the result is 1.00 per cent. By averaging he would get a result of 1.03 per cent. which would not be more than 0.03 per cent. away from the truth in either case, and might be much closer than that, so that in this way it is sometimes advantageous to use the sulphuric bulbs, but whether this advantage is sufficient to compensate for the double labor of weighing two bulbs is perhaps doubtful. In cases where the condensation is on the potash bulbs only as in "1.05", of the first table, and none happens on the sulphuric bulbs, there of course the latter are of no use whatever and the whole error falls on the result as much so as if they had not been used; also if the moisture condensation is confined to the sulphuric bulbs, they are of no avail except to introduce an error into the result, not more than 0.030 per cent. however, although the table shows this to be of infrequent occurrence, both bulbs being usually affected, though rarely to the same degree. As before said, the true remedy is doubtless in the use of smaller bulbs, or in the substitution of soda-lime tubes.

In getting the dummy result it is obviously better to use a small calcium-chloride tube than the potash bulbs; as the dummy result, if any, is simply due, if a preheating furnace be used, to moisture escaping absorption by the drying train, no potash need be used; and also in determining the moisture escaping the prolong, it is better to use the small calcium-chloride tube, making several tests. The dummy results in the table show the impossibility of getting anything like absolute blanks, or anything like true blanks by the usual method in very damp weather.

LABORATORY OF THE KEYSTONE SAW WORKS,
PHILADELPHIA, PA.

THE CHEMISTRY OF CASCARA SAGRADA.[1]

BY ALFRED R. L. DOHME AND HERMANN ENGELHARDT.
Received May 21, 1898.

THE most generally used medicines are most probably laxative medicines, and the most generally used laxative medicine is most probably cascara sagrada bark. This is due to the remarkable property it possesses of being a tonic as well as a laxative, and in no less degree to the fact that its action is

[1] Presented by the Special Research Committee at the Forty-Fifth Annual Meeting of the American Pharmaceutical Association, August, 1897.

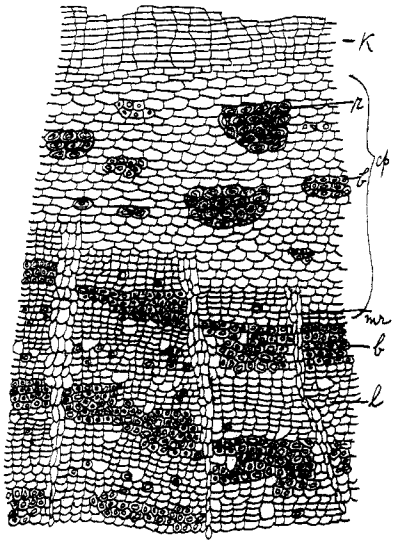
sure and comparatively free from any accompanying unpleasant effects. Most persons can use it regularly for years without it losing its virtues for their particular case. No drug in the pharmacist's armamentarium has sprung into such sudden prominence and has increased in general use to such extent as cascara sagrada. Even conservative Europe, and especially conservative pharmaceutical Europe, has opened its arms and welcomed the "sacred bark" of the Pacific coast as a worthy companion of or possible successor to senna, aloes, or rhubarb. The history of cascara sagrada has been told by Prof. J. U. Lloyd to this association last year at Montreal, and we will not enter upon it here. Quite a number of publications upon the drug and its sister drug, buckthorn bark, have been sent us by the Chairman of the Special Committee of Research of the American Pharmaceutical Association, and we wish to express to him our thanks for the willingness with which he undertook to procure us copies of the various literature we needed for the work. Inasmuch as most of these publications and articles were upon the active principle of the drug and methods of isolating it, and most of them obtained varying results and different compounds, and none of them gave a complete analysis of the drug, we concluded to apply to cascara sagrada the systematic method of plant analysis suggested by Parsons and given in his book upon plant analysis, as well as in Prescott's "Organic Analysis." The result of this proximate analysis of cascara sagrada we will hence give first, giving the detail of the work on the glucoside afterwards.

The cascara sagrada bark used in the investigation was a typical specimen with a light gray cork layer on the outside and a yellowish brown cortical parenchyma layer on the inside. It was gathered in Oregon, and was somewhat less than one year old. It was in thin quills, and markedly bitter when chewed for a few minutes. It was powdered to a number eighty powder and then possessed in that form a yellowish brown color. In cross-section under the microscope it appeared as given in the accompanying sketch.

