

in any way so as to inform the recipients of their poisonous nature.

RULING OF THE POSTOFFICE DEPARTMENT.

For some time, it was ruled by the Postoffice Department that the transmission of poisons through the mail was prohibited. It appears pressure was brought to bear on certain officials, and as a result the following ruling was put in effect:

"Proprietary articles of merchandise, not in themselves unmailable, such as fancy soaps, tobacco, pills, tablets or other preparations such as are used by the medical and pharmaceutical professions, put up in fixed quantities by the manufacturer, for sale by himself and others, which may be sealed in such manner as to properly protect the articles, but to allow examination of such package in its simplest mercantile form, will be accepted for mailing; provided, that poisonous articles, or articles containing poison, and not unmailable, shall be accepted for mailing only when the package bears the label or superscription of the manufacturer or dealer in the article mailed."

Under this ruling, it is possible to send any poison through the mail provided it is used by the medical and pharmaceutical profession and is put up by a physician or pharmacist in fixed quantities for sale by himself or others. It seems that it would be well to call the attention of the postoffice authorities to this matter and inform them it is the law in almost all states that poisonous remedies of the above character must be marked with poison labels indicating their dangerous character. Of course, it probably would be unjust to withdraw the privileges of the mail entirely from remedies of the above character, but the public ought to be protected in some way by suitable labeling at least.

"Skin-bleachers" have also received some consideration at our hands. The active constituents of these preparations consist for the most part of corrosive sublimate mixed with such articles as glycerin, tincture of benzoin and water. The effect of such a mixture is well known to all physicians. It is claimed by the promoters that they are able by the use of these mixtures to turn a black skin white.

The colored race comes in for an additional "soaking" by firms who claim to make curly hair straight by ordinary ointments and oils.

OTHER FRAUDULENT REMEDIES.

One of the most interesting fraudulent remedies claiming to restore "lost vitality" is "Yousouf's celebrated Turkish salve," which an analysis showed to be nothing but a preparation of petroleum containing approximately 20 per cent. of beeswax.

The action of methylene blue is taken advantage of in many cases, and one firm claimed that if the patient would forward a colored "medicated cloth" (which proved on examination to be nothing but cheese cloth), after moistening the same with his urine, they would submit the colored cloth to an examination and report the nature of the disease to the patient.

INTERPRETATION OF THE LAW.

We wish to call attention to several different points that have been encountered and which at present can not be acted on, first, because of the marked division of opinion among the medical profession, and, second, because of the present construction placed on the law governing the use of the mails by the Department of Justice.

The first point is illustrated by a specific case involv-

ing a solution containing a very minute quantity of an organic copper salt, glycerin, phosphates, and, the manufacturer claimed, heroin, which could not be found. The greatest value of this remedy, it was claimed, resided in the very small percentage of copper it contained, which, it was held out by the manufacturer, was a remarkable cure for consumption. An investigation among the best medical authorities showed that they were all ignorant regarding the usefulness of an organic copper salt in the cure of this disease. Literature, however, showed that a number of remarkable cures had been effected by several French physicians, and there was nothing to do but to give the manufacturer the benefit of the doubt and permit him to continue his practice.

Attention is called to the fact that there are at present many remedies that are highly fraudulent and which are relieving the poor people of much of their hard-earned money. The concerns manufacturing these, however, can not be successfully attacked because they have transacted their business in such a way as to come within the rulings of the Department of Justice in the distribution of their remedies.

This ruling is somewhat as follows:

"The privilege of the mail can be withdrawn from parties only when they are using the mail for the distribution of their goods or the reception of money directly from their patients, or both."

There are many that are taking advantage of this situation, chief among which is that much-advertised and highly deceptive product known as "Liquozone."

It might be well to consider the desirability of placing these conditions before our legislators, but the chief difficulty is the point made by certain government officials that many of our senators and representatives are using remedies of this character in their own homes and believe that they have merits.

It would be a gracious thing on the part of the American Medical Association to encourage the Postmaster-General and the Secretary of Agriculture in prosecuting this line of work and to inform them of hearty support and the full co-operation of the Association.

