6.24	149.8	5.78	118.5	268.3	14.0	490.0	32.2	91.0	942.9
Liquid Peptones—Eli Lilly & Company	3.63	4.50	108.0	6.05	124.0	232.0	18.0	630.0	69.6	258.6	829.4
Liquid Peptones, with Creosote—Eli Lilly & Company.	4.34	3.84	92.2	13.47	276.1	368.3	18.0	630.0	110.5	299.5	716.2
Liquid Peptonoids—Arlington Chemical Company	0.23	4.93	118.3	10.57	216.7	335.0	14.0	490.0	100.5	247.5	866.6
Liquid Peptonoids—Arlington Chemical Company	2.02	4.53	108.7	11.53	236.4	345.1	14.1	493.5	103.5	251.5	852.7
Predigested Beef—H. K. Mulford Company	3.40	2.38	57.1	4.37	89.6	146.7	16.0	560.0	44.0	212.0	1011.7
Predigested Beef—H. K. Mulford Company	4.37	2.59	62.2	4.55	93.3	155.5	15.5	542.5	46.7	209.5	1024.3
Nutrient Wine of Beef Peptone—Armour & Company	14.97	0.64	15.4	15.43	316.3	331.7	17.5	612.5	66.3	188.8	757.4
Nutrient Wine of Beef Peptone—Armour & Company	13.70	0.43	10.3	15.57	319.2	329.5	17.0	595.0	65.9	184.9	773.3
Nutritive Liquid Peptone—Parke, Davis & Company	1.02	1.86	44.6	12.89	264.2	308.8	18.8	658.0	74.2	232.1	739.5
Nutritive Liquid Peptone—Parke, Davis & Company	1.95	1.16	27.8	13.19	270.4	298.2	17.7	619.5	71.5	220.2	779.2
Panopepton—Fairchild Brothers & Foster	2.60	6.38	153.1	11.92	244.4	397.5	15.0	525.0	39.8	92.3	775.0
Panopepton—Fairchild Brothers & Foster	4.86	6.33	151.9	10.05	206.0	357.9	17.0	595.0	35.8	95.3	750.2
Peptonic Elixir—Wm. Merrell Chemical Company	3.21	2.54	61.0	11.46	234.9	295.9	16.5	577.5	53.3	157.2	818.6
Tonic Beef S. & D.—Sharp & Dohme	12.91	3.40	81.6	2.36	48.4	130.0	12.0	420.0	13.0	55.0	1300.0
Tonic Beef S. & D.—Sharp & Dohme	12.63	3.28	78.7	2.22	45.5	124.2	13.0	455.0	12.4	57.9	1234.4
Liquid Peptone—Stevenson & Jester Company	.44	1.81	43.4	0.55	11.3	54.7	12.0	420.0	9.8	85.4	1506.8
Cow's milk (3.8 per cent. fat)	....	3.50	84.0	4.80	98.4	182.4	...	....	7.3	1429.6	2000.0

* Total calories *per diem* dose includes the calories of alcohol in the liquid medicinal foods and the calories of the fat in milk.

degree as a food even here, not as a tissue builder, but as a saver of fat and carbohydrate material, and in order to give the preparations in question full value as food products, the calories, represented by the alcohol, are credited to each preparation, as are the proteids and carbohydrates. The factor usually recognized for expressing the calorific value of alcohol is 7. By multiplying the number of grams of alcohol present in 500 grams of material by 7, the number of calories varies from 420 to 658.

On looking over the literature and printed matter distributed by some manufacturers, the physician is frequently left under the impression that these preparations contain all the essential constituents necessary for maintaining normal nutrition of the body, as is clearly shown by the following quotation: "Contains sufficient nutritive material to maintain normal nutrition of the body, a valuable food in typhoid fever, pneumonia, tuberculosis, . . . and all the conditions of the system associated with enfeebled digestion and malnutrition."

In order to show the insidiousness of such representations it is only necessary to give the actual food value of the average daily dose (the average amount to be taken for twenty-four hours) recommended by the various manufacturers for their products. The average adult daily dose recommended varies from 50 to 150 c.c. The total available calories per daily dose based on the proteid and carbohydrate bodies varies from 9.8 to 110.5. Adding to these figures the amount of energy represented by the alcohol, in each case, the total available calories varies from 55.0 to 299.5. The number of calories per diem in sickness should not fall much below 1,500 during twenty-four hours.

In order to get a fair conception of the actual food value of these various preparations, it is desirable to make some comparison which can be readily comprehended by every physician. The amount of good milk necessary each twenty-four hours to sustain the vitality of a patient during a serious illness is not less than 64 ounces, or approximately 2,000 c.c. The food value in calories represented by this amount of good milk may be placed at 1,430. This includes not only the proteid and carbohydrate matter, but the fat as well. By comparing this available potential energy with the total energy available in the predigested foods under consideration, it can be readily seen that if a physician depends on the representations made by some of the manufacturers, and feeds his patient accordingly, he is resorting to a starvation diet. The largest num-

ber of available calories, including alcohol, present in any of the recommended daily doses, is less than one-fifth of the number of calories represented by 2,000 c.c. of milk; and the calories represented by the daily dose of the preparation poorest in food products is only one-twenty-fifth of the amount present in 2,000 c.c. of milk. These figures tell their own story.

Making 2,000 c.c. of milk the basis of calculation, and estimating the amount of the various preparations required to yield this number of calories, it is found that the quantity to be administered daily to supply 1,430 calories, including alcohol, varies from 716.2 to 1,506.2 c.c. In many cases the amount of alcohol exhibited by these quantities would keep the patient in an alcoholic stupor continually. The cost necessary to supply this energy varies from $1.48 down to $3.39. Compare these prices with the cost of two quarts of milk. Is farther comment necessary?

It is urged in justification of the use of preparations of this class that they contain constituents not found in our ordinary foods and in a more perfectly assimilable condition. As pointed out above, these so-called predigested foods contain no fats; the carbohydrates in them are the ordinary sugars present in our common foods, while the proteins belong to the peptone or albumose class. It is for these latter that the greatest claims are made, but even here no value can be pointed out not found in whey, peptonized full milk or peptonized skimmed milk.

There is likewise another point of considerable importance to consider in this connection. The terms *peptone* and *albumose* include bodies of very uncertain composition, and their suitableness as food substances depends largely on how they are prepared. Animal experiments have shown that nitrogen equilibrium may be maintained, for a time at least, by use of enzymic hydrolytic products of the proteins, even where the hydrolysis has been carried far beyond the so-called peptone stage, but it appears to be likewise true that the mixtures secured by acid or high temperature steam hydrolysis have no such value. Some of these, indeed, may exhibit a toxic behavior. This is true in particular of some of the commercial varieties of peptone, and until more is known of the source of the bodies of protein character employed in the make-up of these "predigested" mixtures it is unwise to assume anything concerning the food value of the nitrogen compounds found in them by analysis or even to dignify them by the name of foods.

Your subcommittee makes the following recommendations:

1. No liquid medicinal or predigested food shall be approved by the Council which contains less nutritive value, exclusive of alcohol and glycerin, than milk.

2. At least one-fourth of the nutritive value of the food, exclusive of alcohol and glycerin, shall reside in the nitrogenous matter.

3. The label shall bear a statement whether the peptones and proteoses are produced by enzymes or otherwise.

4. No package or advertising matter of any character shall bear representations which would lead the physician to believe that a food contains more nutrients than it actually does, or that it alone can sustain life for a limited period, if the dose advised contains less than 100 calories, exclusive of alcohol and glycerol, per diem dose.

5. Solid or partially evaporated products shall conform to the above standards when calculated to the water content of milk, viz., 88 per cent.

OXYCHLORINE.

Report of the Council on Pharmacy and Chemistry.

(From The Journal A. M. A., July 6, 1907, 54.)

The following report on Oxychlorine has been submitted to the Council by the subcommittee to which it was assigned:

To the Council on Pharmacy and Chemistry:—Your subcommittee submits the following report: The Oxychlorine Chemical Company, 1326 Wabash Avenue, Chicago, states in its advertising literature that:

"Chemically, Oxychlorine is the tetraborate of sodium and potassium combined with oxychlorid of boron, thus: $6(NaKB_4O_7)BOCl_3$."

Analysis of Oxychlorine showed:

Potassium	12.26 per cent.
Sodium	8.20 per cent.
Chloric acid—CLO_3	25.32 per cent.
Nitric acid—NO_3	21.70 per cent.
Boric acid anhydrid—B_2O_3	18.63 per cent.
Water, calculated	13.29 per cent.

Thus, Oxychlorine is not a definite chemical substance of the composition claimed, but instead is a mixture of alkali chlorate and nitrate with boric acid. Assuming that the chlorate is present as potassium chlorate and the nitrate as sodium nitrate, the analysis above quoted corresponds to a mixture approximately as follows:

Potassium chlorate	37.19
Sodium nitrate	29.76
Sodium and potassium tetraborate	2.18
Boric acid	30.52
Undetermined	0.35
	100 00

Your committee recommends that Oxychlorine be not approved and that this report be published.

The report of the subcommittee was adopted by the Council, and in acordance with the recommendation is published herewith. W. A. PUCKNER, Secretary.

In commenting on the above report it is hardly necessary to call attention to the palpable untruthfulness of the furnished formula, or to its lack of correspondence with the real composition of the preparation, to the imposing claims made by its pseudo-scientific exploiters, or to the absurdities, from a chemical standpoint, of the statements made in their literature. These features are more or less common to all nostrums. The physician who prescribes or uses Oxychlorine under the impression that he is getting a definite and unique chemical compound described as tetraborate of sodium and potassium combined with oxychlorid of boron is, according to our chemists, getting simply a mixture of potassium chlorate, sodium nitrate (or, perhaps, sodium chlorate and potassium nitrate), and boric acid in about equal amounts. More than one-third of this mixture is potassium (or sodium) chlorate, a drug by no means harmless.

In order that there may be no suspicion of unfairness to the promoters of this preparation, we quote from one of the advertising circulars sent out by the Oxychlorine Company:

"Oxychlorine owes it recognition as a therapeutic agent to its six principal qualities:

"1. It will oxygenate the blood at the seat of application, maintain nutrition and heal an uninfected solution of continuity of first intention without scar formation.

"2. It will disorganize all pus and ferment-producing micro-organisms, their toxins, ferments and ptomains.

"3. It will restore an inflamed mucous membrane to its normal condition, except where the membrane is sclerosed or atrophied.

"4. It will destroy pathogenic micro-organism and their toxins in the blood current.

"5. It will stimulate the blood to absorb more oxygen in the lungs that it at the time carries. [We do not know what this means; perhaps the Oxychlorine Company does.]

"6. It is absolutely harmless to the tissues and will not destroy a living cell."

Surely these people must have access to physiologic and chemical authorities not found in modern medical libraries, or else their esoteric researches into the mysteries of life must have carried them far beyond the ken of our most advanced workers along these lines. The scientific world would receive with great interest information as to how a mixture of potassium chlorate, sodium nitrate and boric acid oxygenates

blood, maintains nutrition and causes healing without scar formation. A mixture which will destroy micro-organisms and yet will not destroy a living cell certainly shows a fine sense of selection and discrimination not heretofore expected of a combination of chemicals or of a chemical compound. How like the wonderful elixir of medieval times, which was to the Christian a tonic and to the heathen a poison.

Here is another claim made for this nostrum:

"Two or three rectal injections of a one to two per cent. solution of Oxychlorine and ten grain doses given six to eight times per day is the best and most reliable treatment for typhoid fever."

If eighty grains of Oxychlorine contain thirty grains of potassium chlorate, three rectal injections each consisting of one pint of 2 per cent. solution, would contain approximately 160 grains of potassium chlorate. Such an injection might prove decidedly dangerous, especially when used by one ignorant of its true composition. However, the physician, not the promoters, bears the responsibility.

Oxychlorine sells at $3.50 a pound; the ingredients can be obtained for about 44 cents a pound. Perhaps the margin of profit is intended as a reward due the promoters for the profound physiologic discoveries announced in their reading matter.

PANKREON.

Report by the Council on Pharmacy and Chemistry, with Comments.

(From The Journal A. M. A., April 18, 1908.)

Pankreon, manufactured by the *Chemische Fabrik Rhenania, A.-G., Aachen*, Germany, is sold in the United States by Merck & Co., New York. It is described as a combination of pancreatin with tannic acid. While pancreatin, when administered as such, is destroyed by the action of the gastric juice before it reaches the intestinal canal in which it exerts its specific action, pankreon, it is claimed, is not affected by the gastric fluid, but dissolves in the alkaline intestinal fluids and rapidly develops the action of the pancreatic ferment. If this were true it would be superior to pancreatin.

