Thus it is that the regulation of reaction of blood and protoplasm manifests the very highest stability.[8]

In exactly the same way that neutrality is favored by the ionization constant of phosphoric acid, the excretion of acid is facilitated. By variation of the relative amounts of acid and alkaline phosphates the relative amounts of acid and basic constituents of the urine may be varied in the highest degree, accompanied by the very smallest possible variations of hydrogen ion concentration. Thus the presence of phosphoric acid makes of the urine an ideal regulatory apparatus for the preservation of the normal ratio of acid to base in the blood.

Such are the more striking aspects of this subject. Neutrality is quite as definite, quite as fundamental and quite as important a characteristic of the organism as its temperature, or osmotic pressure, or in fact anything else that we know. And it turns out to possess those remarkable characteristics of stability that have been revealed by the researches of Rubner and others in the case of temperature, only in far higher degree.

Within wide limits of amount any acid or base may be poured into the organism, and the reaction will not vary; nor will it vary if such be produced by the organism, and this constancy will protect all enzymatic processes, the function of respiration and the whole distribution of material throughout the body.

Let us return to Cuvier's vortex. Into it let us pour anything, for example hydrochloric acid. No sooner has it entered than it is neutralized, and neutralized it remains until, on leaving the body, it appears as sodium chloride, ammonium chloride and a slightly heightened excess of acid phosphate over alkaline phosphate in the urine.

The urine is variable, the ingesta are variable, even the products of metabolism are variable; but, while life endures, the dynamical equilibrium of hydrogen and hydroxyl ionizations persists.

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THE PHYSIOLOGICAL SIGNIFICANCE OF SOME SUBSTANCES USED IN THE PRESERVATION OF FOOD[1]

FOOD preservatives are those substances which delay or prevent the decomposition of food as a result of the action of bacteria or other ferment-producing organisms. Other substances, sometimes classed as preservatives, and in the popular mind associated with them, are not so much preservatives as agents for the conservation of some special property of the food in question, as, for example, the use of copper sulphate in the fixation of the color of green vegetables. A large number of bodies may be included under the head of preservatives, but our interest to-day centers in the so-called "artificial" or "chemical" preservatives, because of the question of the permissibility of using them. Some of these bodies have been condemned largely because of their origin, because of their artificial character, which basis of condemnation can not be regarded as sufficient or scientific.

Their merits or faults must be decided on the basis of physiological behavior, essentially, and from this point of view I wish to speak of several substances concerning which the discussions have been

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[8] For a larger survey of this whole subject two articles in the *Ergebnisse der Physiologie*, VIII., 254, 1909 (the author) and XII., 393, 1912 (Sörensen) may be consulted.

[1] A paper read before the Fifteenth International Congress on Hygiene and Demography, Washington, September 23, 1912.

the most heated. These discussions will be necessarily brief.

SODIUM BENZOATE

On certain phases of the behavior of sodium benzoate there is an abundant literature. Following the pioneer investigations of Meissner and Shepard, and Bunge and Schmiedeberg on the synthesis and estimation of hippuric acid it was recognized that benzoic acid, cinnamic acid, quinic acid and other bodies are normally combined in the animal organism with glycine and excreted as hippuric acid. It was shown, also, that many aromatic fruits and vegetables contain these organic acids which go into the benzoyl combination. Numerous later studies have shown the extent of the glycine, or potential glycine, available in the human body for combination.

With the recognition of this normal character of the hippuric acid synthesis no great objection was raised to the administration of large doses of the benzoate in certain diseases, and going back some thirty years we find a considerable record of clinical experience on the dosage of benzoates in pulmonary tuberculosis, rheumatism and diphtheria. It was shown by many physicians that doses of 5 to 25 grams a day might be given without apparent harm to the patient. This extended experience was sufficient to show that the toxic effect of the benzoate was of a very low order, not much greater possibly than that of sodium chloride.

