These crystals were removed from the noncrystalline portion by stirring with Skelly-solve B in which the latter was readily soluble. The crystalline portion was removed by a suction filter. This material when purified by several recrystallizations from a mixture of alcohol and ether, gave rosettes of needles. The crystals melted at 175° C. and its acetate at 195° C. The free alcohol gave a rose to rose purple and finally a deep purple when subjected to the Lieberman-Burchard test for sterols.

Resin Alcohol No. 3.—Prolonged extraction of the nonsaponifiable portion with Skelly-solve B gave a very small amount of material which crystallized in rosettes of needles from the concentrated extract. Several crystallizations from alcohol and ether gave rosettes of platelets. These crystals although appearing to be very pure gave a very indefinite melting point. They appeared to soften at about 220° C. and liquefied at 235° C.

These crystals gave a pink to orange to a red-orange with the Lieberman-Burchard reagent. The amount of material was too small to warrant the preparation of a derivative or further investigation.

SUMMARY

A phytosterol, apparently one of the sitosterols or a mixture of sterols, and three resin alcohols were isolated from the nonsaponifiable portion of the petroleum ether extract of the outer bark of the root of *Celastrus Scandens*.

REFERENCES

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(2) *Biochem. Z.*, 282 (1935), 441.

Incompatibilities in Prescriptions

III. The Use of Inert Powders in Capsules to Prevent Liquefaction Due to Formation of a Eutectic Mixture*,†

By William J. Husa‡ and Charles H. Becker

In filling prescriptions for powder mixtures to be dispensed in capsules, pharmacists frequently encounter difficulties due to liquefaction or formation of a pasty mass (1), (2). The present paper is devoted to the correction of incompatibilities due to formation of a mixture having a melting point below room temperature (eutectic mixture).

One of the methods used in dealing with powders which liquefy or become pasty is to incorporate an inert powder such as starch, magnesium oxide, magnesium carbonate, talc, lactose, etc. In spite of the wide use of such inert powders, apparently no systematic studies have previously been made to determine the relative efficiency of the various powders, or to ascertain the best methods of combining the inert powders with the ingredients prescribed.

The present investigation was carried out to supply practicing pharmacists and teachers of pharmaceutical dispensing with more exact information regarding the best methods of selecting and using inert powders to overcome liquefaction in prescriptions for capsules.

EXPERIMENTAL PART

Prescription No. 1

℞ Camphor	gr. 1/4
Salol	gr. iii

Fac tales capsulæ no. xx. One capsule t. i. d. a. c.

When the ingredients of this prescription were triturated a pasty mass was formed. A study was made to determine the relative efficiencies of eight different inert powders in preventing or obviating the difficulty. In each case the camphor was triturated with the inert powder; the salol was then added and the mixture triturated lightly. The temperature at the time of compounding was from 70° to 74° F. The finished capsules were kept under observation for two weeks in open beakers as well as in closed capsule vials.

With reference to the period of observation, it may be said that many pharmacists lay too much stress on the appearance of capsules at the time they are dispensed, with little consideration of the changes which may occur before all the capsules are used.

Obviously the use of an inert powder increases the size of the capsule to a certain extent depending on the relative quantity of powder used and its bulkiness. This factor must always be kept in mind since many patients find it difficult to swallow the larger capsules. In exceptional cases it may be necessary to divide the material into twice the number of capsules designated and to double the dose

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as to number of capsules. In the present study the size of capsule required in each case was recorded and the results have a bearing on the choice of the quantity and kind of inert powder that would be best to use.

In all the tables in the present paper the following abbreviations are used: L. = soft mass or liquid; P. = dry powder; D. = damp powder; S. D. = slightly damp powder; C. M. = cement-like mass. The quantity of inert powder is stated in grains per capsule.