It is difficult to say approximately what amount of money has been thrown into proper channels by withdrawing the privileges of the mails from many dishonorable concerns during the past two years. This, of course, has brought some ill feeling on the part of certain manufacturers who are recognized as of good standing, some of whom have come out and declared that these firms to whom they were supplying goods were legitimate and honorable, and that they could see no reason why they should be interfered with in any way.

THE INFLUENCE OF SACCHARIN ON THE DIGESTIVE ENZYMES.

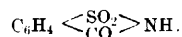
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Saccharin is of interest both from physiologic and economic points of view. Its extensive use as a sweetening agent in canned fruits and vegetables, in syrups, chewing gums, confections, etc., makes it of general dietetic importance. It is also a very common ingredient of lotions, especially of mouth washes. Its use in the diet of diabetics, where sugar can not be tolerated, gives it some importance in medical dietetics. The fact that the food laws of many states prohibit its indiscriminate use, and consider it more or less as a harm-

ful adulterant, makes it incumbent on the pharmacologist to investigate its action on the body; the purpose of the investigation being to find out whether or not it exerts a deleterious influence.

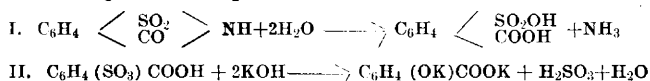
CHEMISTRY AND PROPERTIES OF SACCHARIN.

Saccharin is the imido derivative of ortho-sulphobenzoic acid and is represented by the following formula:



It dissolves with difficulty in cold water and slightly more in hot water. Its sodium salt is readily soluble in water at all temperatures. Saccharin possesses an extremely sweet taste, given usually at from 300 to 500 times as sweet as cane sugar. It is this characteristic sweet taste that makes its use so widespread. Most commercial manufacturers of the substance make much of this point in advertising their product.

For the detection of saccharin it is extracted with ether, or with a mixture of ether and light petroleum spirit. After evaporation of the solvent the intense sweet taste is characteristic. As a confirmatory test a part of the residue is treated with concentrated KOH or NaOH and the dish heated until the mass fuses and is maintained thus for about half an hour. By this means the saccharin is converted into salicylic acid. This can be recognized by its crystalline form, melting point and reaction with ferric chlorid. The reactions on fusing can be represented thus:



On acidifying and extracting with ether, free salicylic acid is liberated from the salt. If salicylic acid is formed in this way outside the body, we thought there was a probability of its formation within the body. It is well known that many reactions which require high heat and the aid of strong acids or alkalies outside the body can take place readily when subjected to the energy of the body cells. On the other hand, benzol compounds in general leave the body in other well known forms. In our experiments, which are given below, we found that not a trace of salicylic acid was formed and that saccharin left the body entirely unchanged.

METHOD OF DETERMINING THE CONDITION IN WHICH SACCHARIN LEAVES THE BODY.

A solution of saccharin (garantose) was prepared by dissolving a known amount in water, by the aid of sodium carbonate. Just sufficient carbonate was used to dissolve the garantose and at the same time keep the reaction of the solution neutral, or very slightly alkaline. The solution was made to a known volume and injected slowly into the femoral vein of a dog. It was allowed to remain in the circulation from two to six hours, and then was washed out through the kidneys with a diuretic— $\text{M}_g \text{Na}_2 \text{SO}_4$. The urine was collected from the ureters, and the amount of saccharin determined by converting it into salicylic acid. By this method we found that when we used from .25 gm. to .5 gm. garantose we could obtain 90 to 95 per cent. of the theoretical amount of salicylic acid in the urine. As commercial saccharin is not chemically pure it is necessary as a control to determine the amount of salicylic acid it will yield. The amount of the diuretic necessary to wash out all, or practically all of the saccharin can be approximately determined by taste. When about 150-200 cc. of the solution of urine and diuretic has been

collected from the ureters, the fluid is practically all $\text{Na}_2 \text{SO}_4$, and fails to give the test for saccharin. It is then made to a known volume and aliquot-portions used in the analysis.

ACTION ON THE BLOOD.