At the time when sodium benzoate was considered important therapeutically the question of its use as a food preservative had not arisen, and the interest attaching to it then and through the following discussions was in no wise influenced by the present practical question. To what extent may benzoic acid be combined or detoxified in the animal organism? The earlier observers soon recognized that ordinarily and normally it combines with glycine to form hippuric acid, and the question of the available supply of this amino acid was discussed for a long time. In 1898, in experiments on rabbits, Wiener[2] concluded that while large doses of benzoic acid, about 1.7 gram per kilogram of body weight, were usually fatal, smaller amounts and up to the quantity yielding 1 gram of hippuric acid per kilogram of body weight, were combined and detoxified. He believed that the value for the combined benzoic acid, that is, the hippuric acid, was rather constant, the maximum being the 1 gram per kilogram of weight. The usual figures were between 0.7821 and 0.8345 gram per kilogram. From this he concluded that the available supply, or stored-up glycine, must amount to 0.3276 to 0.3496 gram per kilogram of weight. He observed that free benzoic acid appeared in the urine when amounts in excess of the maximum values quoted were ingested.

These observations were made at a time when glycine was looked upon as an important intermediary product of protein metabolism, and before much was known concerning the quantitative relations of the amino acids in the protein molecule. It was later shown that the mean glycine content of the ingested proteins is not far from 4 per cent. of their weight, and that the benzoic acid combined to form hippuric acid may be far greater than the weight corresponding to this glycine content. A stored-up reserve of glycine was for a time assumed to account for the remarkable hippuric acid formation reported by several observers, but this view has been pretty generally abandoned. In this connection the researches of Parker and Lusk,[3]

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[2] *Schmied. Arch.,* 40: 313.

[3] *Am. Jour. Phys.,* 3: 472.

Wiechowski,[4] Cohn,[5] Magnus-Levy,[6] Lewinski[7] and others, should be referred to. All of these observers found that in the increased ingestion of large amounts of benzoic acid in animals there was an increased protein metabolism, with increasing amounts of the benzoic acid not combined as hippuric acid. In the Lewinski investigations rather large weights of benzoic acid, as the sodium salt, were given to men. In one case a man of 59 kilograms weight took 12 grams of the acid in 12 hours. All was excreted in combined form and no increase of reducing substances in the urine was noted. This amount of acid is nearly one fifth of a gram per kilogram of body weight, and is relatively less than was ingested in many of the animal experiments. If all combined with glycine it would call for 7.38 grams of the latter, or the glycine existing in about 200 grams of mixed proteins. This amount is probably more than was metabolized in the individual in question.

In another case of Lewinski's a man weighing 67 kilograms took 20 grams of the acid in 12 hours. The urine examination showed the same result as in the other case. Later, the same man took 25 grams of the acid, but it was not all combined, as 1.65 grams were recovered from the urine. When the ingestion was increased to 40 grams still more appeared in the urine uncombined with glycine. In one case on the 40-gram dosage nausea and headache were noted, but these effects seemed less marked with a diet rich in protein. The author concludes that on a high protein diet more benzoic acid may be ingested without ill effects. In one case a man took 50 grams without apparent disturbance, but over 8 grams appeared in the urine uncombined.

All these experiments demonstrate that in man, as well as in animals, ingested benzoic acid may be detoxified in amounts which much more than correspond to the glycine of protein that may be metabolized normally in the same individual, in the same time. The 20 grams of benzoic acid given in one experiment, and which left no free acid in the urine, would correspond to 12.3 grams of glycine.

These papers have been cited because they show the remarkable capacity of the animal organism for the synthesis of hippuric acid and consequent disposition of ingested benzoic acid. It has been shown that the combining power of glycine is not limited to that preformed, or which may be split off in the ordinary metabolism, but that in addition the potential glycine of other amino groups is also available.

It may be urged that this diversion of potential glycine from more complex acids is in itself an abnormal action, and therefore objectionable. This is possibly true, and would have weight, if we were concerned with the question of ingesting daily 5 grams or more of benzoic acid. But the amounts to be practically considered are so far below this that the question of breaking down extra protein does not come to the front at all.

What amounts of benzoic acid are actually in question here? Practically below 500 milligrams daily, if we consider the ordinary solid or semi-solid foods, or below a gram a day, if we consider certain beverages sometimes treated with benzoate. These are probably extreme figures, as for the great majority of food substances benzoate is not used or in any sense required. What then is the physiological behavior of these small amounts of benzoic acid which

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[4] *Hofmeister's Beitraege*, 7: 204.