Pankreon, having been proposed for inclusion in "New and Non-Official Remedies," was assigned to a subcommittee for report. This subcommittee made experiments to determine whether or not pankreon is unaffected by peptic digestion as claimed. The result of the investigations indicated that the compound is promptly digested by pepsin in acid solution, and

hence would be rendered inert before it could reach the alkaline intestinal fluid. The subcommittee recommended that its findings be submitted to the manufacturer through the American agent and that, in the meantime, the further consideration of pankreon be postponed. The report having been adopted by the Council, the findings, in accordance with the recommendation, were forwarded by the American agents to the manufacturer. The manufacturer's reply, having been transmitted to the subcommittee, it presented to the Council the following supplemental report:

"The findings of the referee contained in the report were submitted to Merck & Co. In reply Merck & Co. submit the answer of the *Fabrik Rhenania*, which does not show any inclination to consider the objections made to the product by the subcommittee. Merck & Co. can do nothing in the matter. Your referee recommends that the product be refused recognition."

This report was adopted by the Council and publication of the following directed:

Pankreon is a grayish powder, said to be prepared by the action of tannin on pancreatic material, claimed to contain 10 per cent. of tannin. It is recommended in from four to eight-grain doses for pancreatic affections, disturbances of digestion, diarrheas, dysentery, marasmus, colitis, achylia, nervous dyspepsia, gastritis hyperemesis, jaundice, etc. It is said to be a strong tryptolytic, amylolytic and emulsifiant.

It is repeatedy asserted in the advertising literature that pankreon is "unalterable by the gastric juice," that it is capable of passing through the stomach unmodified, and its medicinal virtue is said to depend largely on this fact. Again it is claimed that: "The characteristic difference that is presented in this newer product is its resistance to the ordinary process of digestion, so that the chief objection to the use of fresh pancreatic substance—which was that it was so readily digested in the stomach—has been largely done away with, and the early conclusions of Langley regarding the destruction of enzymes in the stomach must be modified so far as pankreon is concerned."

Investigation, however, fails to substantiate these statements. On the contrary, it is clearly shown that the enzymic power of pankreon is practically destroyed by subjecting it to the action of an artificial gastric juice. Pankreon was found to digest about forty times its weight of starch in a neutral solution in ten minutes at 40 C. Several mixtures of pankreon and pepsin of proper strength were prepared in a 0.1 per cent. of hydrochloric acid solution and allowed to stand at 40 C. for one-half hour. It was then made faintly alkaline, and various quantities added to different tubes containing 50 c.c. of a 2 per cent. starch paste, and allowed to stand for ten minutes at 40 C. Very little, if any, of the starch was

converted after standing the above time. Various other methods were tried to determine whether or not pepsin and acid affected the enzymic action of pankreon. In every case it was found that the action of pankreon was either destroyed or markedly impaired after being in contact with acid and pepsin for one-half hour or more.

If so marked an effect is produced by the action of artificial gastric juice, it is but reasonable to suppose that the same result would be produced even more promptly and to a more marked degree in the stomach under the influence of the normal gastric fluid. The manufacturer distinctly admits that the enzymic activity of the preparation is diminished by the continued action of a pepsin hydrochloric acid solution, but denies that it is completely destroyed physiologically, in the following sentence: *"Wir geben ja ausdrücklich an, dass bei langdauernder Einwirkung von Pepsin-salzsäure eine Schwächung der Wirkung erfolgt, jedoch ist Vernichtung unter physiolog. Verhältnissen ausgeschlossen."* This statement only tends to substantiate the results obtained in the laboratory. Investigation shows that pankreon does not to any appreciable extent "pass through the stomach unmodified" and that there are good reasons for believing that its enzymic power is completely destroyed by the normal gastric juice. If the product is altered during its passage through the stomach it evidently can not have the physiologic action attributed to it in the advertising matter accompanying the package, nor can it produce many of the therapeutic effects claimed for it by its sponsors.

W. A. PUCKNER, Secretary.

COMMENTS.

The above results serve to emphasize the need of impartial investigation of proprietary products even when put out by reliable manufacturers. This preparation has been largely used in Germany and has been recommended by reputable authors as an agent for replacing the deficient secretion of the pancreas. It has even been proposed to use the administration of pankreon as a means of determining whether the appearance of free fat and undigested muscle fiber in the stools was due to a deficiency in the function of the pancreas or to some other cause. It was reasoned that if the deficiency was due to imperfect functioning of the pancreas it would be supplemented by the action of pankreon and the undigested fat and muscle fiber would disappear from the stools. Consequently it was thought that if pankreon produced a removal of these undigested residues from the feces the evidence was obtained that the abnormal phenomenon had been due to disease of the pancreas.

It is possible that some of the good results attributed to the digestive action of the pankreon were in reality due to the tannin which it contained. This by limiting peristalsis might promote more perfect digestion by giving more time for the natural digestive ferments to act. If this is the method in which it acts it should be an instructive lesson to therapeutists to seek for the possibilities of our well-known remedies without waiting for them to be revealed to us by the investigation of some highly vaunted synthetic which contains their active principle.

PHENOL SODIQUE (Hance Bros. & White).

Report of Examination by Council on Pharmacy and Chemistry and Comments.

(*From The Journal A. M. A., Nov. 9, 1907, 1617.*)

An examination of this article by a subcommittee of the Council on Pharmacy and Chemistry revealed unscrupulous claims which are a positive menace to public health. In view of this the Council has directed the publication of the following comments. W. A. PUCKNER, Secretary.

COMMENTS.

Phenol Sodique was not submitted to the Council by the manufacturers, but was taken up because it is advertised to both physicians and the public. Some advertisements state: "Phenol Sodique was the standard antiseptic thirty years ago. It's the same to-day." If this were true, it would be high time to call a halt; for the unscrupulous claims made for this nostrum, and the effrontery with which they are pushed, are only rivaled by those of the most shameless "patent medicines."

The firm of Hance Bros. & White poses as a reputable pharmaceutical manufacturing house, but how it can reconcile this position with the methods of exploiting this product passes all understanding. In the original package of Phenol Sodique (the latest was purchased on June 20, 1907), there are little booklets and a folder describing the marvelous properties of the nostrum. The booklets do not refer to Phenol Sodique, but they are very instructive. They are entitled: "Dyspepsia," "Worm News," and "Catarrh," advertising "Dyspepsia Stop"—some form of dyspepsia tablets, a remedy for round worms, and "Catarrh Stop," apparently some mild antiseptic tablets. These booklets are addressed frankly to the laity, although recourse to a physician is, generously, advised if the patient does not respond to treatment! The

folly of prescribing "original packages" which contain popular literature has been so often emphasized that further comment seems superfluous. The following from "Catarrh," however, throws an interesting sidelight on the scientific status of Hance Bros. & White:

> "Catarrh is due to a minute insect in the inner lining membrane of the nose. This insect multiplies rapidly, and, unless checked and destroyed, will produce the worst results."

To return, however, to Phenol Sodique: The folder is also evidently intended for the lay public rather than for physicians; at least, if we are to credit Hance Bros. & White with any intelligence whatsoever. It is headed: "Montyon Prize of Encouragement, Awarded by the Institute of France, 1861." This is rather ancient, but what follows indicates that a little restraint would have been better than encouragement. The circular is a compact treatise on self-medication—apparently all that is necessary to retain or regain health is the use of Phenol Sodique, externally and internally. The following conditions are among those specifically named as amenable to this remedy: Smallpox, measles, scarlatina, erysipelas, puerperal fever, typhoid fever, cholera, diarrhea, cramps, burns and scalds, bites, cuts and wounds, excoriations, chilblains, chaps, sore throat, scratches, catarrh, tetter, sunburn, swollen veins, ulcers, hemorrhages, bruises, piles, gangrene, carbuncle, itching, insect stings, ivy poison, cold in the head, bunions, inflamed eyes, eczema, ringworm, rheumatism, pains, toothache, seat worms, etc.—besides numerous diseases of animals.

No antiseptic, whatever its composition, could by any possibility accomplish anything like what is claimed for Phenol Sodique, so that the composition of the article is really of little importance. This is evidently appreciated by the manufacturers, for they have kept the composition a profound secret, except in so far as it is implied in the name. An inquiry addressed to Hance Bros. & White, under date of April 27, 1907, six months ago, has remained unanswered. The Council, therefore, directed an analysis of Phenol Sodique. This was carried out at the chemical laboratory of the American Medical Association, and a check analysis was made by an independent firm of chemists.

This shows that Phenol-Sodique contains something like 0.5 or 0.66 per cent. of phenols, dissolved in about 0.75 per cent. of sodium hydroxid. In other words, it appears to be essentially a very dilute alkaline solution of some impure coal-tar product, presumably of crude carbolic acid. The analysis could not profitably be carried further, because the amount of the antiseptic agent is so very small.

The consideration of this analysis, in connection with the claims made for Phenol Sodique, leaves little doubt as to one reason for the secrecy concerning its composition; although no educated physician could be deceived into believing for a moment that Phenol Sodique could fulfill the promises of its promoters, even if it were "the best antiseptic, hemostatic and disinfectant on the market," as the manufacturers say in their advertisements.

From its composition, it can only have the very moderate and ordinary antiseptic qualities of a dilute phenol or cresol solution, modified only to a very slight extent by the free alkali. According to the manufacturers, however, "Phenol Sodique is a wonderful preparation." Just how wonderful appears from these extracts from the dissertations in the pamphlet which is enclosed in the package. Note particularly the matter which we have put in capitals:

Catarrh, Old Colds, etc.: Drink every morning and evening a glass of water containing ten to thirty drops of Phenol Sodique. . . .

"*SMALLPOX: TO PREVENT ATTACK* take internally three or four times a day, fifteen or twenty drops of Phenol Sodique in one tablespoonful of sugar and water. . . .

"*Measles, Scarlatina and Erysipelas:* Same treatment as for Smallpox.

"*TYPHOID FEVER: TO PREVENT ATTACK* take internally three or four times a day, fifteen or twenty drops of Phenol Sodique.

"*CHOLERA: TO PREVENT* spread sawdust or sand wet with Phenol Sodique, in apartments.

"*THE VERY BEST PRECAUTION* is to drink, morning and evening, a glass of water containing from fifteen to thirty drops of Phenol Sodique. . . .

" . . . *Premonitory Diarrhea:* . . . Drink a teaspoonful of Phenol Sodique diluted in an ounce of water. . . . "

This is the kind of therapeutics and prophylaxis taught to the medical profession by their self-appointed instructors, the proprietors!

But this matter has a serious, as well as a ludicrous, side: What is the proper epithet to apply to those who, knowingly and intentionally, impress on the ignorant lay public that one can with impunity expose himself to smallpox, cholera, typhoid or scarlet fever, or measles, by taking a few drops of very dilute carbolic acid, or by sprinkling a little on sawdust? What must be the consequences to those who trust in these assurances? And what should be the lawful penalty for those

whose blunted moral instincts permit them wilfully to endanger the lives of others for a little financial gain? It would be interesting to know the real opinion of the responsible members of the firm of Hance Bros. & White on these questions.

The Montyon Prize was awarded by the French Institute in 1861—forty-six years ago—how many victims a year?

SULPHO-LYTHIN.

(*Abstracted from The Journal A. M. A., Dec. 8, 1906, 1931.*)

The following report was submitted to the Council by the subcommittee which examined Sulpho-Lythin:

To the Council on Pharmacy and Chemistry:—The following report on Sulpho-Lythin is herewith submitted:

Sulpho-Lythin is sold by the Laine Chemical Company, New York. In the literature sent to physicians it is said: "This product, the sulpho-phosphite of sodium and lithium (non-effervescent), is entirely new and is unique in its action."

Chemical analysis of a specimen of Sulpho-Lythin purchased in the open market indicated its composition to be:

Sodium sulphate, anhydrous	10.51
Disodium hydrogen phosphate, anhydrous	56.67
Sodium thiosulphate, anhydrous	20.78
Sodium chlorid	5.98
Lithium, as citrate	3.12
Sulphur, free	0.16
Moisture	1.53
Loss	1.25

The examination, therefore, shows that Sulpho-Lythin is a mixture consisting mainly of sodium sulphate and sodium phosphate and sodium thiosulphate. The statement that it is a "sulpho-phosphite of sodium and lithium," therefore, is not correct, and a statement that "it is entirely new and unique in its action" appears unwarranted and misleading. It is, therefore, recommended that the preparation be refused recognition. It is also recommended that an article be prepared for publication calling attention to the exaggerated claims made for Sulpho-Lythin.

The recommendations of the subcommittee were adopted by the Council and in accordance therewith the report is published, with the following comments.