I. DETERMINATION OF MOISTURE.

Weighed quantities of the air-dried powder were carefully heated in an air-bath at 110° C. to constant weight, and as the

mean of six determinations we found that it contained 8.3 per cent. of moisture. Its color was not perceptibly altered by the repeated heating at this temperature.



CROSS-SECTION OF CASCARA SAGRADA BARK.

x, 100 diam.; *k*, cork cells; *cp*, cortical parenchyma; *s*, stone cells; *b*, bast fibers; *mr*, medullary rays; *l*, libriform.

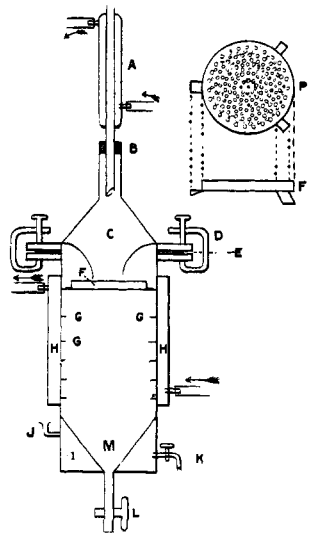
II. DETERMINATION OF ASH.

Weighed quantities of the air-dried powder were carefully incinerated in a platinum dish and finally heated to a bright red heat over a Bunsen burner to constant weight. As the mean of five determinations, the ash was found to represent seven per cent. of the drug, the analysis varying between 6.9 and 7.05 per cent. as extremes. The bark is very difficult to incinerate, as it carbonizes very easily and then cakes, requiring repeated turning and long-continued heating to finally get it all reduced to a uniform gray color. A qualitative analysis of the ash showed the presence of sodium, potassium, and aluminum, with traces of calcium and iron, together with silicic acid and traces of hydrochloric and sulphuric acids.

III. CHLOROFORM EXTRACT.

Although Parsons recommends the use of kerosene to extract

the oils, wax, fat, etc., we found that chloroform answered fully as well. The drug was extracted for five hours in a specially devised apparatus which we constructed, and which is especially adapted to the extraction of large quantities of drug, and is more expeditious than the Soxhlet or Flückiger apparatus. The apparatus is given below.



DRUG EXTRACTION APPARATUS.

A is a Liebig's condenser; *B* is a cork stopper closing head of apparatus *C* and connecting the condenser with it; *C* is the head of the apparatus, which is round like a still and attached to the body of the same by a series of clamps *D* joined by asbestos *E*; *F* are perforated tin plates containing drug and resting upon holders *G* on the inside of the apparatus; *H* is a jacket around the apparatus into which cold, warm, or hot water can be let as wanted; *I* is a similar jacket for bottom of apparatus with inlet *J* and outlet *K*; *L* is the stop-cock of the apparatus; *M* is a funnel-shaped termination of the body of the apparatus, itself terminating in the stop-cocked tube *L*; *P* is a cross-section of one of the perforated plates which have a round piece of filter-paper over all the perforations, and the drug then placed on this.

To operate the apparatus, which is air-tight, charge all the plates, or as many as are needed, with the powdered drug. Pour the menstruum into the apparatus through the condenser tube of *A*, until enough has been added to saturate all the drug and to fill the funnel *M* half full. Then apply a Bunsen burner to the jacket *I*, thus causing the menstruum here to evaporate and pass up through the apparatus and be condensed in *A* and drop

back into the apparatus. If it is a volatile menstruum, the jacket *H* can be supplied with cold water to aid in its condensation; but if, on the other hand, the menstruum is vaporized with difficulty, warm or hot water can be passed into the jacket *H* to facilitate the volatilization of the same and prevent its recondensation before reaching the condenser *A*. After heating the jacket *I*, and continuing the extraction for half an hour or more, pass cold water into the jacket *I*, when all the menstruum in the apparatus will be drawn down into the funnel *M*, whence it can be drawn by the stop-cock *L*. Fresh menstruum is then added as before, and the process repeated until the extract drawn from the stop-cock is colorless.

VOLATILE OIL.