[5] *Jaffe Festschrift*, Braunschweig, 1901.

[6] *Münch. Med. Wochensch.*, 52: 2168; *Biochem. Zeitschr.*, 6: 502 and 523.

[7] *Schmied. Arch.*, 58: 397.

have practical significance? Several lines of enquiry may be followed to find an answer to this question, three of which are comparatively direct: (*a*) the fate in the body; (*b*) the action on digestive ferments; (*c*) the action with reference to general health and metabolism.

(*a*) With reference to the relations under (*a*) we have already sufficient information. Small amounts of benzoic acid are completely united with glycine, and for 500 milligrams 307.5 milligrams of the latter are required, an amount far within the liberation from the ordinary protein metabolism. In the cases of infants or invalids with lower metabolism the possible benzoate ingestion is naturally far below this, and there would doubtless be always, even in such extreme cases, a sufficient glycine content for combination.

With no benzoic acid ingested the larger part of the glycine would probably go to form urea and other products by oxidation. With the benzoic acid we have the synthesis of hippuric acid. Unfortunately, we have no reliable means of comparing the magnitude of or the difficulty in the enzymic work in the two cases. In certain quarters much has been said about the over-burdening of the kidneys with this work of synthesis. As a matter of fact there is no warrant whatever in the assumption that the tax on the organism is any greater in this case than in the other, and those who make the assumption probably overlook the fact that the hippuric-acid synthesis in the human body is normal and constant. Because of a lack of delicacy in the methods employed for the determination of hippuric acid the quantity of this substance excreted daily has usually been greatly underestimated, or neglected entirely.

(*b*) The behavior of benzoic acid toward digestive ferments has been the subject of several investigations. In this direction the action on diastases, pancreatin, pepsin, rennin and the lipases has been studied. A number of such studies have been carried out in my own laboratory, with the general result that while there is naturally an inhibition of digestive activity with certain concentrations of benzoic acid, with those concentrations which have practical importance in the present enquiry the inhibition is very slight or does not appear at all.

In the case of the digestion of starches there is indeed a distinct acceleration in the rate of digestion, as is caused by a number of neutral salts and acids of low concentration. This is true not only of digestions by means of malt infusions, but also in the case of taka-diastase and a number of the pancreatic diastase preparations in general use in this country. Similar results were reported some years ago by Leffmann.[8]

While 0.1 per cent. of sodium benzoate added to egg albumin mixture, such as is used in the official pepsin tests, distinctly retards the rate of digestion, this is not the case with one fifth of this concentration, which is probably above the limit ever found in the stomach after the ingestion of benzoated foods. This relation has been observed in a number of mixtures of fibrin as well as egg albumin, and with a variety of pepsin preparations. Analogous results have been reported by Gerlach in his lengthy study of the benzoate question.[9]

Very weak concentrations of either benzoate or benzoic acid have no influence on the rennin coagulation of milk, but with an increase in the concentration there is a gradual inhibition. Our results in this

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[8] *Jour. Frank. Inst.*, 147: 1899, p. 97.

[9] Wiesbaden, 1909.

respect are not essentially different from those of Weitzel.[10] In the clinical feeding of infants sodium benzoate has been frequently added to milk.

According to Amberg and Loevenhart[11] the activity of lipase, as measured by the splitting of ethyl butyrate, is not diminished by the presence of 0.1 per cent. of sodium benzoate. Dakin, working in Herter's laboratory, has made a careful redetermination of many of the digestive constants in presence of benzoate.[12]

(*c*) We now come to the most important part of the subject, the behavior of benzoic acid with reference to general health and metabolism. At the time when this substance was extensively used in medical practise, that is, from 1875 to 1880, it was recognized by some physiologists that large doses were followed by increased elimination of nitrogen, which, it was assumed, must come from the breaking down of body proteins. E. Salkowski, especially, from experiments on dogs,[13] concluded that high doses might occasion a considerable loss in man. But in the dog experiments the ingested benzoate amounted in the mean to about one third of a gram per kilogram of body weight, which proportion if applied to a man of 50 kilograms weight would call for nearly 17 grams of benzoate, or 25 grams for a man of 75 kilograms weight. Somewhat similar observations were made by other physiologists, but on the other hand the reports from clinical practise failed to show any such losses. To follow these discrepant observations farther is not necessary in this place, as the question of the increased nitrogen excretion has been pretty fully handled in the investigations of Magnus-Levy,[14] Ringer, and Epstein and Bookman,[15] and others already referred to.