W. A. PUCKNER, Secretary.

According to the above analysis, this wonderful new remedy, "which surgeons of this city (New York) have used . . . after laparotomies . . . with excellent results" is simply a mixture of well-known salts obtainable in any drug store, and which any third-year student knows how to prescribe and even to compound.

Sodium sulphate in the crystallized form is commonly known as Glauber's salts; disodium hydrogen phosphate is ordinary, common, every-day sodium phosphate. We presume every physician knows what Glauber's salts are good for, and that phosphate of soda is an excellent saline laxative, although it has not been known before that it possesses antiseptic properties. Sodium thiosulphate is familiar to physicians as sodium hyposulphite, and to photographers as "hypo," while every one knows, of course, that sodium chlorid is common salt.

Examinations and analysis of various specimens of this product demonstrated that its composition is not always the same. Thus analysis of one specimen indicated only 5.12 per cent. of anhydrous sodium sulphate instead of more than 10 per cent. in the first specimen; also this specimen contained 10.46 per cent. of water instead of 1.53 per cent. Apparently, therefore, the manufacturers are not competent to prepare a product of constant composition. Or is it simply that they do not care to do so and believe that anything is good enough for the doctor? That the first is the more probable cause is indicated by the report of one chemist which calls attention to the fact that different portions taken from the same bottle differed widely in composition. The following is taken from his report:

> The analysis shows Sulpho-Lythin is not a definite chemical compound, but a mixture of sodium phosphate, sodium thiosulphate and some compound of lithium. That it is only a mixture is shown by the fact that in the examination for thiosulphate when the substance was examined without first being thoroughly mixed, results were obtained varying from approximately 27 per cent. in the first portions taken from a bottle, to 42 per cent. in the last portions of the same bottle.

As a further sign of the ignorance and incompetence of the promoters of this nostrum it is interesting to note that the label on one of the bottles purchased states that it is a "sulphophosphate" instead of a sulphophosphite. Apparently the gentlemen who presume to instruct us in regard to this remedy do not know the difference between a phosphite and a phosphate. Or do they know the difference, but feel perfectly safe that in our own ignorance we will not note such contradictions?

The attempt to make a "true hepatic stimulant, antizymotic and uric acid eliminant," all in one, out of simple laxative salts, is surely bold enough to excite one's admiration, even if it does not inspire one's faith. Certainly those who have the brazen assurance to offer a combination to physicians

as a new and valuable remedy must have a pretty high opinion of the intelligence and of the credulity of that profession. Some occult and wonderful skill must be used in mixing Glauber's salts, phosphate of soda, etc., to produce a medicine which will do the wonderful things claimed for Sulpho-Lythin by its promoters.

WONDERFUL VIRTUES OF THE NEW COMPOUND.

According to one circular, this simple mixture of salts is a great remedy for:

> Disorders of the Liver, Inflammation of the Gall Bladder and Bile Ducts, Acute Congestion of the Liver, Gall Stones, Intestinal Indigestion, Chronic Constipation, Rheumatic and Gouty Conditions, Diabetes, Nephritis, Acute or Chronic, Bright's Disease, Genito-Urinary Diseases, Miasmatic (Malarial) Fevers, Skin Eruptions, Corpulency or Obesity, Convalescence from Alcoholism and the Treatment of Drug Habits.

In another circular we read:

> "It is not itself a cathartic or even a laxative, but catharsis results from its administration because of the bile that is poured out into the intestinal tract, and the sulphur liberated by its decomposition."
>
> "Sulpho-Lythin is absorbed and passes into the circulation, where it exerts an antifermentative and antitoxic action, restoring and preserving normal alkalinity of the blood and preventing or counteracting septic processes throughout the body. It is also a *solvent for uric acid.*"
>
> "Sulpho-Lythin acts also on the skin, stimulating the perspiratory glands and removing discolorations and eruptions on its surface."
>
> "Sulpho-Lythin is particularly effective in all forms of derangements of the liver, because it is one of the very few hepatic stimulants, which increases the secretion of bile and causes it to be discharged into the bowels."
>
> "In the preparation of patients for surgical operations, Sulpho-Lythin is especially valuable because it restores and preserves the normal functional activity of the liver, bowels, kidneys and skin, and places the patient in the best possible condition to withstand the shock of the operation and to recuperate therefrom. . . . The length of time required for efficient preparation will depend on the character of the operation and the condition of the individual patients when they come under observation. As a rule, Sulpho-Lythin should be administered for one, two or three weeks prior to the operation to obtain the best result."

What need for universities to erect laboratories for the prosecution of laborious animal experiments in search of biliary stimulants when the discovery has already been made in a New York office building?

Our distinguished surgeons are no doubt proud to honor American commercial enterprise by sitting at the feet of progressive "chemical" (?) companies to receive instruction regarding the manner in which they should prepare their patients for operation.

NOT ADVERTISED TO THE PUBLIC.

This nostrum is not advertised to the public. Oh, no! It is put up solely for physicians' use (*sic*). But the physician is repeatedly advised in the advertisements to "order always an original (6 ounce) bottle to prevent substitution." 'Twas ever thus. The physician prescribes as ordered and then wonders why his patients buy "patent medicines." The patient, in this instance, gets plenty of advice as to the use to which he can put the nostrum. "An original (6 ounce) bottle to prevent substitution" has labels on three sides of the bottle.

On one side the patient reads that Sulpho-Lythin is a "true hepatic stimulant, antizymotic, uric acid solvent and eliminant."

On side No. 2 he learns that it is indicated in: "Disorders of the liver, intestinal indigestion, chronic constipation, inflammations of the gall bladder and bile ducts, gallstones, jaundice, rheumatic and gouty conditions, uric acid diathesis, diabetes, albuminuria, malarial fevers, skin eruptions, corpulency, preparation of patients for surgical operations and convalescence therefrom, convalescence from alcoholism and drug habits."

Label No. 3 tells the patient how to use it.

In the language of a wise man, "What fools we mortals be." We not only allow adventurers to humbug us, but we permit ourselves to be used as agents to humbug the trusting layman.

THE EXPLOITERS OF THE STUFF.

And now, who and what is this Laine Chemical Company? Is it a regular pharmaceutical or chemical company engaged in the business of manufacturing drugs and chemicals? If so, where is its manufacturing establishment and its laboratory? One of the phases connected with this proprietary medicine business is that many of these preparations are foisted on our profession by promoters who have gone into the business as they would go into the business of humbugging people with a "patent medicine," into a scheme for exploiting stock in a salted mine, or into any other get-rich-quick scheme. This is not a reckless statement on our part; we have plenty of evidence to prove it, and we believe that physicians can verify it if they will make a little inquiry into the standing and character of some of the so-called "chemical" or "pharmacal"

"companies" whose preparations they have been deluded into prescribing. We can not swear whether or not the Laine Chemical Company is of this character. We have been trying to find out. From one source we learn that the "business was started nearly two years ago for the purpose of putting up a proprietary remedy, but nothing was known in the trade as to the individuals composing the firm. After being in business for some time the firm was incorporated, the certificate of incorporation being dated Albany, N. Y., Jan. 29, 1906. The names given in the certificate were A. C. Aubrey, W. L. Clark and W. L. Sohl." Our informant said that apparently W. L. Sohl was the secretary and manager, but that nothing definite could be learned.

Not having received any satisfactory information from the sources tried, we asked Dr. Robert A. Hatcher, professor of pharmacology in Cornell University Medical School, to make a personal investigation and to learn, if possible, what kind of a concern it is. Under date of July 25 Professor Hatcher reports that:

> He went to the office of the Laine Chemical Co., Room 25, 83 Fulton St., an office building, and found the company domiciled in a small room, in which were three girls typewriting. There were also advertising circulars, a number of bottles in a case, and a few cases marked for shipment. There was also present a man, apparently about 35 years of age, in charge. Professor Hatcher could get no information whatever from him nor from any other source that was satisfactory. From what he was able to find out, however, it would seem that the company is made up of men who know nothing whatever about pharmacy, chemistry or medicine; that the business of this "chemical company" is selling to physicians the nostrum sulpholythin.

After reviewing Professor Hatcher's report the Laine Chemical Company was requested to furnish the following information:

> "1. Who are the members of the firm, or corporation, known as the Laine Chemical Co.?
>
> "2. Is either of the members of this firm, or corporation, a registered pharmacist, a chemist, or a physician?
>
> "3. What, if any, other preparation does the Laine Chemical Co. manufacture or sell?
>
> "4. Is the 'Sulpho-Lythin' made by the Laine Chemical Co.? If so, where is the laboratory or factory? Please give street and number.
>
> "5. Is 'Sulpho-Lythin' a definite chemical compound, or a mixture? If a chemical compound, what is its chemical formula? If a mixture, what are the ingredients, and

the proportion of each ingredient to a given amount of the produce?"

When we wrote the above letter we were aware that it was a presumptuous thing to do, but nevertheless the information asked for would be willingly furnished by any legitimate pharmaceutical house, and, for that matter, by any business concern, no matter what the business might be. Some might object to furnishing the names of all persons connected financially with the firm, but none would object to giving the names of those in direct and responsible charge. However, in a few days the following letter was received:

"NEW YORK, Aug. 21, 1906.

"*Dear Doctor:*—The officers of our company are at present absent on their vacation and immediately on their return we will send you a full reply to your communication under date of August 17.

"Trusting that this is satisfactory, we are, yours very truly, LAINE CHEMICAL CO."

After waiting nearly three months—a rather long vacation for the officers to take—the following communication was received:

"NEW YORK, Nov. 9, 1906.

"*Dear Doctor:*—Reverting to your communication of August 17, receipt of which was acknowledged under date of August 21, we will state that the Laine Chemical Co. is a corporation, incorporated under the laws of the State of New York; that Sulpho-Lythin, exploited to the medical profession exclusively, is the only product now manufactured by the Laine Chemical Co.; that Sulpho-Lythin is manufactured under the immediate supervision of the Laine Chemical Co. by a regular graduate in pharmacy, and that the active constituents of Sulpho-Lythin are combined in a Sulpho-Phosphate of Lithium and Sodium.

Very truly yours, LAINE CHEMICAL CO."

It looks as though each of the above letters is signed by the same individual, and the writing bears a similarity to that of W. S. Sohl; at least, his signatures to the letters which were written to physicians and druggists and forwarded by them to us, bear an extremely marked similarity to the writing of one who signed the letters quoted, all of which make it appear that "the officers of our company" were taking their vacation in the City of New York. It will be noted that the important questions in our letter of August 17 were not answered.

Possibly we ought to apologize for devoting so much space to such an insignificant nostrum. If any apology is necessary, we offer the following:

Sulpho-Lythin literature carries testimonials written by men of influence and standing in the profession—not many, happily—and it is advertised in medical journals supported—only in part, it must be admitted—by educated and thoughtful members of our profession.

Sulpho-Lythin is a sample of hundreds—shall we say thousands?—of so-called "ethical proprietaries" that are being used by physicians; it is no worse and no better than most of the others. It illustrates beautifully various phases of the "ethical proprietary." They are not made under responsible and intelligent supervision. The vast majority of them are made, or at least sold (for not a few have their preparations made for them by others, as do many of the "patent medicine" vendors), by men who have absolutely no knowledge of drugs or of medicine, but who not only presume to sell medicines of their own compoundings, but also to arrogate to themselves the right to tell physicians how to treat their patients, advice which every physician with any self-respect would scorn to accept, did he know who gave it.

Most of these preparations are simple mixtures of well-known drugs that physicians are prescribing every day, and which require as much skill in compounding as can be found in a drug-store bottle washer.

But granting that some of these mixtures may possess good qualities and be convenient, their secret nature and the irresponsiblity of their makers give the physician no guarantee that their composition will remain uniform, and that the materials used will be of good quality. If these preparations are to be used, it is evident that some control is necessary by some authority acting in the interests of the medical profession. It ought to be evident by this time that the Council on Pharmacy and Chemistry had an important mission to perform, and that such a body was created none too soon.

TYREE'S ANTISEPTIC POWDER.

Report of the Council on Pharmacy and Chemistry and Some Comments Thereon.

(*From The Journal A. M. A., Oct. 20, 1906, 1316.*)

Tyree's antiseptic powder was assigned for examination to a subcommittee of the Council, which made the following report:

To the Council on Pharmacy and Chemistry:—Your subcommittee, to whom was assigned Tyree's Pulv. Antiseptic Comp., marketed by J. S. Tyree, Washington, D. C., reports as follows:

The label on the package states: "This preparation is a scientific combination of borate of sodium, alumen, carbolic acid, glycerin and the crystallized principles of thyme, eucalyptus, gaultheria and mentha, in the form of a powder," etc.