The result of the extraction with chloroform was a dark greenish brown oil of a pronounced odor, reminding strongly of the drug. The yield was 7.5 per cent. of the air-dried drug. We supposed from the pronounced odor that a volatile oil was contained in this extract, and were not mistaken in our conjecture, as we found upon treating the extract with steam that a yellowish green oil passed over with some of the chloroform. This oil was separated from the chloroform, in which it is soluble with very great difficulty, and after redistillation in a vacuum was obtained comparatively pure, but in very small quantity. It is extremely volatile, and possesses, to a marked degree, the characteristic odor of cascara sagrada bark, which hence in all probability derives its odor therefrom. Too little of it was obtained for an analysis, and efforts to saponify it proved fruitless on account of its volatility and the fact that when treated in a sealed tube with saponifying agents it was completely resinified.

FIXED OIL.

The oil remaining in the distilling flask after all the volatile products had been driven off by steam, was again heated with water, and the latter drawn off and tested for alkaloids with potassium mercuric iodide. As no precipitate was obtained, no alkaloids were extracted by the chloroform. Treatment of the aqueous solution with basic lead acetate gave no precipitate,

showing absence of glucosides. It was then warmed slightly with dilute sulphuric acid to recover possibly present free alkaloids, but the effort resulted negatively also. It was then boiled with caustic potash to saponify the fixed oil, and after a short while it was entirely dissolved. After cooling, the solution was extracted with ether which left on evaporation a colorless oil. This oil soon became solid upon standing. It was recrystallized from alcohol and thus obtained in white leaflets melting at 24°–26° C. An analysis by combustion with copper oxide in a stream of oxygen, by the open tube method, gave the following results :

I. 0.107 gram substance gave 0.3024 gram CO_2 and 0.172 gram H_2O.

II. 0.1315 gram substance gave 0.3715 gram CO_2 and 0.210 gram H_2O.

Calculated for $C_{12}H_{26}O$. Per cent.	Found. I. Per cent.	II. Per cent.
C = 77.42	C = 77.07	C = 77.2
H = 13.98	H = 14.4	H = 14.5

The substance is hence one of the numerous possible isomeric dodecyl alcohols, probably the normal dodecyl alcohol which melts at 24° C. It was found to be quite a difficult matter to separate and obtain pure the two fatty acids which are combined with the above dodecyl alcohol to make up the fixed oil of cascara sagrada. However, we believe our results hardly leave any doubt as to their identity. To obtain them, the alkaline liquid, which has been extracted with ether to obtain the above alcohol, was heated to remove all the ether and then treated with hydrochloric acid, which precipitated an oil. This oil soon became solid and was then found to melt at 30° C., although all efforts to purify it by crystallization from alcohol proved futile. The potassium salts of the acids were hence prepared by dissolving the substance in caustic potash and then purified by fractional crystallization from alcohol. As obtained therefrom, it crystallized in pearly leaflets and the acid obtained from it melted at 57° C. An analysis of the acid potassium salt showed it to be a mixture of stearic and palmitic acids. The neutral potassium salt was of course obtained when the fatty oil was saponified by means of caustic potash, but on treating this

with alcohol or water it was converted into the acid salt. The analyses follow:

0.211 gram substance was incinerated and heated to constant weight with sulphuric acid and gave 0.032 gram K_2SO_4.

0.178 gram, similarly treated, yielded 0.027 gram K_2SO_4.

		Found.	
		I.	II.
	Per cent.	Per cent.	Per cent.
Calculated for acid potassium palmitate..	K = 7.09	.....	.....
" " " " stearate ...	K = 6.43	K = 6.8	K = 6.9

The analyses would indicate that the salt obtained was most likely acid potassium palmitate, but the melting-point of the free acid at 57° C., which is below that of palmitic acid, 69.2° C., and that of stearic acid, 62° C., indicates that it is very likely a mixture of both, as a mixture of several substances nearly always tends to lower the melting-point of either. The conclusion reached is then that the fixed oil of cascara sagrada is a mixture of dodecyl palmitate and dodecyl stearate, and we regret that we were unable to definitely settle this point, and hope to be able to do so during the course of the coming autumn.