But these early reports have had one very important effect, which must be recalled here. They left the impression that the ingestion of sodium benzoate is in general followed by increased protein metabolism, tissue metabolism possibly, an undesirable result, and this statement is frequently repeated as applicable to all doses of benzoate. A number of lengthy metabolism experiments have shown that for ordinary ingestions of benzoate this increased protein metabolism does not occur. In the last few years the results of several such investigations have been published. One of these investigations was conducted under the auspices of the Bureau of Chemistry of the United States Department of Agriculture, and from it the conclusion was drawn that small doses of benzoic acid or benzoates exert a harmful action on man, a slight loss in weight being affirmed in some cases. It is not my purpose to criticize this work here beyond saying that the published data do not seem to warrant the conclusions drawn, which opinion is shared in a lengthy review of the work by K. B. Lehmann, recently published.[16]

I wish to speak more particularly of the results of the extended studies carried out by Chittenden, Herter and myself, as members of a commission appointed by the Secretary of Agriculture to investigate the question anew.[17] In Herter's work four men were observed through periods of four months, while in the investigations of Chittenden and myself six men on a definite

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[10] *Arbeiten aus dem kais. Gesundheitsamt*, 19: 1902.

[11] *Jour. Biol. Chem.*, 4: 1908.

[12] Herter, *Jour. Am. Med. Assoc.*, 54: 1774.

[13] *Virchow's Archiv*, 78.

[14] *Loc. cit.*

[15] *Jour. Biolog. Chem.*, 10.

[16] *Chemiker Zeitung*, November 28, 1911.

[17] Report No. 88, U. S. Department of Agriculture, 1909.

diet containing sodium benzoate were observed through a period of four months.

These studes covered lengthy observations on the general metabolism of the men, the qualitative changes in the urine, the effects on the blood, effects on the intestinal flora, and daily clinical observations on the weight and general condition of the men. Under the head of metabolism determinations were made of the nitrogen balance and utilization, the distribution of nitrogen, the distribution of sulphur and the utilization of fat. From the data of Chittenden and myself, which were fuller in detail than those of our colleague, certain facts are clearly shown. In Chittenden's series of experiments the doses of benzoate were administered as follows:

	Days	
Fore period	14	no benzoate
Low benzoate period	62	300 mg. daily
After period	10	no benzoate
Medium benzoate period	7	600 mg. daily
First high benzoate period	7	1,000 mg. daily
Second high benzoate period	7	2,000 mg. daily
Third high benzoate period	7	4,000 mg. daily
After period	10	no benzoate
Total	124	71.8 grams

This is an average dosage of 718 milligrams daily, for dosage periods. In my series of experiments the amounts were as follows:

	Days	
Fore period	25	no benzoate
Low benzoate period	60	300 mg. daily
Medium benzoate period	14	600 mg. daily
High benzoate period	18	1,000 mg. daily
After period	7	no benzoate
Total	124	44.4 grams

This is equivalent to an average dosage of nearly 483 milligrams daily for the dosage periods. In either case the dosage more than covers the practical consumption and is doubtless better adapted to throw light on the subject than are the excessive doses previously given. Larger ingestions of benzoate are no more suited to prove its practical physiological action than would 150 grams of sodium chloride, kilograms of sugar or half liters of vinegar daily be suitable for these substances. With such large ingestions even the common food substances or condiments might be made to appear highly injurious.

Time will not permit me to go into details with reference to all these experiments. It is sufficient to say that no effects whatever were observed which pointed to a modification of the nitrogen or fat utilization, the nitrogen balance or distribution, the sulphur metabolism, the body weight or the hemoglobin content and red and white counts in the blood. The order of nitrogen distribution remained always the same in the period averages, and it was only when doses of 4 grams of benzoate daily were given that Chittenden noticed a slight, but to be expected, percentage decrease in the urea excretion.