A neutral solution, prepared as above, and containing .25 gm. was injected into the femoral vein. After two hours some blood was withdrawn and its action on hydrogen peroxid tested. Normal blood from the same animal was used as a control. The results are as follows:

I.	II.
2 c.c. blood (sacch.)	2 c.c. Blood (normal).
10 c.c. water.	
2 c.c. H_2O_2 .	10 c.c. water.
Gas given off in 30 minutes:	2 c.c. H_2O_2 .
12 c.c.	13.5 c.c.
Gas in 2 hours:	
14 c.c.	14.0 c.c.

The only action here is a slight retardation of the oxidation.

In a second experiment normal blood was taken from the carotid artery and dry saccharin added to it.

I.	II.
2 c.c. blood.	2 c.c. blood.
0.1 gm. sacch.	3 c.c. H_2O_2 .
3 c.c. H_2O_2 .	
Gas in 10 minutes:	
18 c.c.	27 c.c.

Here the larger amount of saccharin causes a marked diminution in the oxidative power. On standing a longer time only a slight change was found in the relative and absolute volumes given in the table.

ACTION ON THE OXIDATION OF SUGAR IN THE BLOOD.

Every animal can oxidize a certain amount of a mono-saccharid if it is injected directly into the circulation. The total amount that can be oxidized before sugar appears in the urine can be called the oxidizing coefficient of the animal. This amount will, of course, vary with different sugars, depending on the ease with which the sugar can be oxidized. In other work one of us (McGuigan) found that levulose is very much easier oxidized than any of the other common sugars. Consequently in this work we started with levulose. If the oxidizing power of the animal is lessened by the injection of saccharin—a fact which we have shown fully—then less sugar can be oxidized by an animal with saccharin in its blood than can be oxidized by a normal animal. To test this point we selected two dogs of about equal size and age. Dog 1 was used as a control. A solution containing 15 grms. levulose and 1 gm. sodium bicarbonate made to 500 cc., was injected into the femoral vein at the rate of 10 cc. every 5 minutes. Sugar commenced to appear in the urine when 250 cc. had run in. No sugar appeared before this time. The same strength of sugar solution with the addition of 2 grms. of garantose to 750 cc. of the solution, was run into the femoral vein of Dog 2 at the same rate as in Dog 1. Sugar appeared in the urine in this case when 140 cc. had been injected. If we assume that the dogs possessed the same oxidizing power, then clearly the addition of garantose materially lessens the oxidative power. This is corroborated by the rest of our work and is strikingly brought out by the work of Bornstein.¹ We are aware that most diuretic salts and many anesthetics will produce a condition of glycosuria, and have been careful to avoid the use of such. In all this work chloretone was used as the anesthetic. In this last experiment no diuretic was used.

1. Zeit. für klinische Medizin, vol. 40 p. 208. This reference also contains a résumé of the literature of the work on saccharin.

INFLUENCE OF SACCHARIN ON THE FERMENTATION OF SUGAR.

The urine containing levulose from the above experiments did not ferment with yeast. A solution of pure levulose was then tried and it fermented rapidly. If, however, a slight amount of saccharin was added, fermentation was entirely inhibited. Garantose is only slightly soluble in water; it is yet sufficiently soluble to prevent fermentation. This point is worthy of consideration in diabetic diets.

INFLUENCE ON THE WORKING OF SALIVA.

The influence of saccharin on the diastatic action of saliva is more pronounced than on any other enzyme of the body. Even traces exert an enormous retarding influence, while larger quantities completely arrest the action of the enzyme. This is shown by the following experiments:

	I	II	III	IV	V
Dry sacch. grms.2	.1	.05	.01	0
Saliva, c.c.	2	2	2	2	2
Starch paste, 2 per cent., c.c.	5	5	5	5	5

The solutions were mixed in vitro and placed in a thermostat at 40 degrees C. The results were as follows:

V—All digested in 8 minutes.
IV—All digested in 16 minutes.
III—All digested in 40 minutes.
II—Only trace digested in 360 minutes.
I—No digestion in 360 minutes.