The statement that the powder contains the crystalline principles of thyme, eucalyptus, gaultheria and mentha is vague and misleading, since the chief medical constituents of eucalyptus and gaultheria are liquids, but it tends to convey the impression that the powder contains the essential constituents of these drugs, namely, thymol, oil of eucalyptus or eucalyptol, oil of wintergreen, or methyl salicylate, and menthol.

The literature supplied to physicians *claims* its composition to be: "Parts, sod. bor., 50; alumen, 50; ac. carbol., 5; glycerin, 5; the cryst. principles of thyme, 5; eucalyptus, 5; gaultheria, 5, and mentha, 5."

The composition, therefore, might be expressed as follows:

Sodium borate (borax)	50 parts, or	38.46 per cent.
Alum	50 parts, or	38.46 per cent.
Phenol (carbolic acid)	5 parts, or	3.85 per cent.
Glycerin	5 parts, or	3.85 per cent.
Thymol	5 parts, or	3.85 per cent.
Oil of eucalyptus or eucalyptol	5 parts, or	3.85 per cent.
Oil of gaultheria (or methyl salicylate)	5 parts, or	3.85 per cent.
Menthol	5 parts, or	3.85 per cent.

Analysis of specimens purchased from different sources in the open market were made under our direction. The reports of the chemists show that Tyree's antiseptic powder contains no borax, or mere traces only, and that it contains no alum, or mere traces only. Instead, the analyses show that boric acid and zinc sulphate are the essential constituents. The amounts of carbolic acid, thymol, menthol, etc., contained in the powder, if present, were far below the quantities indicated by the formula. The presence of glycerin could not be demonstrated, and, if present, the amount must be very small.

One chemist reports:

> The result of analysis shows that different samples differ slightly in composition, but that the following indicates the average composition of the product:

	Per cent.
Zinc sulphate, anhydrous	15.56
Boric acid	81.26
Volatile matter at 100° C. for four hours	0.45

> The undetermined portion consists of salicylic acid, carbolic acid, menthol and eucalyptol; possibly other antiseptic agents may be present in very minute quantities.
>
> From the above findings we conclude that Tyree's antiseptic powder is a mixture of boric acid and dried zinc sulphate and antiseptic bodies, such as menthol, salicylic acid and carbolic acid, eucalyptol, etc. From this it can be readily seen that the label which is supposed to set

forth the composition of Tyree's antiseptic powder is not in accord with the facts. The powder does not contain either borate of sodium or alum, and the presence of glycerin could not be established. The antiseptic agents, exclusive of the boric acid, are present only in small amounts.

The report of another analysis concludes as follows:

It evidently contains less than the amount stated of the principles of thyme, eucalyptus, wintergreen and mint. It also contains a very small amount indeed of carbolic acid, much less than that stated. We have been unable to identify certainly the presence of glycerin, and it is doubtful if it be present.

From the result of the analysis we feel confident that the preparation is to all intents and purposes a mixture of boric acid and sulphate of zinc.

The carbolic acid, thyme, eucalyptus, wintergreen, etc., if present, are present only in sufficient amount to give the compound a satisfactory odor.

In view of the fact that J. S. Tyree has given wide publicity to a formula which the preceding report has shown to be a deliberate misrepresentation of facts, it is recommended that the article be refused recognition by the Council on Pharmacy and Chemistry, and that this report be published in THE JOURNAL of the American Medical Association.

The recommendation of the subcommittee was adopted by the Council in accordance with which the report is published.

W. A. PUCKNER, Secretary.

Mr. Tyree, in a letter to Dr. Simmons (which he states he writes at the request of Dr. Kebler, of the Drug Laboratory of the Department of Agriculture, though he is under no moral or financial obligation to do so), says that it has been his intention to inform the medical profession of his reasons for changing the formula of Tyree's Antiseptic Powder from an alum and borax base to a boracic acid and zinc base. He states that this change was made at the suggestion of prominent physicians connected with hospital clinics on nose and throat, venereal and other conditions and that he has had in contemplation the omission from the label of the various conditions to which the preparation is applicable.

Mr. Tyree, it will be seen, assumes the right to sell to physicians a preparation with a descriptive formula which he acknowledges is false, and that he presumes to use his own pleasure as to the time when he will inform them of its true composition.

Mr. Tyree does not state when he changed the formula. We do not know whether it was a year ago, five years ago or ten years ago, but we do know that the package which was

used in making the first analysis was purchased as early as last February, and the first chemist's report was submitted to the Council March 5, 1906. On April 4 Mr. Tyree was notified by the Council that the composition of "Tyree's Antiseptic Powder" did not correspond with the formula published by him.

Whether or not Mr. Tyree is justified in offering our profession a preparation as composed chiefly of borax and alum when in reality it is chiefly composed of boric acid and zinc sulphate, we leave physicians to judge.

Discrepancies Between Facts and Claims—Unfortunate Attempts of Mr. Tyree at Explanation.

(From The Journal A. M. A., May 18, 1907, 1692.)

A report from the Council on Pharmacy and Chemistry on Tyree's Antiseptic Powder appeared in THE JOURNAL, Oct. 20, 1906. This showed that the preparation, advertised as a "scientific combination of borate of sodium, alumen, carbolic acid, glycerin and the crystallized principles of thyme, eucalyptus, gaultheria and mentha, in the form of a powder," was essentially a mixture of boric acid and sulphate of zinc—approximately four-fifths of the former to one-fifth of the latter. "The carbolic acid, thyme, eucalyptus, wintergreen, etc., if present, are present only in sufficient amount to give the compound a satisfactory odor." As will be remembered, in the correspondence published at that time, Mr. Tyree attempted to explain the discrepancies between his statements and the proven facts by intimating that he had recently changed the formula, and that it was his intention "on or about the first of February to state to the medical profession his reasons for changing the formula," and that the change had been made "a short time ago, at the suggestion of several prominent gentlemen." Since that time, through circulars and other advertisements, Mr. Tyree has attempted to explain the matter in various ways. In his latest circular letter he seems to make a deliberate attempt to mislead our profession and to misrepresent facts to a degree that makes it almost impossible to believe that the circular came from a man who claims to be honorable.

First, however, we shall take this opportunity to publish some matter which we have had in reserve since the first exposé was made last October. When it was realized that Mr. Tyree intended to defend himself by claiming that a change had recently been made in the powder, we took occasion to try to secure some of the preparation that had been on the market for a long time. In this we succeeded very

well. From a Chicago druggist one package was bought which had been in the store at least since July, 1902—how much longer is not known. The druggist from whom the powder was obtained bought the drug store in July, 1902, and this powder was on hand at that time, none having been bought since. This particular powder was analyzed by a chemist, who found the composition practically the same as that given in the Council's report, this chemist estimating that it contained approximately 81 per cent. boric acid and 14 per cent. anhydrous zinc sulphate. Bearing in mind that for at least four years and ten months Tyree's Powder has been essentially the same as it is to-day, this letter is very interesting: (The comments in brackets are, of course, ours.)

"J. S. TYREE,
"CHEMIST,
"WASHINGTON, D. C.

"April 16, 1907.

"Dr. ——— ———,
"_____,

"*My Dear Sir:*—Doctors and medical publications of extreme and prejudicial minds often hold and express opinions in honorable faith, but like all critics, they are not always familiar with the conditions composing their opinions, and are often given to expressing them without complete knowledge of the true motives and facts in the case.

"If you will read an article that appeared in one of the medical weeklies some time ago [THE JOURNAL of the American Medical Association, of course] and which has been copied by several of its offsprings, [not many we regret to say] relating to Tyree's Antiseptic Powder, you will see that I had previously informed the editor as well as his council of investigators, that at the suggestion of prominent physicians, extensive clinical experimenting [sic] were being made with some slight [! ! !] changes in my powder, the object being to develop and extend its usefulness in new lines. [It had already been recommended for about everything.[1]] and at the same time make it more acceptable to the general run of the profession. I also notified this editor that these investigations

1. From the circular accompanying a package bought over a year ago, we find the powder recommended for the following conditions: "For Leucorrhea, Gonorrhea, Vaginitis, Pruritus, Ulcerated conditions of the mucous membrane. . . . Scrofulous, Syphilitic and Varicose Ulcers, . . . for Spraying the Nose and Throat, . . . for immediate deodorizing and disinfecting . . . for prickly heat, poison oak, squamous eczema and other conditions of similar nature. . . . As a deodorant and prophylactic in dental work, . . . for disinfecting offensive cavities, . . . for profuse and offensive perspiration, swelling, soreness and burning of the body and feet. . . . As a delightful toilet preparation after the bath and shaving."

would not be completed until the first of the present year, after which time these slight [! ! !] changes in the formula of Tyree's Powder would be announced. [It is now the middle of May; when and where were the changes announced?[2]]

"There is nothing new, startling or dangerous in such changes in formulas. The Pharmacopeias and national books of authority are continuously improving their formulas. It is the same with every preparation on the market. [Mr. Tyree, as a nostrum maker, is in a position to know. His plea evidently is: "I am no worse than others."] The apparent difficulty in my case is caused by my exceptional frankness ["exceptional frankness" is good under the circumstances] with the profession in telling them [when and where?] about this improvement before I was ready to announce full details and particulars, or place my improved [sic] powder on the market. Yours very truly,

"J. S. TYREE."

For years Mr. Tyree has been misleading physicians by making false statements regarding the composition of his powder and regarding its value as a therapeutic agent. When exposed he tries to defend himself and his business by statements and excuses that are worthy of a schoolboy trying to get out of a bad scrape. We would respectfully suggest to him that he either take his wonderful powder off the market, or—which would probably amount to the same thing—tell the truth, and the whole truth, about it.

URON AND THIALION.

Report of the Council on Pharmacy and Chemistry.

(From The Journal A. M. A., Nov. 3, 1906, 1500.)

The following reports were submitted to the Council by subcommittees which examined Uron (Uron Chemical Company) and Thialion (Vass Chemical Company):

To the Council on Pharmacy and Chemistry:—The following report on Uron is herewith submitted:

Uron is sold by the "Uron Chemical Co., Box A, St. Louis, Mo." In the literature distributed to physicians and in advertisements appearing in current medical journals $LiC_{13}H_7N_4O_2$ is given as the chemical formula of Uron.

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2. Last January the national Food and Drugs Act went into effect: one of its provisions is that the label must not lie. This is not the exact verbiage, but it means the same thing. So, instead of repeating the old false statements, the new label of Tyree's antiseptic powder contains nothing whatever about the composition—the law does not require that it should—unless the preparation contains certain specified drugs. Why is the formula omitted?

According to analyses, this article is not a chemical compound, but is a mixture of lithium benzoate and hexamethylenamin[1] in approximately the following proportions:

Lithium benzoate	58 per cent.
Hexamethylenamin	42 per cent.

It is recommended that Uron be refused recognition and that this report be published.

To the Council on Pharmacy and Chemistry:—We beg leave to report on Thialion as follows:

Thialion is sold by the Vass Chemical Co., Danbury, Conn. In the literature supplied to physicians and in the advertisements in medical journals, Thialion is stated to be "a laxative salt of lithia" with the chemical formula "$3Li_2O.NaO.SO_3,7HO$." Sodio-trilithic anhydrosulphate" is given as a synonym. An elaborate graphic or structural formula is also given.

According to analyses, this preparation is a mixture consisting chiefly of sodium sulphate and sodium citrate with very small amounts of lithium, the average of several estimations indicating the following composition:

Sodium citrate	58.6
Sodium sulphate, anhydrous	26.6
Sodium chlorid	3.3
Lithium citrate, anhydrous	1.8
Water	9.7

Thus, the advertising literature is a deliberate misrepresentation of the facts. It is, therefore, recommended that the preparation be refused recognition, and that this report be published.

The recommendations of the subcommittees were adopted by the Council and in accordance therewith the above reports are published. W. A. PUCKNER, Secretary.

In publishing the above report, the Council is presenting to the medical profession another object lesson, and one that illustrates how easily our profession is being humbugged. There are several things that we may learn from the report on these two nostrums, but at this time we will take up only one phase of the lesson. Many of the scientific chemical compounds and derivatives given us by the German chemists have been distinct advancements and have proved to be valuable additions to our therapeutic agents; further, they were received with so much favor by physicians that they have been profitable for those who made them. It is not strange, therefore, that imitators should appear. One of the first was our old friend, Antikamnia (which was introduced as a "new synthet-

1. We once more remind our readers that hexamethylenamine is the absurdly long but official name for the article that is sold under the proprietary names: Urotropin, Formin, Cystogen, Aminoform, Hexamin, Uritone, etc.

ical" compound). This was followed by Ammonol, Phenalgin, Salacetin, and a host of others having acetanilid as their principal ingredient.