Qualitative Changes in the Urine.—In all of our work frequent examinations were made for the appearance of sugar or other reducing bodies, traces of albumin, casts, aromatic oxyacids, or other things which might indicate a change in the nature of the excreted bodies. There was never any indication of an alteration in this direction. The occasional appearance of a trace of albumin or of a hyaline cast was no more frequent in the dosage periods than in the fore periods, and was without practical significance.

During the progress of the work frequent determinations were made of the so-called normal reduction of the urine of the men working in my laboratory, by means of a delicate ammoniacal copper solution. No definite changes were noted which could be connected in any way with the benzoate. After the conclusion of the 124 days of regular experimentation two of the men in my group who had followed the regular routine continued for seven days longer, with higher dosage. They began with 5 grams a day and finished with 10 grams, the average being 7.5 grams daily. With this large dosage there was no reduction which could be noticed with Fehling solution, and nothing which was outside the normal limits for the ammoniacal solution, although there appeared to be a slight increase from the former figures. Other changes were absent. A third man who had not been a member of the experimental squad, but who had followed the same diet routine, took doses beginning with 5 grams and ending with 7.5 grams on the seventh day. No abnormal behavior of any description was noted in his excretion or general condition. In this case it could not be urged that the man had become accustomed to large doses through gradually increasing small doses.

Temperature, Pulse, Respiration.—All these factors were systematically noted from day to day for each man. Absolutely no variations from the normal were observed which might in any way be attributed to or connected with the dosage of benzoate.

Conclusions.—From all these observations the conclusion was drawn that in the dosage administered, which is large enough for practical purposes, sodium benzoate exercises no recognizable physiological action on the human organism, beyond the slight increase in hippuric acid excretion, a change which is often exceeded after hearty meals of certain berries and fruits which are frequently consumed in quantity. I have recited the facts in some detail because of the long-continued and persistent attempts to create the impression, especially in this country, that sodium benzoate exerts a toxic action, sufficiently marked to warrant its exclusion from use with foods.

Gerlach's Studies.—Attention must be called here to an elaborate investigation carried out by Dr. Gerlach, of Wiesbaden, on the effects of sodium benzoate as used in the food industries. These experiments were continued through a long period and appear to have been conducted with great care. From the numerous clinical and metabolism observations made Dr. Gerlach draws the conclusion that sodium benzoate causes no changes in the body which may be considered as harmful, or which may be taken as pointing to departure from the normal in any direction.[18]

COPPER SALTS

It has long been a popular notion that copper salts are decidedly toxic and the older medical literature contains many references to poisoning by verdigris and other combinations of copper. Modern study, however, has shown that these assumed effects were greatly exaggerated. The subject has practical interest now because of the custom, which had its origin in France, apparently, of fixing the color of certain green vegetables by cooking them in the canning process in contact with small amounts of copper sulphate, or other copper salt. The effect depends on the formation of a very stable green compound of copper and a derivative of chlorophyll.

The permissibility of the process has been much debated, especially in France, Germany and Belgium. In France the discussion has been a prolonged one and several scientific commissions have taken part in it. Some of the older commissions made reports finding against the use of

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[18] Dr. med. V. Gerlach, "Physiologische Wirkungen der Benzoesaeure und des benzoesauren Natron," Wiesbaden, 1909.

copper in this way, but in the more recent studies the results seemed to point to the practical harmlessness of the metal in green peas and beans. In consequence of these French investigations, and later ones in Germany, the use of copper in limited amounts is now tolerated by the food laws of most European countries.

There seems to be no question regarding the physiological action of relatively large amounts of copper salts. They behave as irritant poisons and produce nausea, vomiting, purgation, while the small quantities absorbed exhibit characteristic lesions in the liver, spleen, kidneys and other organs. We are concerned, however, with amounts far below those necessary to cause any such violent symptoms, amounts which could scarcely exceed 15 to 20 milligrams of copper daily in any case, and usually much below this. In the coloring of peas and beans the amount of sulphate used is generally less than 1 gram per kilo, a part only of which becomes fixed in the product, the actual copper content being from 25 to 150 mg. per kilo, ordinarily.