The point when digestion was completed was indicated by the iodine test. No digestion was shown by failure to reduce Fehling's solution.

ACTION ON PEPTIC DIGESTION.

A 1 per cent. neutral solution of saccharin was prepared and the following experiments carried out:

	I	II	III	IV	V	VI
Pepsin, 2 per cent. acid reaction, c.c.	4	4	4	4	4	4
Sacch. sol., c.c.	5	4	3	2	1	0
Water, c.c.	1	2	3	4	5	6
Fibrin, grms.	2	2	2	2	2	2

The above were shaken in test tubes and placed in the thermostat at 40 degrees. Results:

VI—All digested in 45 minutes.
V—All digested in 60 minutes.
IV—All digested in 85 minutes.
III—All digested in 100 minutes.
II—All digested in 130 minutes.
I—All digested in 350 minutes.

The retarding influence here is very apparent.

ACTION ON TRYPTIC DIGESTION.

Experiments were carried out with commercial pancreatin; with fresh pancreatic extracts and with pancreatic extract mixed with extract of the duodenum (dog). The proteolytic action of pancreatin and extract of the pancreas alone was only slightly affected by the addition of small amounts of saccharin. The diastatic action is materially decreased by the addition of saccharin, though not to so great an extent as the diastatic action of saliva. The most striking results are obtained when extract of the pancreas and duodenum are mixed.

An extract of the pancreas and duodenum of a dog was prepared by grinding the organs to a pulp and macerating 30 minutes with a 5 per cent. Na_2CO_3 solution. The extract was then filtered and added to fibrin as follows:

	I	II	III	IV	V
Filtered ext., c.c.	5	5	5	5	5
Sacch. dry grms.1	.05	.02	.01	0
Fibrin, grms.	1	1	1	1	1

The mixtures were placed in the thermostat at 40 degrees C. and observed at short intervals, with results as follows:

V—All digested in 45 minutes.
IV—All digested in 105 minutes.
III—Almost digested in 270 minutes.
II—About half digested in 270 minutes.
I—Practically no digestion in 270 minutes.

No observations were made again for twelve hours, when the same condition was found as at the end of 270 minutes. These results indicate clearly enough the inhibitory action of the substance on pancreatic digestion.

ACTION ON THE OXIDATIVE POWERS OF MUSCLES AND GLANDS.

The muscular and glandular tissues of the body will all liberate oxygen from hydrogen peroxid. The amount of oxygen liberated by a given amount of the dried tissue is roughly proportional to its oxidative powers. If saccharin is added, the oxidation is lessened; if sufficiently large amounts are added, the oxidative power is entirely overcome. This influence is illustrated by the following experiments:

The tissues were prepared by grinding the fresh material to a fine pulp and macerating in 95 per cent. alcohol for 24 hours. It was then filtered, washed with alcohol and ether and dried in the air. After drying it was ground very fine and run through a fine sieve. The first experiment was with rabbit's muscle, 2 grms. in each:

	I	II	III	IV
Dry sacch., grams.1	.05	.01	0
Water, c.c.	5	5	5	5
H_2O_2 , c.c.	2	2	2	2
C.c. gas in 5 minutes.	0	0	.8	2.5
C.c. gas in 10 minutes.	0	0	1.5	3.4
C.c. gas in 30 minutes.	0	0	2.0	5.5
C.c. gas in 60 minutes.	0	0	2.2	5.8

In a second experiment rabbit's liver was prepared in the same way; using .2 grms. gave the following results:

	I	II	III	IV	V
Saccharin, grams.2	.1	.05	.01	0
Water, c.c.	5	5	5	5	5
H_2O_2 , c.c.	2	2	2	2	2
Gas in 5 minutes.	0	0	2	4.5	12.0
Gas in 10 minutes.	0	1.5	3.0	6.0	15.0
Gas in 30 minutes.	0	2.5	3.8	8.0	17.2
Gas in 45 minutes.	2	2.6	4.8	9.6	18.0
Gas in 60 minutes.	2	3.0	6.5	12.4	19.0

In Experiment 3, dog's muscle and liver were treated in the same manner, with the following results:

DOG'S LIVER, TWO-TENTHS GRAM IN EACH.

