colate that has once established a saturation equilibrium with the extractive material in the plant cells. The second series of experiments seems to indicate that a large amount of the difficulty in extraction, which has been ascribed to the impenetrability of the plant cells to the menstruum, is probably not due to that at all, but likely due to the fact that the menstruum is functioning simultaneously as solvent for the alkaloids and the inert extractive material and that the relative proportions of each extracted are determined by the relative quantities present. Therefore after the removal of a portion of the extractive material, the relative quantity of alkaloid that will dissolve in any given portion of the menstruum is greater and thus a smaller quantity is required.

It is interesting to note that the quantity of solvent required ultimately reaches a minimum, which fact is in accordance with the theory discussed in the foregoing paragraphs, namely, the equilibrium theory, which puts the extraction problem in the realm of an experiment in osmosis.

CONCLUSION.

A search for a solvent in which inert extractive matter is quite insoluble and alkaloidal salts wholly dissolve, would seem to be the next reasonable investigation of this problem.

SOME OBSERVATIONS ON GLYCERIN SUPPOSITORIES.*

BY WILBUR L. SCOVILLE.

One of the simplest preparations in the Pharmacopœia from a chemical standpoint, is that of glycerin suppositories, but from the physical standpoint it is the most complex.

Chemically they consist simply of glycerin in which is dissolved sufficient sodium stearate to form a solution, which when cold is firm enough to hold its form and can be handled easily, and yet will melt or dissolve in the body secretions at body temperature. The U. S. P. suppositories are thus composed, and in addition they contain a slight excess of sodium carbonate and a little water. In making the suppositories some water is necessarily formed in the reaction between the stearic acid and sodium carbonate, and more is introduced by dissolving the sodium carbonate in water as the easiest method of manufacture.

The official suppositories are of fair consistence, but they are opaque. Most of the glycerin suppositories of commerce are transparent, or at least translucent. This quality adds to the appearance of the suppository, though it makes no difference with its medicinal value.

As compounded, the U. S. P. formula produces the following composition:

Glycerin	80.00%
Sodium Stearate	6.50%
Sodium Carbonate	0.17%
Water	13.33%
	100.00%

* Read before Section on Practical Pharmacy and Dispensing, A. Ph. A., Buffalo meeting, 1924.

The main objection to these suppositories is that they are opaque. Manufacturers supply transparent suppositories which are more attractive; they suggest glycerin by their appearance.

Now since the opacity must be due to either (1) imperfect saponification of the stearic acid, or (2) imperfect solution of the soap formed, or some reactionary product, or (3) hydrolysis of the soap, it is evident that to secure transparent suppositories one must be sure that the stearic acid is completely saponified and that too much water is not present. We know that sodium stearate is completely soluble in glycerin, and since an excess of sodium carbonate is used the stearic acid must be completely saponified if sufficient heat is employed for the reaction and solution. We also know that water hydrolyzes sodium stearate, liberating an acid soap which is not completely soluble, and thus will give an opaque solution. So it follows that if we wish a transparent suppository we need only to reduce the amount of water and we will get the transparency. A trial proves this to be the case, but the mass is then too soft. It is so soft, in fact, that it will not come out of the moulds intact.

This change in consistence is unexpected, but it apparently indicates that a little more sodium stearate will remedy that defect and settle the problem. Another trial launches us into "the perversity of inanimate things," for the second experiment comes out even softer than the first, although the sodium stearate content is greater. Evidently there is something more to this problem than simply adjusting the proportions of glycerin and sodium stearate.

If we now tackle the problem systematically we may note first that the U. S. P. formula contains about 15% excess of sodium carbonate above what is needed for saponifying the stearic acid. Is that necessary? A few experiments will demonstrate that a nearly neutral soap, even if completely saponified, gives us more opaque suppositories. The excess of alkali helps to produce the transparency. On the other hand the excess of alkali softens the suppository mass. A few trials disclose that the best results are secured when there is present an excess of alkali of from 10% to 15% above the theoretical need. This ratio of excess appears to give the most satisfactory balance between the tendency to opacity and that toward softening.

Therefore, an excess of alkali is not merely an easy assurance of complete saponification but it is a promoter of transparency.

Now turn to the question of the water content. Here we quickly learn that water has the opposite effect from the alkali. The less water there is present the softer is the mass, and the more transparent. When no water is present beyond that formed in the reaction, the mass is beautifully clear, but so soft that it cannot be moulded well.

The following three formulas will illustrate the effects of changing proportions:

	1.	2.	3.
Glycerin	80.00	80.00	80.00
Stearic Acid	5.33	8.00	10.00
Sodium Carbonate, U. S. P.	1.33	2.00	3.50
Water	13.37	10.00	7.50
To make	100.00	100.00	100.00

The first formula is that of the U. S. P. IX. The suppositories are fairly firm but opaque. They would be more satisfactory if they were a little harder, particularly for the infant's sizes and shapes.

The second formula produces a suppository which is translucent and is firmer than the first. It is more satisfactory in both respects. The third formula produces a suppository which is much softer than either of the others—though it contains the most sodium stearate, but is transparent.