But there are hundreds of other so-called "new chemical" compounds among the "ethical" proprietaries on the market aside from the acetanilid mixtures. These wonderful compounds, by the mysterious union of their ingredients, possess therapeutic properties different from, or more powerful for good than the drugs from which they are made. At least, this is what we are told, and this is what many believe or they would not sell so well.

There is another factor worth noting connected with this subject: When to the claim that the mixture is a "chemical compound" is added a complex chemical formula, it prevents the impertinent question, "What is it?" or isn't the "formula" there, and is not the information given without the asking? Most of us have been so overcome by the display of the chemical knowledge of the nostrum maker that we have been afraid to expose our ignorance by asking for information or explanation. And thus the promoter avoids perplexing questions, which, if answered truthfully, would spell bankruptcy.

URON.

The Uron Chemical Company informs us, concerning Uron, that it has the chemical formula of $LiC_{13}H_7N_4O_2$. Now this formula looks very dignified and scientific to those who are not up in chemistry. To the chemist, however, the formula signifies nothing. A few simple tests reveal the composition of the mixture, and it is surmised that the "formula" is the result of an attempt to combine the formulas of the two ingredients, i. e., $LiC_7H_5O_2$ and $C_6H_{12}N_4$, the addition being faulty.

THIALION.

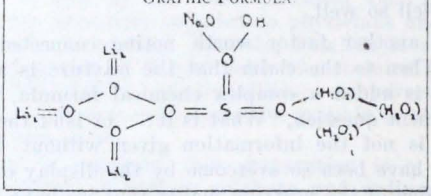
In regard to Thialion, the formula furnished by the Vass Chemical Company is even worse. To a physician who possesses but little knowledge of chemistry, it will seem impressive, and he may absorb the idea that it stands for a preparation that is the result of exhaustive scientific research. To the chemist, this formula will appear as a jumble of symbols and numbers that mean nothing.

It is not worth while to call attention to the simplicity of this simple mixture of ordinary salts, for it is too self-evident. As to the remarkable therapeutic qualities of Thialion, the reader is referred to that ably edited "scientific" periodical, the *Uric Acid Monthly*, and to the mass of "literature" relating to this wonderful remedy.

While there is a ridiculous side to this business, there is also a serious one. Those who have been making money out of us undoubtedly laugh in their sleeves at our gullibility, but to us as members of a presumably learned and intelligent profession, it is not a laughing matter. The whole nostrum business is a shame and a disgrace.

CHEMICAL FORMULA: $3Li_2O.\ NaO,\ SO_3.\ 7HO$ (*Sodio-trilithic anhydrosulphate*).

GRAPHIC FORMULA:



This picturesque "graphic formula" for Thialion appears with many of the advertisements. To most of us it looks formidable, wonderfully and deeply scientific and non-understandable; to a chemist it looks absurd.

VIN MARIANI.

Report by Council on Pharmacy and Chemistry—With Comments Thereon.

(*From The Journal A. M. A., Nov. 26, 1906, 1751.*)

This preparation was assigned to a subcommittee of the Council and the following is an abstract of the report of the committee:

Samples of Vin Mariani and of the literature distributed by the manufacturers were examined.

It appears that the beverage or medicine known as "Vin Mariani" is a preparation of red wine, apparently imported from Bordeaux, and fortified, in this country, by an alcoholic preparation of coca leaves or other parts of the coca plant.

The committee considered first, the character of the red wine as imported. A sample received from the port of New York, March 10, 1905, from Henry Clausel & Co., Bordeaux, and consigned to Mariani & Co., on analysis was found to have the following composition:

Specific gravity		0.9959
Alcohol by volume	per cent.	10.00
Extract	per cent.	2.279
Volatile acids	per cent.	0.0914
Ash	per cent.	0.2801
Reducing sugar		trace.
Pol. direct	degrees	—0.8
Pol. invert.	degrees	—0.7
K_2SO_4	Mg. per liter	0.092

MARIANI WINE

4/- PER BOTTLE. 45/- PER DOZEN.

MARIANI WINE possesses truly remarkable **Sustaining, Stimulating** and invigorating powers. Its success and merits are appreciated by all who have tried it, and numberless are the testimonials received from members of all classes of society and professions suffering from

GENERAL DEBILITY,

DEPRESSION, LASSITUDE, EXHAUSTION AND

WANT OF ENERGY.

As a **restorative** and **stimulant** of the highest order. MARIANI WINE is without rival; its high medicinal value has caused it to be recognised and

RECOMMENDED BY 8,500 PHYSICIANS

Before and After

THE BEST AND SUREST TONIC ✱ RESTORATIVE

Delivered free from Wilcox. 49. Haymarket. S.W.. or of all Chemists and Stores.

[The above is the first page of a four-page circular accompanying the bottle of Vin Mariana as sold direct to the public in England.]

A sample of Vin Mariani, as bought in the open market in an original package, has also been analyzed and found to have the following composition:

Specific gravity		1.0125
Alcohol by volume	per cent.	16.15
Extract	per cent.	8.602
Ash	per cent.	0.277
Glycerin	per cent.	0.444
Volatile acids	per cent.	0.0747
Tartaric acid	per cent.	0.2400
Alkaloids (coca bases)	per cent.	0.0250
Cane sugar	per cent.	2.35
Reducing sugar	per cent.	3.38

The increased alcoholic strength of Vin Mariani over the Bordeaux wine, from which it is made, as shown by this analysis, doubtless comes from the alcohol extract containing the coca bases, as already stated. Approximately 6 per cent. of sugar is also added to the wine. Judging from the analysis, therefore, Vin Mariani corresponds to a mixture of an alcoholic preparation of coca leaves and ordinary Bordeaux red wine, with the addition of about 6 per cent. of sugar.

Vin Mariani conflicts with Rule 5, which requires that "No article will be admitted or retained, concerning which the manufacturer or his agents make misleading statements as to geographical source, raw material from which made, or method of collection, or preparation," by stating in the advertising literature that: "The United States government, under the Pure Food Law of March 3, 1903, further emphasizes all previous analyses of Vin Mariani by admitting Mariani's wine as absolutely pure and unadulterated."

Whatever may have been the intent of the above statement, its effect is to deceive. The conjunction of the terms "Vin Mariani" and "Mariani's wine" can only be construed as meaning the same thing. Inasmuch as it does not appear that Vin Mariani is imported into this country, it would not have been possible for the United States government to inspect it, and as to the wine obtained from Henry Clausel & Co., from Bordeaux, it is not in any sense Mariani's wine except that of ownership. It is the opinion of the committee that this phrase can only result in deception and the construction of the language strongly favors the supposition that it is intentionally meant to deceive.

This false claim is practically repeated in the other pamphlets published by the Vin Mariani Company, although not always in the same words.

This preparation also conflicts with Rule 6, which states that "No article will be admitted or retained of which the manufacturer or his agents make unwarranted, exaggerated or misleading statements as to therapeutic value," in that the firm's letter-heads have printed on them the following:

"Vin Mariani purifies the blood stream, strengthens the circulation, stimulates muscular fiber and nerve tissue, is a respiratory stimulant, strengthens the heart muscles, and is an emergency food in the absence of all other nutriment. Successfully employed as an adjuvant in anemia, debility, diseases of the chest, nervous troubles, muscular or mental overstrain, neurasthenia, and allied conditions, and in certain cases of protracted convalescence."

The committee believes that Vin Mariana is intended as a beverage rather than as a medicine.

The report concludes:

"The committee recommends, therefore, that Vin Mariani be refused recognition and that this report be published in full or in part."

In accordance with this recommendation the above extract of the report is herewith published.

W. A. PUCKNER, Secretary.

VIN MARIANI MADE IN THIS COUNTRY.

According to the above report, Vin Mariani as imported is simply an ordinary cheap French wine, the preparation sold in this country as Vin Mariani being compounded in this country. Yet the advertising literature, the label on the bottle, etc., state directly or indirectly that it is a French preparation. Until recently—presumably until the vendors realized that the truth regarding this point would come out—the advertisements in medical journals contained an analysis made by a chemist in Paris. The shape of the bottle, the character of the printed matter accompanying the bottle, etc., are evidently intended to convey the impression that it is imported. So far, then, as this point is concerned, Vin Mariani is sold under gross misrepresentations and is a fraud.

ADVERTISED TO THE PUBLIC.

Vin Mariani was at one time advertised to the public in this country, but, so far as we know, it is not at the present time; at least, not directly. Yet it is most effectively advertised to the public indirectly, and this with little expense to the promoters, the cost of the circular around the bottle being the only expense—doctors who prescribe it do the rest. If those who are in the habit of prescribing Vin Mariani will examine the advertising that goes into the hands of their patients they will realize how true it is that our profession is responsible for much of the "patent-medicine" taking. Few laymen could withstand the temptation to buy the stuff for any ailment that comes along when they read in the circular that this "medicine," which their doctor evidently thinks is a

good thing, is so highly recommended, for all the ills that befall us mortals, by the Pope of Rome, the Czar and the Czarina of Russia, the Queen of England, the Shah of Persia, the King of Norway and Sweden, the Queen of Portugal, the Queen of Saxony, the Crown Prince of Cambodia, Ferdinand of Bulgaria, and by a whole list of ambassadors, generals, politicians, musicians, actresses, etc. The testimonials of these great men and women are enough to convince the most skeptical that this remarkable medicine will do everything but raise the dead—and under favorable circumstances accomplish even this. And still more—it will win battles! Witness this from the governor-general of Madagascar: "We were refreshed by Vin Mariani, and before morning carried the stronghold." Alexandre Dumas and Emile Zola are credited with calling it "the elixir of life." One very strange thing about the testimonials in the circular used in this country is that all are written by foreigners. But Americans (President McKinley—think of it—among others) are honored by having their testimonials quoted in the circulars used on the other side of the Atlantic. Why? Is it possible that the testimonials are fakes?

AN ETHICAL CURE-ALL.

Here are a few of the conditions that the circular says Vin Mariani is good for: "Anemia, winter cough, debility, vocal weakness, la grippe, continued fevers, bronchitis, nervous troubles, muscular weakness, diseases of the aged, malaria, melancholia, overwork, neurasthenia, impotence, malnutrition, depression, heart troubles, wasting diseases, mental overstrain, and in certain cases of protracted convalescence."

The following quotations are taken from blotters—circulated in this country—which are evidently intended for the laity, as well as for physicians:

"Vin Mariani creates and sustains vigor and energy. Guards against wasting diseases. When everything else has failed try it to prove merits."

"Lung, Throat and Stomach Troubles benefited by Vin Mariani; this Ideal French Tonic strengthens entire system of Body, Brain and Nerves."

"Most Efficacious, Most Agreeable, Unequaled by anything in Fortifying, Strengthening, Refreshing."

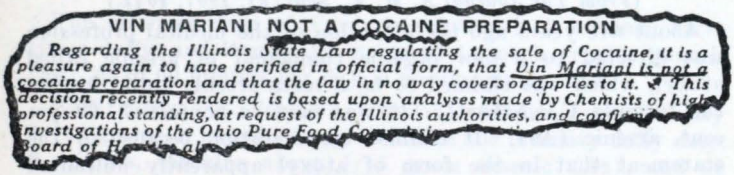
WHY BLAME THE LAYMAN FOR USING NOSTRUMS?

Can we blame the layman for using peruna, wine of cardui, etc., simply because they are advertised, when there are physicians who, for the same reason, prescribe concoctions that are just as quackish and just as useless? And can editors of medical journals consistently find fault with newspapers for

carrying advertisements of fraudulent "patent medicines" when they themselves admit to their pages advertisements of nostrums that are no less fraudulent and of no more value?[1]

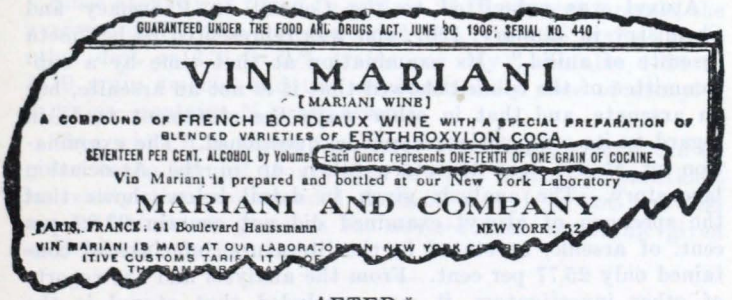
MEMBER OF PROPRIETARY ASSOCIATION.