What are the effects of small doses, up to 20 milligrams of copper daily? To answer this question experiments have usually been made with the sulphate or other soluble salt, but it should be recognized that this does not exactly correspond to the practical situation, since in the pea or bean the copper is largely combined as phyllocyanin compound, which in its solubility is very different from the ordinary salts, and is much more stable.

The results of a long series of experiments carried out in my laboratory in the last two years have convinced me that the copper perfectly combined in this chlorophyll derivative is practically without any evident physiological action in amounts up to 12 or 15 milligrams daily, which amounts would be contained in a weight of the vegetable as large as any one could eat with a relish for more than a short period. There appears to be no effect on body weight, nitrogen metabolism, blood factors or qualitative or microscopic blood findings. Nausea is not produced. But the case is somewhat different when we turn to small doses of copper salts given in tea, coffee, milk or beer. Here in time we notice some effect, especially in causing nausea and digestive disturbances, and also in some cases a slight modification of the nitrogen partition and some of the blood factors.

In young vegetables with high chlorophyll content the copper sulphate used in small amount appears to be very perfectly combined. This compound is remarkably stable and resists the action of the digestive ferments to a degree which prevents any great absorption of the copper. In the case of the green pea especially the chlorophyll is largely in the hulls, and these, still green with their copper compound, may pass through the alimentary tract and be found in the feces but little changed. This copper-chlorophyll complex is but slowly broken up by hydrogen sulphide or ammonium sulphide.

In older vegetables, however, where the chlorophyll has become considerably destroyed this copper compound can not be formed to the same extent and the copper added in the canning operation goes into a union with proteins which is easily broken down. In this case the copper acts much as it does in the ordinary inorganic salts. In experiments I have found it possible to add 250 to 300 milligrams of copper per kilo to old green peas, and others have reported still higher additions. Much of this copper may be separated easily by dilute hydrochloric acid.

The fact that the non-ionic copper in the phyllocyanate is practically inert physiologically has been noticed by others. Reference here may be made to the work of Tschirsch,[19] Spiro[20] and Brandl.[21] These writers agree that other compounds of copper have a much more marked effect. From these other combinations, as well as from imperfectly coppered vegetables, the metal may reach the liver and other organs and in time produce a marked effect. In a series of experiments by Chittenden this absorption has been clearly shown. As long as it is not practically possible to limit the use of copper in greening to the youngest vegetables only, and in a specified small amount, it would seem that it might be well to prohibit its use altogether in foods, where, indeed, it serves no useful purpose beyond imparting a bright green color.

SULPHUROUS ACID

Sulphurous acid is used in two essentially different ways in the treatment of food products. First, in the free state or the oxide, and secondly, as a salt, usually sodium sulphite, but sometimes the bisulphite. Some years ago there was for a time a limited application of the true hyposulphite, but this seems to have been abandoned. Sulphurous acid found its first uses in this connection in the protection of must before fermentation, and in the racking off or transfer of wines from one vat to another, or just before bottling. These uses are still in vogue, and other uses have been introduced, especially in the clarification of cane juices before boiling down for sugar, and in the treatment of certain fruits in the sun-drying process. Within comparatively recent times the application of sodium sulphite in some of the minor meat industries and in the canning of certain vegetables was introduced.

It will be seen at a glance that we have here two rather distinct conditions. In the application of the sulphurous acid in the sugar, wine and fruit industries there is finally a pretty complete combination of the product with the sugars to form the aldehyde compounds, from which the sulphite is gradually oxidized. These carbohydrate-containing substances hold also certain organic salts, the acids of which are in part displaced by the sulphurous acid. The protein and fatty substances of meats, however, are in themselves inert toward sodium sulphite, and the latter remains unmodified or combined. The fats, in addition, protect the sulphite from rapid oxidation. Among food chemists there seems to be a practical recognition of this distinction in the active condition of the two classes of sulphured products, and the question of permissibility of use has been advanced generally with reference to the sulphites, rather than as concerns the carbohydrate combinations.