IV. EXTRACT WITH EIGHTY PER CENT. ALCOHOL.

The residue from the chloroform extract, which had assumed a slightly darker color after being dried, was extracted for twelve hours with eighty per cent. alcohol. The menstruum extracted twenty-seven per cent. of the original air-dried powder. After distilling off the alcohol, there remained a brown, rather hard residue, possessing the characteristic bitter taste of cascara sagrada. It was boiled for half an hour with absolute alcohol, which dissolved the greater portion of it. The solution obtained in absolute alcohol was heated until all the alcohol had passed off, and then extracted with warm water and the aqueous solution treated with basic lead acetate. The result was a reddish brown precipitate, which we believe consisted of a mixture of the lead salt of the glucoside with the lead salts of the tannates present, inasmuch as the precipitate formed by treating the pure glucoside with the same reagent is brick-red in color. It was filtered off and stirred up with water while hydrogen sulphide was passed through to remove all the lead. The lead sulphide was filtered off and the filtrate evaporated to dryness,

resulting in a brown amorphous residue which is soluble in alcohol, acetone, and ethyl acetate. Recrystallized from any of these it forms fine, dark brown needles, but only in small quantities, the majority separating out again in an amorphous condition. This is the glucoside of cascara sagrada which we have named purshianin, analogously to the glucoside frangulin obtained from Rhamnus frangula. That portion of the residue from the eighty per cent. alcohol extract found to be insoluble in absolute alcohol, was treated with hot water and the resulting solution treated similarly with basic lead acetate. The result was a dirty yellow precipitate which, after removal of the lead, gave a dark brown resinous substance, different in color from that obtained from the portion soluble in absolute alcohol. We will enter into the details of the work on these glucosides later.

V. HOT WATER EXTRACT.

The residue from the absolute alcohol extraction, which had now assumed a dark brown color and was practically devoid of taste, was macerated for twelve hours with water and then filtered. The aqueous extract was evaporated to dryness and found to represent about 12.3 per cent. of the weight of the original air-dried drug. It had a dark brown color and was devoid of any taste. The residue from this aqueous extract was boiled with dilute sulphuric acid (1 : 100) to invert all starches present, and the residue filtered off and dried. The amount of starches, sugar, etc., so extracted was not determined, but will appear in the final résumé of the analysis as difference after everything else has been determined.

VI. DILUTE ALKALI EXTRACT.

The dried residue from the hot water extraction was treated with a half per cent. caustic potash solution, which extracted 21.3 per cent. of the original powder, including most all of the remaining coloring-matter. The residue from this extraction was treated with calcium hypochlorite to bleach it, and then yielded 16.1 per cent. of practically white cellulose.

Summed up, these analyses show that cascara sagrada is made up as follows :

	Per cent.
I. Moisture	8.3
II. Soluble in chloroform	7.5
III. Soluble in eighty per cent. alcohol	27.5
IV. Soluble in hot water	12.3
V. Soluble in dilute alkali	21.3
VI. Cellulose	16.1
VII. By difference, starch, etc	7.0
	100.0

THE GLUCOSIDES OF CASCARA SAGRADA.

We next desire to speak in detail of the work we have done upon the glucosides of cascara sagrada. The literature on the glucosides of buckthorn and cascara sagrada is quite extensive, and we will give a general account of what has been done upon them by other investigators. Buckthorn bark (Rhamnus frangula) had been investigated quite considerably before cascara sagrada was known and studied. Casselmann,[1] and later Enz,[2] worked on buckthorn bark and obtained therefrom citron-yellow silky crystals, which were tasteless and odorless, and melted at 226° C. Their composition was for a long time a matter of dispute among chemists, Hesse[3] claiming that the formula was $C_{20}H_{20}O_{10}$ which was also verified by Faust; but Casselmann set up the formula $C_5H_6O_3$ as the result of his analyses. Faust then decomposed the substance by treating it with alcoholic hydrochloric acid and discovered that it was a glucoside, as it yielded him sugar and an acid which he named frangulinic acid. This he obtained in golden yellow crystals, melting at 248°–250° C., difficultly soluble in water, chloroform, and benzene, but easily soluble in ether and alcohol, as well as in alkalies, in which latter it dissolved with formation of a purple-red color. Later investigations showed that this frangulinic acid was the same as emodin, which is trioxymethylanthraquinone. According to Baeumker[4] it is quite an active laxative. Thorpe and Robinson[5] and Thorpe and Miller[6] went into the matter more closely and

[1] Casselmann: Ann. Chem. (Liebig), 104, 77.

[2] Enz: Vierteljahr. d. prakt. Pharm., 16, 106.

[3] Hesse: Ann. Chem. (Liebig), 117, 349.

[4] Baeumker: Exper. Beitr. zur Kenntniss der pharm. Wirkung von Frangulasäure, Göttingen, 1880.

[5] Thorpe and Robinson: J. Chem. Soc., 57, 38.