	I	II	III	IV
Sacch., grams.1	.05	.01	0
Water, c.c.	5	5	5	5
H_2O_2 , c.c.	2	2	2	2
Gas in 5 minutes.	0	0	1.5	4.0
Gas in 10 minutes.	0	0	2.3	5.5
Gas in 20 minutes.	0	.5	4.0	8.5
Gas in 40 minutes.	0	1.0	5.2	9.5
Gas in 60 minutes.	0	1.8	6.8	9.6

DOG'S MUSCLE, TWO-TENTHS GRAM IN EACH.

	I	II	III	IV
Sacch., grams.1	.05	.01	0
Water.	5	5	5	5
H_2O_2	2	2	2	2
C.c. gas in 5 minutes.	0	0	1	2
C.c. gas in 15 minutes.	0	0	1.5	2.5
C.c. gas in 30 minutes.	0	0	2.0	3.0
C.c. gas in 45 minutes.	0	0	2.5	3.5

From these results it is evident that saccharin in small amounts retards oxidation, and in larger amounts prevents oxidation both in herbivorous and carnivorous animals. These results agree fully with those of Bornstein,¹ who found that the administration of saccharin caused an increased elimination of total nitrogen. The amount of nitrogen in the urine was less than before the using of saccharin, but the amount in the feces was greatly increased, so that the average of the two was greater than before using it. This means either a decreased hydrolysis or a decreased absorption of proteid, or both. As a matter of fact, Bornstein proved that absorption was materially lessened by the use of sac-

charin. He also observed that on those days in which he used it he suffered from headache and other symptoms of gastrointestinal derangement.

The experiments recorded above confirm the work of Reigler,² although it seems that we noted a more powerful action than that reported by him. This is undoubtedly due to the using of different brands of saccharin. In our work we used the "garantose" handled by Merck & Co. Reigler used that manufactured by Fahlberg, List & Co. The commercial products vary in strength, and to obtain uniform quantitative results a chemically pure preparation must be used.

PHARMACOLOGY OF SACCHARIN.

Saccharin is used in medicine solely on account of its sweetening properties. As we have shown, it has a retarding influence on the action of the digestive juices, especially that of the saliva and pancreas. Its prolonged use would, therefore, tend to produce digestive disorders. When injected into the circulation of an animal it produces depression and stupor, followed by labored respiration similar to asphyxia. This is evidently due to its inhibitory action on the enzymes in the blood and also in the tissues in general. This action very probably accounts for the headache and other symptoms which follow its use. Like many of the other benzol compounds, it may be considered a general protoplasmic poison, in that it inhibits nearly all the fermentative processes of the body. Consequently it interferes with and decreases the general body metabolism.

LEPROSY, BLASTOMYCOSIS, LUPUS, SYPHILIS, ALOPECIA AREATA, LUPOID SYCOSIS.*

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CASE 1.—J. G., male, aged 20, a native of Russia, came to this country six years ago, and has since that date lived in one of the western states contiguous to Illinois.

History.—Three years ago he began to suffer from a series of febrile attacks, accompanied by chills and by eruptive symptoms of an erythematous type, which were supposed to be syphilitic in character and for which he was subjected, without remedial results, to a course of specific treatment. Aside from the symptoms referred to, he has enjoyed fair health. There is no history of venereal disease; he has occasionally indulged in tobacco smoking; his family record is good. His father, who accompanies him, is a healthy-looking, though somewhat undersized, Polish Jew.