As observed with relatively large ingestions all these products exert, of course, a somewhat toxic action, and the toxicity of the carbohydrate combinations seems to run parallel with their rates of dissociation as aldehyde compounds. For the pure aldehydes the rate is rather rapid in the glucose compound, as the lengthy investigations carried out by Rost and Franz and by Kerp have shown.[22] But in their experiments the rate of dissociation of the glucose aldehyde compound is undoubtedly far greater than would be the case in the commercial combinations of fruits and

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[19] "Das Kupfer vom Standpunkte der gerichtlichen Chemie, Toxikologie und Hygiene," Stuttgart, 1893.

[20] *Muench. Med. Wochenschr.*, 56: 1, 1070.

[21] *Arb. aus dem kais. Gesundheitsamt,* 13: 104, 1897.

[22] *Arb. aus dem kais. Gesundheitsamt,* 21: 1904.

syrups, for example, where there is always a great protecting excess of the sugar present. In most of the experiments carried out to test the pharmacological action the dosage of the sulphur compound has been so relatively large as to render difficult a conclusion regarding the behavior of small doses, or those which have practical importance. This is especially true of the experiments of Kionka frequently quoted.[23]

In Lehmann's experiments on dogs and cats, with doses running up to 37.5 and 62 milligrams of sulphurous oxide (150 to 250 milligrams of sulphite) daily, and extending through about 200 days, no definite harmful effects were seen. Lehmann considered these doses relatively large.[24]

I can refer but briefly to the work of two recent French commissions which have studied the behavior of sulphurous acid in wine, with respect to the health of the consumer. As a result of these investigations an official announcement was made about a year ago in France, advancing the allowable content of sulphurous oxide in wine from 350 to 450 milligrams per liter, of which not over 100 milligrams may be in the free state. I have not heard that this tentative standard has been modified.

This whole question is now under review by the commission appointed by the Secretary of Agriculture of this country, but the lengthy investigations undertaken have not yet been brought to a conclusion, and can not, therefore, be discussed here.

JOHN H. LONG

THE THOMAS PENNANT COLLECTION

SINCE the death of Gilbert White's correspondent, Thomas Pennant (1726–1798), the author of "British Zoology," "A Tour in Scotland, Wales and Ireland," and other important works, the collections made by him have remained almost as he left them, at Downing Hall, Holywell, Flintshire. This estate, with the collections, was inherited by a former Countess of Denbigh, and the present owner, the Earl of Denbigh, C.V.O., being about to dispose of it, has presented the whole of the Pennant Collection to the trustees of the British Museum. Accompanying the Collection are several volumes of a manuscript catalogue in which the specimens were, for the most part, entered and numbered. A fairly large proportion of the specimens still bear numbers corresponding with those in the Catalogue, a very fortunate circumstance, since most of the labels that have been preserved had become dissociated from the specimens to which they referred. The Catalogue is accompanied by letters and lists from several of Pennant's distinguished correspondents. Among the 140 birds are the only two known specimens of the extinct British race of capercailzie, as well as the originals of many birds figured in the "British Zoology" (1766). There are also a few mammals, fishes and crustaceans. The recent shells include 16 type-specimens and 70 figured specimens, all described in the "British Zoology." The fossils run to more than 1,000 specimens and include many from foreign localities presented by the Italian naturalist, Allioni, and others. Three of the British Silurian corals were described by Pennant in 1757, and a mammoth tooth from Flintshire was referred to by him in 1771. Of minerals there are about 860 specimens, of which 340 still retain their original labels. Pennant appears to have begun this section of his collection when he visited the Rev. William Borlase, author of "The Natural History of Cornwall," and from him he received specimens from time to time. Other donors were Bishop E. L. Pontoppiden, author of "The Natural History of Norway," and Emannuel Mendes da Costa, author of "The Natural History of Fossils" (1757). Among the Welsh minerals the most important are those from Flintshire which formed the basis for the description of Flintshire minerals published in "The Tour in Wales" (1778). Additions to

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[23] *Arch. Hygiene*, 22: 1896.

[24] *Arch. Hygiene*, 66: 303, 1909.