[6] Thorpe and Miller: *Ibid*, 61, 1.

determined that the glucoside had the formula $C_{21}H_{22}O_9$ and was split up by acids into emodin and a dextrorotatory sugar, which is not glucose, however, but was identified by them as Rhamnose. Schwabe's[1] work on cascara sagrada is quite extensive, and he concluded that the active principle is emodin, which melts at 254° C., and whose formula he determined to be $C_{15}H_{10}O_5 + H_2O$. The cascarin of Le Prince[2] is certainly not a pure substance, to judge by the description given.

Summed up, the work done indicates that buckthorn bark contains a glucoside frangulin and that this is split up into emodin, which is trioxymethylanthraquinone, and a sugar, Rhamnose or isodulcite, and further, that cascara sagrada contains emodin but not frangulin. We proceeded as follows in obtaining the glucoside of cascara sagrada which had, up to the time of our work, not been obtained. The drug was extracted with chloroform to remove fats, etc., and the residue extracted with eighty per cent. alcohol, and the resulting extract dried and dissolved in hot water. On cooling, some resinous, waxy substance separated and was filtered off. The filtrate was treated with lead acetate, which produced a yellow precipitate. This was filtered off and stirred with hot water on a water-bath. As the lead tannates are difficultly decomposable by hydrogen sulphide it is advisable to pass this gas through the suspended precipitate of lead salts at a temperature of about 100° C. This was done until on shaking the flask, whose mouth was closed by the thumb, the latter was raised by the pressure of the gas. The lead sulphide was filtered off and the filtrate evaporated to dryness, resulting in a dark brown substance which consisted mainly of tannins, as portions of them dissolved in water gave good inks on treatment with ferric salts. This tannate mass appears to be composed of several tannins which we did not undertake to investigate, reserving that for a later time, should Prof. Trimble not find time to undertake the same. The filtrate from the lead tannin was treated with basic lead acetate and gave a dark red-brown precipitate of lead glucosides. It is not by any means pure, or it would be colored more nearly cinnabar-red. The precipitate is stirred with hot water in a flask and treated with hydrogen

[1] Schwabe: Archiv. d. Pharm., **226**, 569.
[2] Le Prince: Compt. rend., **115**, 286.

sulphide as before. The filtrate from the lead sulphide on evaporation yields a hard, brown-red substance which is very difficult to obtain in a crystalline form, as efforts to crystallize it from acetone and ethyl acetate resulted only in our obtaining a few dark brown-red needles melting at 237° C., the most of it separating out in an amorphous condition. Not sufficient of it was obtained to make an analysis, but we could confirm that it was not emodin, as it gave no purple color on being treated with caustic potash. It is the glucoside of cascara sagrada which has so far eluded capture, and we have named it purshianin as already explained, being analogous to the frangulin of buckthorn bark. On heating it with alcoholic hydrochloric acid we obtained a sugar and a product which proved to be emodin. The product obtained by heating the purshianin with alcoholic hydrochloric acid was poured into cold water, when a yellow crystalline substance separated out. This was recrystallized from ethyl acetate, which proved the best solvent for the purpose, and separated therefrom in reddish yellow needles melting at 254° C. (one lot melted at 265° C.) and producing a blood-red color on treatment with caustic alkalies. The crystals were dried at 110° C. and appeared to lose some moisture during the process, which was not, however, determined. The analysis of these reddish yellow needles, dried at 100° C., resulted as follows:

I. 0.257 gram gave 0.6304 gram carbon dioxide and 0.0972 gram water or 66.9 per cent. carbon and 4.2 per cent. hydrogen.

II. 0.091 gram gave 0.02330 gram carbon dioxide and 0.032 gram water or 66.83 per cent. carbon and 3.9 per cent. hydrogen.

Calculated for $C_{15}H_{10}O_5$.	Found. I.	Found. II.
C = 66.6	C = 66.9	C = 66.83
H = 3.7	H = 4.2	H = 3.9