We can now conclude that a moderate excess of alkali is necessary to secure transparency, and that water is necessary to produce the desired firmness of the mass, but that too much of either will offset the effects of the other. That is, too much alkali makes a soft mass, and too much water produces an opaque one. A proper balance of the two will secure the better results.

Just to satisfy ourselves that this theory is sound, a few lots of suppositories were made, using sodium hydroxide in place of sodium carbonate, the hydroxide being properly related to the stearic acid used. These experiments confirmed our conclusions. When a neutral soap was attempted the mass was opaque. When about 10 to 12% of excess alkali was used, the mass was transparent, but softer. When 20 per cent. of alkali was used the mass was too soft. Variations in the proportions of water gave the opposite effects as in the first experiments.

But the experiments with hydroxide developed another point. It was noticed that with the caustic alkali the suppositories were clearer than those made with carbonate. This suggested that the carbon dioxide liberated in the carbonate reaction was a factor in the transparency. Suppositories containing free caustic alkali are inadmissible, although they are easier to make and are more attractive. So the next set of experiments involved the degree and amount of heat to be used. Lots were made at varying temperatures, from 90° C. to 130° C. The carbon dioxide was driven out quite rapidly at temperatures of 120° C. and above, and the suppositories were quite clear—but soft. Under 100° C., a longer heating was necessary to get rid of the dissolved gas, but the consistence of the mass was better.

Temperatures above 100° C. appear to drive out some of the water, and so produce a soft mass. A temperature of about 95° C., such as is obtained on a steam-bath, is safer. In small lots of 100 to 125 grams, about one-half hour of heating was found to be necessary to drive out the excess of gas. Several lots were heated five or six hours at this temperature (95° C.) in a wide-mouth flask—almost a beaker—and found to yield a satisfactory mass. Hence the mass should not be heated above the temperature obtained from a steam-bath, but the heating should be continued, with occasional vigorous stirring, until the gas is driven out and the liquid is perfectly clear. This promotes transparency.

One other suggestion came to us in the course of the experiments. Since water is needed to produce a sufficiently firm mass, but tends to spoil the transparency, how would alcohol do in place of part of the water? We know that alcohol is used to make transparent soaps, and it might be expected to improve the suppositories.

Trial found that this is correct, so far as improving the transparency is concerned. When alcohol is used in place of a part of the water, the suppositories are clearer—but softer. In the experiments made, the added clearness was considered to be more than offset by the decreased hardness.

Thus the best substitute for the U. S. P. IX formula that I have to offer at present is the following:

Glycerin	80.00 Gm.
Stearic Acid	8.00 Gm.
Sodium Carbonate, Monohydrated	2.00 Gm.
Water	10.00 Gm.
To make	100.00 Gm.

COMMERCIAL SUPPOSITORIES.

As before stated, the commercial suppositories are nearly all transparent—or at least translucent. Some of them claim to contain 95% of glycerin.

To learn if there are any chemical tricks in making these, six different brands were obtained and a partial analysis made of them. The glycerin was estimated by simply acidulating the melted suppository mass, adding water and extracting the fatty acids with ether. Then the acid liquor was titrated with standard dichromate solution. If any alcohol were present, it would be estimated as glycerin, and would figure as more glycerin than alcohol. Since a marked alcoholic odor was observed when the bottle was first opened, in two instances there is reason to think that alcohol is used in some of the commercial suppositories. This will make the glycerin estimations high, and the figures for glycerin should be taken with a mental allowance. The results are probably high in several instances.

	% Glycerin.	% Ash grav.	% Ash vol.	% Fatty acid.	M. p. fatty acid.	Reaction.	Appearance.
U. S. P.	80	1.13	1.13	5.33	56° C	Alk.	Opaque
No. 1	61	1.38	1.38	4.32	55.5	Alk.	Transluc.
No. 2	87	2.58	2.58	6.16	55.5	Alk.	Transluc.
No. 3	93	0.82	0.78	4.02	52.2	Sl. alk.	Transluc.
No. 4	90	1.63	1.48	9.12	55.5	Sl. alk.	Transluc.
No. 5	94	1.75	1.65	4.13	55.0	Alk.	Transluc.
No. 6	88.5	1.17	1.06	6.27	54.5	Sl. alk.	Transluc.

The U. S. P. suppositories were not analyzed. Those figures are theoretical and are given for comparison.

An attempt was made to estimate water directly by distributing the melted suppository on asbestos fiber and drying in a vacuum over sulphuric acid, but the results were so obviously of no value that they were discarded.

The ash was first weighed, then titrated and figured as sodium carbonate. The results show that the ash consisted mostly of sodium carbonate in all cases.

The melting points of the separated fatty acids show that these consisted of stearic acid in all cases but one (No. 3) in which a mixture of stearic acid and some other fat may have been used.

An attempt was also made to estimate the free alkali by titration, but the results were not good. The analyses are far from complete, but are sufficient to show that essentially the suppositories all consist of a solution of sodium stearate in glycerin. In other words they are simply modifications of the U. S. P. formula.

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