Examination.—The face of the patient is seen to be the seat of a diffuse infiltration, chiefly conspicuous about the nares, the brows, the lips, and the ears. The infiltrated area, though diffuse, is studded here and there with smaller and larger tubercles. There is marked alopecia of the brows. On the forearms, hands, legs, and the dorsum of the feet, there are larger and smaller poorly defined areas of punctate pigmentation; and here, as also where no such coloration exists, there are areas distinctly insensitive to hot and cold applications and to the prick of a pin. On the extensor surface of the left wrist is a large, coin-sized keloid developed from a burn which, he states, at the time of its infliction, produced no pain. The ulnar nerves are enlarged and somewhat corded, but the ascending great auricular nerve is not involved. This special nerve is said to be implicated in nearly 90 per cent. of similar cases, and its induration is readily demonstrated in the patient whom I shall next present to you. There is a deep, funnel-shaped ulcer in the sole of the left foot corresponding in char-

acter with the symptoms of *mal perforant du pied*. This young man has had frequent attacks of epistaxis. The mucous membrane of the nasal cavity is studded with small pin-headed and larger tubercles and irregular, shallow ulcers, thus explaining largely the catarrhal symptoms of which he complains.

This patient was first examined on Dec. 4, 1904, at which time a small nodule was excised for examination. The section when stained exhibited numerous lepra bacilli and the same micro-organisms were thickly dispersed in a smear of the nasal secretion.

Points of Special Interest.—Though presenting typical and unmistakable symptoms of tubercular leprosy, with an admixture of lesions commonly found in anesthetic types of that disease, this patient presents several points of special interest.

His youth and the relatively brief period of time during which he has suffered from the disease may be named first in order. These promised well if an appropriate therapy were instituted. He was placed on chaulmoogra oil, beginning with five minims in a glass of milk administered three times daily, the dose being progressively increased to nearly a teaspoonful. With this were administered ferruginous tonics; and a carefully directed hygiene was insured.

The results have surprised all who have watched the progress of the case. The general appearance and health of the patient have greatly improved. The skin is fairer, less muddy, less infiltrated. Over the brows the tubercles are now scarcely evident. The catarrhal symptoms are less severe. The only feature of his case in which there has not been corresponding improvement is the plantar ulcer. This we shall treat surgically.

Second: The origin of the disease. The youth almost certainly contracted leprosy in Russia. Instances of this malady, originating in the United States, are, indeed, few. My colleague, Dr. Ormsby, has reported one such case, the patient having been exhibited to this clinic last year. In his published report of this case, Dr. Ormsby makes reference to the case of the child of a leprosy patient presented by me before this clinic several years ago, in which it seemed highly probable that the child, a native American, contracted the disease, presumably from the father, in the state of Nebraska.

Third: The demonstration of lepra bacilli in great numbers in the nasal secretion would seem to argue in favor of the opinion long sustained by Dr. Morrow, of New York, that most cases of leprosy are contracted by the medium of nasal secretions. It should be added, however, that in most of the leproseria visited by me the organs, apart from the skin and viscera, most frequently involved were without question the eyes. The number of blind lepers in any asylum devoted to this class of patients is pitifully large.

CASE 2.—This patient, F. B., aged 27 years, a native of Australia, left his home seven years ago to become a sailor.

History.—In the course of his voyages he has visited Ceylon, India, Norway, Sweden, China, and the West Indies, and has lived an irregular sexual life in all these countries. At one time he was associated with a bunk-mate supposed to have the same disease and with whom he occasionally exchanged clothing. It appears, however, that before he left Australia an odd-looking "patch" appeared on his back, which may possibly have been the first symptoms of the disease with which he is now affected. There is a leper asylum in the vicinity of his native town. His history, prior to the development of the present disease, is not significant. His parents are healthy and free from symptoms of his ailment. The tip of the left index finger has been removed as the result of a traumatism. His functions are regularly performed.

Examination.—At the present time, the dorsum of the trunk is seen to be symmetrically, though irregularly, overspread with circular and ovoid patches having a faintly erythematous central area surrounded by annular bands from one to two centimeters in width, pigmented in yellowish-brown shades. There are about a score of these visible, varying in size from the section of a hen's egg to the palm of a hand; some of them are insensitive to both superficial irritation and to cold and heat. There are other areas of anesthesia where the pigmentation and color changes are absent, as, for example, about the popliteal spaces, but more particularly over the posterior

2. Archiv. für Exp. Path. u. Pharmacologie, vol. 35, p. 306.

* A clinical lecture delivered before the Visiting Alumni of Rush Medical College at the Commencement of 1905.