These figures, together with the melting-point 254° C., leave little doubt but that the substance in hand was emodin, which has also been found to be the active principle of buckthorn bark and likely in a measure of rhubarb. The sugar that is formed when purshianin is saponified appears to be dextrorotatory and non-fermentable, but we have not yet examined it with sufficient care to arrive at a definite conclusion as to what it is. It will

be necessary to obtain a quantity of it, make its osazone, and endeavor to recognize it by the properties and analysis thereof. It appears that the glucoside purshianin is certainly one of the active principles of the drug as in doses of one-fifth of a grain it produces the effects of the drug as far as these affect the bowels. Purshianin is tasteless and odorless, and soluble in alcohol, ethyl acetate, acetone, alkalies, and hot water. We wish to reserve for ourselves its further study, which we hope will bring to light wherein the difference between frangulin and purshianin lies. Frangulin is an orange-yellow powder melting at 225° C., according to Thorpe and Robinson, while we find that purshianin is a dark brown-red crystalline substance melting at 237° C. Curiously enough, both are glucosides and yield the same substance on being saponified; *viz.*, emodin. The difference cannot hence lie in anything but the sugars that are combined with the emodin to form the glucosides, or perhaps in the way in which these are combined. A fact it is, nevertheless, and notwithstanding the above apparent marked similarity, that cascara sagrada acts more agreeably and effectively than buckthorn bark, which it has practically supplanted. It may be possible that both of these drugs do actually contain as their active principle the identical glucoside, and that the cascara either contains more of it or produces a happier result on the patient by virtue of its other accompanying constituents. We hope to be able to solve this question this autumn, and also to isolate the bitter principle of the bark and determine in what way magnesia or lime removes or alters the same so as to render the preparation free from bitterness.

LITERATURE UPON RHAMNUS FRANGULA AND RHAMNUS PURSHIANA.

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1876, Liebermann and Waldstein: *Ber. d. chem. Ges.*, **9**, 1775; *J. Chem. Soc.*, **31**, 477.
1879, Prescott: *Am. J. Pharm.*, **51**, 165.
1885, Kennedy and Wiltrout: *Proc. Am. Pharm. Ass.*, **33**, 499.
Limousin: *J. Pharm. Chim.*, (5), **6**, 80; *Pharm. J. Trans.*, **15**, 615.
1885, Wise: *Western Druggist*, 7, 89.
1886, Wenzell: *Pharm. Rundschau*, **4**, 79; *Pharm. J. Trans.*, **16**, 918.
1887, Butterfield: *Pharm. J. Trans.*, **18**, 473.
1888, Meier and Webber: *Am. J. Pharm.*, **60**, 87.
1888, Eccles: *Drug. Circ.*, **32**, 54; *Proc. Am. Pharm. Ass.*, **36**, 402.

1888, Schwabe: *Archiv. Pharm.*, **226**, 569; *Proc. Am. Pharm. Ass.*, **37**, 491.
1889, Findlay: *Pharm. J. Trans.*, **20**, 491.
1889, Fuge: *Pharm. J. Trans.*, **19**, 736.
1889, Zeig: *Proc. Am. Pharm. Ass.*, **37**, 261.
1890, Rusby: *Proc. Am. Pharm. Ass.*, **38**, 203; *Bulletin Pharm.*, **5**, 115.
1892, Blanc: *Revue Therapeutique*, 326.
1892, Le Prince: *Compt. Rend.*, **115**, 286; *Pharm. J. Trans.*, **23**, 183; *Proc. Am. Pharm. Ass.*, **41**, 691.
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1893, Braeutigam: *Pharm. Centralh.*, **34**, 385.
1890, Thorpe and Robinson: *J. Chem. Soc.*, **57**, 38.
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BALTIMORE, AUGUST 1, 1897.

MOLECULAR WEIGHTS OF SOME CARBON COMPOUNDS; A FEW WORDS MORE.

BY C. L. SPEYERS.

Received May 26, 1898.

IN a short review by Noyes[1] of an article by me,[2] Noyes writes: "No discussion of the results is given, however, nor is any evidence of their accuracy presented, which is particularly unfortunate, since, according to the reviewer's experience, a Beckmann thermometer, which is subjected to considerable variations of pressure, may give quite unreliable readings, owing to the imperfect elasticity of the bulb."

In regard to the discussion of the results, I would state that the measurements made at the boiling-points under ordinary pressures need no discussion; such measurements have been thoroughly discussed by others. In regard to the measurements made under reduced pressure, I would state that I am altogether at a loss to account for the peculiar results obtained. The values given under "cor." in my article show that the rise in the temperature is, in most cases, probably the rise actually caused by the substance dissolved and that the rise is not appreciably influenced by irregular boiling nor by the very slight change in pressure during a set of determinations.

In regard to an error that might seem to come from the imperfect elasticity of the thermometer bulb, I would state that

1 *Rev. Am. Chem. Research*, 4, 55 (*1898*).
2 *J. Phys. Chem.*, 1, 766 (*1897*).