One word more: There is an organization known as the Proprietary Association of America, but it is usually referred to in common parlance as the "patent-medicine" men's association. It will be remembered that last year we printed a list of the members of this body, among which was the Vin Mariani Company. It will be remembered also that in the list were the names of certain firms who were supplying medicines


VIN MARIANI NOT A COCAINE PREPARATION

Regarding the Illinois State Law regulating the sale of Cocaine, it is a pleasure again to have verified in official form, that Vin Mariani is not a cocaine preparation and that the law in no way covers or applies to it. This decision recently rendered is based upon analyses made by Chemists of high professional standing, at request of the Illinois authorities, and confirm investigations of the Ohio Pure Food Commissi... Board of H...

BEFORE.*


GUARANTEED UNDER THE FOOD AND DRUGS ACT, JUNE 30, 1906; SERIAL NO. 440

VIN MARIANI

[MARIANI WINE]

A COMPOUND OF FRENCH BORDEAUX WINE WITH A SPECIAL PREPARATION OF BLENDED VARIETIES OF ERYTHROXYLON COCA.

SEVENTEEN PER CENT. ALCOHOL by Volume—Each Ounce represents ONE-TENTH OF ONE GRAIN OF COCAINE.

Vin Mariani is prepared and bottled at our New York Laboratory

MARIANI AND COMPANY

PARIS, FRANCE: 41 Boulevard Haussmann NEW YORK: 32

VIN MARIANI IS MADE AT OUR LABORATORY IN NEW YORK ... ITIVE CUSTOMS TARIFF ... OF ...

AFTER.*

* Advertisements of Vin Mariani before and after national Food and Drugs Act went into effect.

to physicians, but practically all these resigned from membership and their resignations were published by us. We have not had the pleasure of publishing the resignation of the Vin Mariani Company. On the contrary, we note that at the last annual meeting of the "patent-medicine" men's association this firm was still an active member, Mr. A. L. Jaros, who stands for the Mariani Company in this country, being one of those registered at the meeting.

PART II.

CONTRIBUTIONS FROM THE CHEMICAL LABORATORY.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION.]

ATOXYL.

W. A. Puckner and A. H. Clark.

(*From The Journal A. M. A., Sept. 21, 1907, 1041.*)

About five years ago the attention of the medical profession was directed to a new organic compound of arsenic called atoxyl, which was claimed to be a meta-arsenic anilid having the formula $C_6H_5NHAsO_2$. It was said to contain 37.69 per cent. arsenic (As). It claimed consideration because of the statement that in the form of atoxyl apparently unlimited amounts of arsenic could be administered without toxic effect.

Atoxyl was submitted to the Council on Pharmacy and Chemistry in January, 1907, and was represented to be "meta arsenite of anilid." Its examination at that time by a subcommittee of the council showed that it is not an arsenite, but an arsenate, and that in other ways the statement made in regard to its composition should be questioned. The examination of atoxyl was therefore taken up in the Association laboratory. The analysis given in detail below shows that the specimen of atoxyl examined did not contain 37.69 per cent. of arsenic, as stated in the literature, but instead contained only 25.77 per cent. From the analysis and the reports of other investigators, it was concluded that atoxyl is the sodium salt of arsenic acid in which one hydroxyl radical of arsenic acid has been replaced by a molecule of anilin. Agreeing with this, the manufacturers now have adopted this formula—i. e., $C_6H_4(NH_2)(AsO.OH.ONa)_2$—as indicating the composition of atoxyl, whereas heretofore they have given the following: $C_6H_5NHAsO_2$. While our analysis indicates that the atoxyl molecule is combined with 3 molecules of water, the results of other chemists make it appear that the water content is variable. It is desirable, therefore, that the amount of arsenic in atoxyl, as found on the market, be controlled from time to time. To facilitate such control, the method of examining atoxyl used by us is published in detail.

Since physicians in using this new compound of arsenic will wish to compare its effect with other arsenic compounds, a

comparison of the dosage of atoxyl with Fowler's solution will be of interest at this time. As atoxyl contains the arsenic as an arsen*ate* while in Fowler's solution it is present as an arsen*ite*, the doses are compared by calculating in each case the weight of the element arsenic itself.

In the advertising literature it is stated for atoxyl that "forty times as much arsenic may be assimilated in this form as when the element is exhibited in Fowler's solution or other of the ordinary arsenical preparations." The average dosage is stated to be from 1/3 to 4/5 grain, given every other day. It is also stated that the dose may be cautiously increased to as much as 3 grains daily.

The ordinary dose of Fowler's solution is 3 minims, three times daily, and it may be increased to much greater quantities; 30 to 60 minims per day is no uncommon dose.

Each minim of Fowler's solution contains approximately 1/133 grains of arsenic (As), therefore the ordinary daily dose, 9 minims, contains about 1/15 grain arsenic (As), and 60 minims contain nearly 1/2 grain of arsenic (As).

Since atoxyl was found to contain 25.77 per cent. arsenic, the average daily dose recommended (1/3 to 4/5 grains every other day, or 1/6 to 2/5 grains per day), contains 1/24 to 1/10 grain arsenic, and the maximum daily dose of atoxyl—3 grains—contains 3/4 grain arsenic.

Thus while it is stated that forty times more arsenic can be given in the form of atoxyl than in other arsenic preparations, in reality the recommended dose of atoxyl is but one and one-half times as great as the advised dose of arsenic given as Fowler's solution.

[Contribution from the Chemical Laboratory of the American Medical Association.]

BURNHAM'S SOLUBLE IODIN.

W. A. Puckner and A. H. Clark.

(*From The Journal A. M. A., March 28, 1908.*)

Burnham's Soluble Iodin, according to the manufacturers, is one of the most noteworthy "discoveries" of the age. The advertisements aim to create an impression that while the product contains iodin, pure and simple, yet by some secret process this element has been so changed as no longer to possess its usual properties. The Burnham Soluble Iodin Company makes such extravagant claims for its product and gives such wide publicity to these claims that it seemed advisable, in the interests of the profession, to determine the nature of the prepa-

ration. Its examination was accordingly taken up in the laboratory of the American Medical Association.

From the analysis,[1] given in detail below, we conclude that Burnham's Soluble Iodin is a solution of iodin in alcohol made miscible with water by the presence of some iodid. Wilbert[2] and other investigators have arrived at practically the same conclusion.

Whatever the secret process, hinted at in the advertisements, by which this preparation is evolved, the fact remains that when one prescribes Burnham's Soluble Iodin, one is prescribing iodin, together with an iodid, the nature of which is hard to determine. The iodid is not present as potassium iodid nor, entirely, at least, as hydrogen iodid (hydriodic acid), but this is of slight importance compared with the fact that it is a solution in alcohol of free iodin and an iodid, and therefore is essentially the same as Lugol's solution.

The amount of iodin found corresponds approximately to 3.0 gm. of free iodin and 2.0 gm. of combined iodin in 100 c.c. of the solution. Lugol's solution contains 5.0 gm. free iodin, and 10.0 gm. potassium iodid in 100 c.c.

BURNHAM'S SOLUBLE IODIN TABLETS.

Burnham's Soluble Iodin Tablets are a light brown compressed tablet, stamped with the letters B. S. I. in mono-

1. ANALYSIS OF BURNHAM'S SOLUBLE IODIN: At different times two specimens were purchased in the open market and examined. In the report they are referred to as Specimen No. 1 and Specimen No. 2. Burnham's Soluble Iodin is a reddish brown liquid, having a slight odor of iodin and is miscible with water in all proportions.

Iodin: The presence of free iodin is shown by the usual starch test and the violet color when extracted with chloroform.

Free Acid: When mixed with water and decolorized with sodium thiosulphate the solution obtained is distinctly acid in reaction. Also, if all iodin is extracted with chloroform the colorless solution which remains is strongly acid in reaction.

Iodids: The colorless acid solution obtained when all free iodin is removed by extracting with chloroform responds to tests for iodids, i. e., gives with silver nitrate a yellow precipitate which is insoluble in nitric acid; on the addition of sulphuric acid followed by ferric chlorid, hydrogen dioxid, potassium permanganate or potassium dichromate, free iodin is liberated.

Glycerin: By evaporating on a water bath, Burnham's Soluble Iodin leaves a thick dark brown residue which is volatile only after prolonged heating. The usual milk of lime method for separation of glycerin failed to demonstrate its presence.

Alcohol: In a portion of Burnham's Soluble Iodin the free iodin was destroyed with sodium thiosulphate, the solution made alkaline with sodium hydroxid and distilled. Ethyl alcohol was detected in the distillate by the iodoform test.

Ethyl Acetate: The solution remaining after the removal of free iodin with sodium thiosulphate has an odor closely resembling ethyl acetate.

gram. Each tablet is said to contain 3 minims Burnham's Soluble Iodin.

The average weight of each tablet was found to be 0.3526 gm.; since Burnham's Soluble Iodin was found to have a specific gravity of .8527 and to contain 4.5 per cent. total iodin, the tablets should contain approximately 2.3 per cent. total iodin, about one-half to two-thirds of which, depending on the condition of the "Soluble Iodin" from which they are made, should be free iodin. Instead of this, only 0.317 per cent. free iodin and 1.57 per cent. total iodin was found. The analysis in detail is given below.[3] It shows that Burnham's Soluble Iodin tablets contain approximately one-fourth the amount of free iodin and approximately two-thirds the amount of total iodin which should be contained therein if, in accordance with the label, each tablet contains 3 minims of Burnham's Soluble Iodin.

COMMENT.

The literature put out by the Burnham Soluble Iodin Company is in itself enough to condemn the products it advertises. The much emphasized statement of the company that

> **"Something had to be done: and Burnham's Soluble Iodin is that which has been done"**

fulfils, in its blatant assertiveness, all the requirements of nostrum advertising. The results of the analyses are not, therefore, a surprise.

Estimation of Free Iodin: A weighed quantity of Burnham's Soluble Iodin was added to 10 c.c. of water and titrated with tenth normal sodium thiosulphate volumetric solution.

Estimation of Total Iodin: (1) A weighed quantity of Burnham's Soluble Iodin was added to a solution of 2 gm. of potassium hydroxid in 10 c.c. of water, evaporated nearly to dryness, a little starch added to facilitate desiccation, the mixture then brought to dryness and ignited. The residue was then extracted with hot water and in this solution the iodin determined as silver iodid. (2) The same procedure as in (1) was used except that in place of precipitating the iodin as silver iodid it was liberated by the addition of hydrochloric acid and ferric chlorid, extracted with chloroform and titrated with tenth normal sodium thiosulphate volumetric solution. (3) Free iodin was reduced to iodid with sulphurous acid and in the clear solution total iodid determined by precipitation as silver iodid. (4) Free iodin was extracted with chloroform. To the clear liquid remaining in the separator sulphuric acid and ferric sulphate were added and liberated iodin extracted with chloroform. The combined chloroformic extracts were then titrated with tenth normal sodium thiosulphate volumetric solution, or each titrated separately and the two results then combined.

Estimation of Free Acid: A weighed quantity of Burnham's Soluble Iodin was added to 10 c.c. of water and the iodin titrated with tenth normal sodium thiosulphate volumetric solution. To the colorless liquid phenolphthalein was then added and the free acid determined by titration with tenth normal alkali. The volume of alkali consumed was then calculated to hydrogen iodid and from

Secrecy is just as essential to-day to the successful exploitation of this class of proprietaries as it was before the demand for formulas became so universal. The requirement of publicity is evaded, therefore, in one of two ways: Either a formula is given which is false, or at least meaningless, or else the claim is made that the method of preparing the product is a unique and remarkable secret that is possessed only by the manufacturers. The Burnham Soluble Iodin Company uses the latter device.

Meanwhile, physicians will be perfectly justified in viewing with suspicion all claims based on such conspicuously unscientific premises, more especially so when these claims fail to find substantiation on careful and painstaking analyses. In brief, whenever the physician wishes to administer free iodin, Lugol's solution (Liquor Iodi Compositus, U. S. P., Physician's Manual, page 84) is an inexpensive and perfectly available preparation.

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this the figures representing combined iodin, in the table under Combined iodin, calculated from acidity, were calculated. It will be seen that the amount of iodin here indicated added to the free iodin found exceeds the total iodin by a large amount. It is plain, then, that this acidity is not due entirely to hydrogen iodid and may be due to another acid entirely and the iodid ions otherwise combined than with the hydrogen ions. It will be seen that as the free iodin increases in Specimen No. 2, the acidity decreases in proportion, the sum of the two being always about the same. The results are here tabulated.

	Free Iodin.	Total Iodin.				Combined Iodin.	
		Method 1.	Method 2.	Method 3.	Method 4.	1. Total iodin less free iodin.	2. Calculated from acidity.
Specimen No. 1.	2.65	4.45	4.50	...	...	1.83	2.45
	2.57	4.52	4.51	...	...	1.95	2.40
Specimen No. 2.	2.40	4.67	...	4.58	4.58	2.21	2.55
	3.06	4.66	...	...	...	...	...
	3.14	...	...	...	...	...	2.02
	3.23	...	...	...	...	...	1.91

Alcohol: To 25 c.c. Burnham's Soluble Iodin, sodium thiosulphate was added in quantity just sufficient to decolorize. The solution was at once added to 5 gm. of potassium hydroxid dissolved in 100 c.c. of water. Of this mixture, exactly 100 c.c. was distilled over and the specific gravity of the distillate determined; all measurements being made at a temperature of 15.6 C., 92 per cent. by volume of ethyl alcohol was indicated.

Specific Gravity: The weight of 25 c.c. of Burnham's Soluble Iodin is 21.3177 gm., indicating a specific gravity of .8527.

2. Proc. Am. Pharm. Assn., 1903, li, 409.

3. Three packages of 100 tablets each were purchased in the open market. From each package 25 tablets were removed, powdered and thoroughly mixed, and the mixture was used for the determinations.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION.]

CALCIDIN—ABBOTT.

W. A. Puckner and A. H. Clark.

(*From The Journal A. M. A., Sept. 7, 1907, 866.*)

[The following has been submitted to, and its publication approved by, the Council on Pharmacy and Chemistry.

W. A. PUCKNER, Secretary.]

In the advertising literature of the Abbott Alkaloidal Company it is claimed that Calcidin—Abbott produces therapeutic effects entirely different from those obtained from iodin in any other form. In view of this and similar extravagant claims, and because the statements made in regard to its composition are vague and confusing, it was considered of interest to determine the nature of this proprietary article. Accordingly an original package of calcidin was purchased in the open market and submitted to analysis.

From this analysis we calculate the composition of calcidin to be:

	Per cent.
"Available iodin (liberated on acidulation)	9.20
Calcium iodid (CaI_2)	5.71
Calcium oxid (CaO)	18.45
Calcium carbonate ($CaCO_3$)	34.45
Corn starch (anhydrous)	16.13
Iron and aluminum	Traces
Magnesium oxid (MgO)	.35
Water (by difference)	15.71
	100.00

In other words, we conclude that calcidin is essentially a mixture of iodin, calcium iodid, lime and corn starch and that the preparation is made by mixing ordinary iodin, lime and corn starch, the calcium iodid and some calcium iodate being

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Free Iodin: Of the powder prepared as above 5 gm. was mixed with 50 c.c. of water and starch paste added. A faint blue color developed indicating the presence of iodin. On drop of a tenth normal sodium thiosulphate volumetric solution discharged this blue color. On standing a few moments the blue color returned and another drop was added. This was repeated until a solution free from blue color remained even after standing one and one-half hours. A total of 1.26 c.c. tenth normal sodium thiosulphate was used indicating .317 per cent. iodin.

Total Iodin: A weighed quantity of the powdered tablets was mixed with a solution of 2 gm. of potassium hydroxid in 10 c.c. of water, evaporated and ignited. The residue was extracted with hot water and in the solution the total halogen determined by precipitation as silver halid. It was found that 2.4213 gm. of Burnham's Soluble Iodin Tablets gave .0716 gm. of silver iodid, indicating .03865 gm. or 1.59 per cent. iodin. In a duplicate 2.9341 gm. of the tablets gave .0841 gm. of silver iodid, indicating .04544 gm. or 1.55 per cent. iodin.

formed by the action of the lime on the iodin in the presence of moisture. The exact amount of calcium iodid found in different specimens of calcidin will vary in accordance with the amount of moisture present and the age of the product.

While it is claimed that calcidin produces "therapeutic effects entirely different from those obtained from iodin in any other form," in reality the introduction of calcidin into the acid stomach contents results in such chemical changes that it corresponds to giving iodin, calcium iodid and calcium chlorid, each 65 mg. (1 grain) of calcidin being equal to about 6 mg. (1/10 grain) iodin, 4 mg. (1/15 grain) calcium iodid and 50 mg. (4/5 grain) calcium chlorid.

As a comparison the average dose of Liquor Iodi Compositus, U. S. P. (Lugol's solution) is 0.2 c.c. (3 min.), and these 3 minims contain 10 mg. (1/6 gr.) of iodin. The dose of calcidin is given as ⅓ to 2 grains, and this will contain 1/30 to 1/5 of a grain of iodin. In other words, the full dose (2 grains) of calcidin contains a little less iodin than 3 minims of Lugol's solution.

CALCIDIN TABLETS.

Having in mind past experiences, where proprietary preparations put up in different forms have differed more or less in composition, sometimes to the extent that the different forms resembled each other in name only, and also realizing the difficulty of making a mixture of lime and iodin into tablets without serious decomposition, the examination of calcidin tablets was taken up.

This examination demonstrated the fact that calcidin tablets do not have the same composition as calcidin itself, but instead are essentially tablets of calcium iodid. While 1 grain of calcidin is equal to 1/10 grain of iodin, 3 calcidin tablets, which represent 1 grain of calcidin, are equivalent to but 1/83 grain iodin. While the recommended dose of calcidin itself will contain 1/30 to 1/5 grain of iodin, the same amount given in the form of calcidin tablets is equivalent to only 1/250 to 1/40 grain iodin.

The analysis shows that the attempt to produce calcidin tablets was a failure because of the tendency of iodin to react with bases to form iodates and the tendency of the iodates to decompose with formation of iodids, which facts are well known to chemists.

COMMENTS.

Two points are especially worthy of emphasis in the above report by the Association chemists. The first is the old, old story so common in the history of nostrums and "patent medi-

cines," of discrepancies between the extravagant, unscientific and absurd claims made by the manufacturers or promoters and the actual facts as revealed by a scientific examination. Inspection of the advertising matter for calcidin shows that its promoters make the following statements regarding it:

> Calcium Iodized, Calcidin—Abbott—is an entirely unique substance, being neither a true chemical compound, nor a simple mixture of its ingredients. Briefly, it is calcium carrying an excess of freely available iodin.

In a circular discussing the nature of the product is this statement:

> It is a new compound of iodin and calcium easily broken up when in contact with acids and of remarkable therapeutic value.

Another advertisement states:

> Calcidin—Abbott (Calx Iodata) is a unique product. It consists of lime unchanged or modified except by hydration, bearing a definite percentage of available iodin. There is no essential chemical union between the two, neither is it a mere mechanical mixture of calcium and iodin, but by a peculiar [?] process (which is stopped at precisely the right moment [sic]) the lime becomes a carrier for the iodin, which is liberated when the substance is brought in contact with acids in the digestive tract.

It is also claimed that calcidin produces "therapeutic effects entirely different from those obtained from iodin in any other form;" that it is "the most effective and only non-injurious preparation of iodin for internal use," and that it possesses all of the valuable properties of iodin with all of the objectionable effects left out.

This enthusiastic eulogy of the preparation closes with the following climax:

> If it is a case in which iodin (divested of all its objecable features) would be "the remedy of choice" use calcidin and rest assured the result will be satisfactory.

Certainly a preparation possessing such startling and epoch-making qualities is worthy of careful investigation.

It is somewhat disappointing, after having our expectations brought up to such a point, to be informed that calcidin is simply a mixture of iodin, lime and corn starch, and that the results of its administration are exactly stimilar to those obtained when giving an equal amount of ordinary iodin, calcium iodid and calcium chlorid. Had the promoters of this preparation advertised their product as a convenient method of administering a certain amount of these three chemicals, there would have been no ground for criticism. It is a different mat-

ter, however, to make extravagant and ridiculous claims of unique and unequaled therapeutic properties, which are not, in any sense, borne out by the facts in the case.

One other point worthy of emphasis in this connection is that, according to the advertisements of calcidin, the great advantage presented by the use of calcidin tablets is that they contain "free iodin." Calcidin and calcidin tablets are supposed to be practically the same thing, but, as is so often the case in proprietary preparations, the statements made by the manufacturers are not borne out by the chemical analysis. Calcidin tablets are said to contain ⅓ of a grain of calcidin and hence should contain 1/30 of a grain of "free iodin" per tablet. As a matter of fact each tablet contains only 1/250 of a grain of "free iodin," an amount so small as to be of no practical value, the remaining iodin being in the form of calcium iodid, *a substance condemned by the manufacturers of calcidin as practically inert.* The advertising matter specially emphasizes the statement that "free iodin" alone is of value and that iodids are practically useless. Such being the case, it is unfortunate that calcidin tablets contain practically no "free iodin" at all and that all of the iodin present is in the form of iodids. In other words, the preparataion does not contain the form of iodin which it is claimed to contain, and does contain the form of iodin which the promoters insist is of little value.

The practical lesson to be drawn from the above report is that any manufacturer who makes extravagant claims, or any product which is advertised by means of statements of marvelous methods of manufacture, unique properties, unheard-of-chemical contents and the like, is to be viewed with suspicion. Calm statements of scientific and chemical facts are one thing and circus poster methods of advertising are quite another.

[Contribution from the Chemical Laboratory of the American Medical Association.]

UNOFFICIAL PREPARATIONS OF HYDRASTIS (GOLDEN SEAL).

W. A. Puckner.

(*From The Journal A. M. A., July 4, 1908.*)

In the price-lists issued by most manufacturers of pharmaceutical products there are to be found listed under fluidextracts, the following preparations of golden seal (hydrastis): "Golden seal U. S. P.," "Golden seal, aqueous," "Golden seal,

colorless." As the term, "fluidextract," or "fluid extract," designates a class of pharmaceutical preparations of which 1,000 c.c. represent 1,000 gm. of the drug, the several golden seal preparations should be of the same drug strength. It is difficult, therefore, to understand why these preparations should differ so widely in prices. Thus, a recent price-list (Ray Chemical Company) quotes them at $3.60, $2.75, and $1.25 a pint, respectively, in the order named above.

The price-lists of some manufacturers shed light on this subject to some extent, at least. Thus H. K. Mulford Co.'s catalogue contains under fluidextracts, "Hydrastis U. S. P.," "Hydrastis, Aqueous (without alcohol)," and "Hydrastis, Colorless (non-alcoholic)," but a foot-note explains that the last preparation is one of those which "differ from fluidextracts in that they are not made 1 gm. to the c.c." So also the price-list of Parke, Davis & Co., which quotes "Golden Seal," "Golden Seal, Aqueous" and "Golden Seal, Colorless," contains an explanatory note which states that "Golden Seal, Colorless" does not represent the crude drug minim for grain.

On the other hand, the price-list of Hance Bros. & White contains an explanatory note which leads to the inference that their golden seal preparations are all of the same strength, thus:

"The Golden Seal used in our preparations is assayed to the standard of 2 per cent., white alkaloid Hydrastin, this being the alkaloid which produces the characteristic physiologic effects.

"We list three Fluid Extracts: Golden Seal, U. S. P., Golden Seal, Aqueous, and Golden Seal, Colorless. Fluid Extract Golden Seal, U. S. P., contains resinous matter and will not make a clear solution with water. Fluid Extract Golden Seal, Colorless, contains only the white alkaloid Hydrastine in an aqueous solution and is especially prepared for medication of the genito-urinary mucous membrane. It makes clear solutions with water and does not stain linen."

Yet the preparations are offered, respectively, at $4.50, $3.75, and $3 per pint.

Evidently, therefore, there is something radically wrong in the system which lists under fluidextracts, Golden Seal, Aqueous and Golden Seal, Colorless. To investigate the matter further, the products of a number of manufacturers were purchased in the open market and examined.

GOLDEN SEAL, AQUEOUS.

The table below gives the descriptions as they appear on the labels of the products supplied by the manufacturers and also the percentage of the alkaloid hydrastin which they were found to contain when examined by the process of the U. S. Pharmacopeia and by a modification of the official method (Method B). The results of the assays by the latter

method, as has been explained elsewhere,[1] are somewhat higher than those obtained by the official method. The latter determinations were made, and the results are recorded only as a verification of the values obtained by the first, the official method. It should be remembered that the official strength of fluidextract of hydrastis is 2 gm. alkaloid to the 100 c.c., whereas, the preparations mentioned below varied from 0.58 to 1.79 gm.

The following table shows that, with one exception (No. 8), the "non-alcoholic," "aqueous" hydrastis preparations examined should not be designated as fluidextracts since they do not contain the amount of the alkaloid hydrastin which the Pharmacopeia directs for fluidextract of hydrastis (2 per cent.). Only one product, that of Stearns, approached the alkaloidal strength the official fluidextract. In reply to an inquiry, Frederick Stearns & Co. claimed that the preparation was made in April, 1907, and at that time assayed exactly 2 per cent. hydrastin.

Two firms, Eli Lilly & Co., and Parke, Davis & Co., do not use, on the label, the word "fluidextract," but instead, call their preparations, respectively, "Fluid Golden Seal, Non-Alcoholic," and "Fluid Golden Seal, Aqueous." These firms also state the amount of alkaloid which these preparations contain, viz., 1.25 per cent., and 1 per cent., respectively, and the examination confirms these claims in a general way.

The results of the analyses were submitted to the several firms interested who were requested to state how these results agreed with those obtained by their own chemists. The replies received, indicate that either the preparation is made and sold without control of its alkaloidal strength or, if assayed, no attempt is made to meet the official standard for fluidextract of hydrastis.

In brief, this examination demonstrates that few of the so-called "non-alcoholic" or "aqueous" fluidextracts of golden seal, deserve the title, "Fluidextract." It also indicates that, in addition to the claim that the inert constituents have been removed, equal prominence should be given to the fact that, to a large extent, the chief active constituent also has been removed. The replies of the manufacturers generally indicate that being an unofficial preparation, little attention is paid to its strength (something on the order of the "eggs good enough for custard," of Mr. Peck's illustrious son); but they also show a willingness to improve the quality of the product or to label it properly.

1. Pharmaceutical Review, May, 1908, p. 132.

GOLDEN SEAL AQUEOUS.

No.	Firm.	Title on label.	Claims made.	Grams of hydrastin in 100 c.c. of preparation. By U. S. P. Method	Grams of hydrastin in 100 c.c. of preparation. By Method B.
1.	Hance Bros. and White.	"Fluid Extract Golden Seal aq."	"The irritating resin of golden seal is eliminated and only the alkaloid retained."	1.43	1.49
2.	Eli Lilly & Co.	"Fluid Golden Seal (Non-alcoholic)."	"The resin and other inert matter is eliminated while the hydrastin and berberin are retained in natural combination, 1.25 gm. hydrastin in 100 c.c."	1.09	1.16
3.	H. K. Mulford Co.	"Fluid Extract of Hydrastis aqueous."	"Represents the medicinal properties of hydrastis but excludes the resinous extractive."	0.58	0.64
4.	Parke, Davis & Co.	"Fluid Golden Seal, Aqueous"	"Represents the medicinal properties of hydrastis. The resinous extractive has been excluded." "Standard, 1 per cent. hydrastin."	0.93	0.95
5.	Ray Chemical Co.	"Ray's Fluid Ext. Golden Seal non-alcoholic."	"Represents the medicinal properties of hydrastis. The resinous extractive has been excluded."	0.77	0.82
6.	Schieffelin & Co.	"Aqueous Fluid Extract of Hydrastis."	No statement[2] except "contains no alcohol."	1.31	1.35
7.	Sharp & Dohme.	"Fld. Extr. Golden Seal Aqueous."	"Each cubic centimeter represents 1 gram . . . of Golden Seal."	1.50	1.62
8.	Frederick Stearns & Co.	"Fluid Extract Hydrastis Aqueous."	"No claims made.	1.79	1.79
9.	Truax, Greene & Co.	"Fld. Ext. Golden Seal without alcohol."	"Contains all the native principles of the drug except the inert, gummy and resinous matter. . ."	1.04	1.10
10.	Wm. Warner & Co.	"Fluidextract Golden Seal without alcohol.	No claims made.	1.26	1.35

2. In Schieffelin & Co.'s prices current of March 30, 1907, it is stated that "Hydrastis, aqueous" is standardized to U. S. P. strength. On corresponding with this firm it appeared that the sample analyzed was of old stock, of which Schieffelin & Co. said:

GOLDEN SEAL, COLORLESS.

On the labels of the trade packages of the so-called "Golden Seal, Colorless" preparations, the following descriptions appear:

Hance Bros. & White: "Liquid Golden Seal, Colorless." "One fluidounce represents one and one-quarter grains(0.081 gm.) hydrastin."

"This preparation is simply a solution of the White Alkaloid of Hydrastis Canadensis in approximately the proportion in which it exists in a prime quality of the drug—twenty grains to the pound—and without the addition of any ingredient intended to increase its action."

Eli Lilly & Co.: "Liquor Hydrastin."

"This preparation, frequently called 'Colorless Hydrastis,' contains the colorless medicinal principles of Golden Seal."

H. K. Mulford Co.: "Fluid Hydrastis (Colorless)."

"Each pint of the fluid contains 20 grains of white alkaloid, the only valuable constituent of Hydrastis."

Parke, Davis & Co.: "Fluid Golden-Seal, Colorless."

"Each fluidounce of this fluid contains 1¼ grains of Hydrastin, the white alkaloid of Hydrastis (Golden Seal)."

Ray Chemical Co.: "Ray's Fluid Extract Golden Seal (Colorless)."

Sharp & Dohme: "Fluid Golden Seal, Colorless."

"Each pint contains 20 grains Hydrastin, White Alkaloid, the principal and most valuable constituent of Golden Seal."

F. Stearns & Co.: "Fluid Golden Seal (Colorless)."

"Each fluidounce of this preparation contains 1¼ grains of Hydrastin (White Alkaloid), to which, recent investigations have shown, the valuable properties of Golden Seal (Hydrastis) are due."

Truax, Greene & Co.: "Liquid Hydrastin."

"Fluid Golden Seal, Colorless."

"One pint of this solution contains an amount of the 'White Alkaloid' Hydrastin equivalent to that contained in one pound of fresh Golden Seal root of average quality.."

H. K. Wampole & Co.: "Fluidextract Golden Seal, Colorless."

"Each pint contains, in a non-alcoholic menstruum: Hydrastin, 20 grains."

Wm. R. Warner & Co.: "Fluidextract Golden Seal, Colorless."

"Each pint contains 20 grains Hydrastin."

The above shows that only a few firms use the word "fluid extract" on the label; nor, with one or two exceptions, is any attempts made to make it appear that the preparation approaches fluidextracts in strength. In general, the labels show that they are weak solutions of salts of hydrastin. While the fluidextract of hydrastis contains 2 per cent. of alkaloid, these preparations contain less than 0.3 per cent.

"None of the old stock should have been sent out subsequently to the issuing of the price list, and we regret to find that a few liters of what we had on hand were sent out. Therefore, we have no doubt that your analytic results are correct, and we can only express our mortification that our oversight should have put us in this position." Analysis of a new specimen submitted showed the amount of alkaloid present as represented—that is of standard U. S. P. strength.

The statement made by Truax, Greene & Co. that one pint contains an amount of hydrastin equivalent to that contained in one pint of fresh golden seal root is, to say the least, misleading. Casual reading gives the impression that this preparation contains an amount of alkaloid equivalent to that prescribed for the official fluid extract. The word, "fresh," however, which probably will, and perhaps is intended to escape the reader, is of considerable importance in this case. According to J. U. Lloyd[3] and Alice Henkel[4] every 100 pounds of fresh golden seal, when dried for the market, yields only 28 to 30 pounds.

Since the U. S. Pharmacopeia requires that golden seal contain 2.5 per cent. hydrastin, the "fresh" drug should contain only 0.6 per cent. The preparation of Truax, Greene & Co., however, does not contain even this amount; examination[5] indicating that it contains less than 0.25 per cent. of hydrastin. To a considerable extent, the same criticism applies to the product of Hance Bros. & White, who state that the alkaloid is contained in their liquid Golden Seal, Colorless, "approximately in the proportion in which it exists in a prime quality of the drug." This is followed by the acknowledgment that it contains 20 grains to the pound. Hance Bros. & White apparently feel confident that physicians are quite unfamiliar with the alkaloidal content of drugs!

THERAPEUTIC INDICATIONS.

In conclusion, the following statements taken from the label for these preparations show the extent to which some manufacturers go in their desire to tell physicians (and others?) the various uses to which this remedy may be put:

"It is indicated in atonic dyspepsia, gastritis, and in the treatment of catarrhal affections of the mucous surfaces; also a wash in conjunctivitis and an injection in gonorrhea, vaginal leucorrhea and inflammation and ulceration of the mucous lining of the bladder. It is free from all staining properties. When used as a wash or injection, it should be diluted with from four to twelve times its volume of water." (HANCE BROS. & WHITE.)

"Non-irritant, permanent, will not stain, contains no alcohol. Will be found useful wherever Golden Seal is indicated."

"Medicinal Uses: It is recommended for various inflammatory and catarrhal conditions of mucous membranes; as an injection in gonorrhea, leucorrhea, and other catarrhal affections of the genito-urinary tract; also in inflammatory conditions of the nasal and air passages. Internally is employed in fermentative dyspepsia, malarial troubles, biliousness, gastric catarrh, gastritis, etc. May also be used in combinations, according to the discretion of the prescribing physician." (STEARNS & CO.)

3. Drugs and Medicines of North America, vol. i, p. 84.
4. U. S. Department of Agriculture, Bull. 51, part 6, p. 14.
5. See Pharmaceutical Review, May, 1908, p. 132.

The examination demonstrates that these unofficial preparations, while listed and sold more or less directly under the titles of fluidextracts, do not comply with the standard adopted for the official fluidextract of golden seal; the results may serve as a suggestion to physicians to make some attempt to learn the composition of unofficial remedies. The analyses emphasize the fact that, with hydrastis as with many other drugs, as soon as the physician leaves the official preparations he is dealing with unknown quantities.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION.]

IODIDE OF LIME (NICHOLS').

W. A. Puckner and A. H. Clark.

(*From The Journal A. M. A., Nov. 2, 1907, 1540*).

Having determined the composition of Calcidin (Abbott), it was deemed of interest to determine the composition of a similar product sold as "iodide of lime (Nichols')" by the Billings Clapp Co., Boston.

Iodide of Lime (Nichols') is said to have been originated about forty years ago by Dr. James R. Nichols of Boston, who was one of the original members of the firm of Billings Clapp Co. A specimen of this preparation was purchased in the open market and analysis in the Association laboratory indicated its composition to be, approximately:

"Available" iodin (liberated on acidulation)	10.66
Calcium iodide (CaI_2)	.65
Calcium carbonate ($CaCO_3$)	3.77
Lime (CaO)	49.06
Alumina (Al_2O_2)	1.87
Magnesia (MgO)	13.89
Silica (SiO_2)	1.22
Water (by difference)	18.88
	100.00

Iodide of Lime (Nichols') is, therefore, essentially a mixture of lime and iodin containing about 10 per cent. iodin. The other constituents apparently are impurities in the lime used in its manufacture.

Calcidin (THE JOURNAL A. M. A., Sept. 7, 1907, page 865), was found to contain 14.13 per cent. iodin, of which 9.2 per cent. in the presence of the acid of the stomach acted as free iodin, while the remaining portion acted as calcium iodid. The Iodide of lime (Nichols') contains 11.22 per cent. iodin, practically all of which (10.66 per cent.) is "available," i. e., liberated as free iodin by the acid of the stomach.

IODIDE OF LIME TABLETS (NICHOLS').

Examination of the tablets of "Iodide of Lime," sold by Billings Clapp Co., demonstrated that, like "Calcidin Tablets," they differ in composition from the original substance which they are supposed to represent. Iodide of Lime (Nichols') was found to contain approximately 10 per cent. "available" iodin. Each ⅓ grain tablet should, therefore, contain about 1/30 "available" iodin. Instead, it was found that each tablet was equivalent to 1/128 grain of free iodin.

It is worthy of note in this connection that the tablets appeared decidedly brown in color, which might be taken to indicate that they really did contain a considerable amount of free iodin. The examination, however, showed that brown color to be due to the presence of large amounts of iron oxid.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION.]

EXAMINATION OF TABLETS OF BISMUTH, OPIUM AND PHENOL.

W. A. Puckner and A. H. Clark.

(*From The Journal A. M. A., July 25, 1908.*)

The demand for "palatable and convenient" medicaments has led manufacturing pharmacists to attempt to produce in tablet form mixtures which, from the nature of the case, are not suited to that method of compounding. In such cases it becomes a question as to what reliance the physician may place in such products and so an examination of a type of these preparations was made in the Association's laboratory.

Nearly every manufacturing pharmacist lists in his catalogue a tablet composed of bismuth, opium and phenol (carbolic acid). According to the price lists and labels, each tablet contains either five or three grains of bismuth subnitrate, one grain of aromatic powder, one-half grain of powdered opium and one-half grain (in one case one-eighth grain) of phenol.

Specimens of different makes of this tablet were purchased, in open market and from the manufacturer, and were examined to determine the amount of phenol each contained. A long series of experiments, the details of which will be published elsewhere, were carried out to determine the best metho