Table I.—Prescription No. 1. With Inert Powders

Capsules Stored in Open Containers

Inert Powder, Grs.	Size of Capsule	Time in Days 0	1	2	4	14
Heavy Magnesium Oxide						
1	2	D.	L.	L.	L.	L.
2	1	S. D.	D.	D.	L.	L.
3	1	P.	P.	P.	S. D.	D.
4	0	P.	P.	P.	S. D.	D.
5	0	P.	P.	P.	S. D.	D.
Light Magnesium Oxide						
1	2	P.	L.	L.	L.	C. M.
2	1	P.	D.	D.	L.	C. M.
3	0	P.	P.	P.	P.	S. D.
4	00	P.	P.	P.	P.	S. D.
5	00	P.	P.	P.	P.	S. D.
Talc						
1	2	L.	L.	L.	L.	L.
2	1	D.	L.	L.	L.	L.
3	1	S. D.	S. D.	D.	D.	D.
4	1	S. D.	S. D.	D.	D.	D.
5	0	S. D.	S. D.	D.	D.	D.
Lactose						
1	2	L.	L.	L.	L.	L.
2	1	D.	D.	L.	L.	L.
3	1	S. D.	D.	D.	D.	D.
4	1	S. D.	S. D.	S. D.	D.	D.
5	0	S. D.	S. D.	S. D.	D.	D.
Magnesium Carbonate						
1	2	P.	P.	P.	P.	P.
2	1	P.	P.	P.	P.	P.
3	0	P.	P.	P.	P.	P.
4	00	P.	P.	P.	P.	P.
5	00	P.	P.	P.	P.	P.
Corn Starch						
1	2	L.	L.	L.	L.	L.
2	1	D.	D.	L.	L.	L.
3	1	S. D.	S. D.	D.	D.	D.
4	1	S. D.	S. D.	S. D.	D.	D.
5	0	S. D.	S. D.	S. D.	S. D.	D.
Wheat Starch						
1	2	L.	L.	L.	L.	L.
2	1	D.	L.	L.	L.	L.
3	1	S. D.	S. D.	D.	D.	D.
4	1	S. D.	S. D.	S. D.	S. D.	D.
5	0	S. D.	S. D.	S. D.	S. D.	D.
Potato Starch						
1	2	L.	L.	L.	L.	L.
2	1	D.	L.	L.	L.	L.
3	1	S. D.	S. D.	D.	D.	D.
4	1	S. D.	S. D.	S. D.	D.	D.
5	0	S. D.	S. D.	S. D.	S. D.	D.

Table I shows that magnesium carbonate was most effective in preventing liquefaction, one gr. per capsule being sufficient to maintain the ingredients as a powder. Light magnesium oxide was somewhat better than heavy magnesium oxide but both of these powders were less efficient than magnesium carbonate. Talc, lactose and the starches were rather ineffective. It was observed that all capsules containing light magnesium oxide developed a pink color, which was more intense with the smaller proportions of light magnesium oxide. With the use of one or two grs. of light magnesium oxide per capsule, the ingredients eventually formed a mass of cement-like hardness. In all cases of liquefaction or pastiness, the ingredients shrunk to about half of the original volume. The results with the capsules stored in closed vials were similar to those with the capsules placed in open beakers; for this prescription, tight closure of the container was of no distinct advantage.

Since various textbooks have recommended that starch should be dried at 100° C. for use in powders, experiments were carried out to determine whether or not such dried starch had an advantage over ordinary starch. Similar comparisons were made with the other inert powders used in the present study. In each case, a portion of the powder was dried to constant weight at 100° C. The percentage loss in weight on drying was as follows: potato starch, 15.1; corn starch, 12.0; wheat starch, 11.7; magnesium carbonate, 2.6; heavy magnesium oxide, 1.5; light magnesium oxide, 1.0; talc, 0.2; lactose, 0.1.

Prescription No. 1 was filled using the same procedure as before, except that the oven-dried inert powders were used; the results are given in Table II.

Table II.—Prescription No. 1. With Oven-Dried Inert Powders

Capsules Stored in Open Containers

Inert Powder, Grs.	Size of Capsule	Time in Days 0	1	2	4	14
Heavy Magnesium Oxide						
1	2	D.	L.	L.	L.	L.
2	1	P.	S. D.	D.	D.	D.
3	1	P.	P.	P.	P.	S. D.
4	0	P.	P.	P.	P.	S. D.
5	0	P.	P.	P.	P.	S. D.

Table II.—(*Continued*)

		Light Magnesium Oxide				
1	2	P.	L.	L.	L.	C. M.
2	1	P.	P.	S. D.	S. D.	S. D.
3	0	P.	P.	P.	P.	S. D.
4	00	P.	P.	P.	P.	S. D.
5	00	P.	P.	P.	P.	S. D.
		Talc				
1	2	D.	L.	L.	L.	L.
2	1	S. D.	L.	L.	L.	L.
3	1	S. D.	S. D.	D.	D.	D.
4	1	S. D.	S. D.	D.	D.	D.
5	0	S. D.	S. D.	D.	D.	D.
		Lactose				
1	2	L.	L.	L.	L.	L.
2	1	D.	D.	D.	L.	L.
3	1	S. D.	S. D.	D.	D.	D.
4	1	S. D.	S. D.	S. D.	D.	D.
5	0	S. D.	S. D.	S. D.	D.	D.
		Magnesium Carbonate				
1	2	P.	P.	P.	P.	P.
2	1	P.	P.	P.	P.	P.
3	0	P.	P.	P.	P.	P.
4	00	P.	P.	P.	P.	P.
5	00	P.	P.	P.	P.	P.
		Corn Starch				
1	2	L.	L.	L.	L.	L.
2	1	D.	D.	L.	L.	L.
3	1	S. D.	D.	D.	D.	D.
4	1	P.	S. D.	S. D.	D.	D.
5	0	P.	S. D.	S. D.	D.	D.
		Wheat Starch				
1	2	L.	L.	L.	L.	L.
2	1	D.	D.	L.	L.	L.
3	1	S. D.	D.	D.	D.	D.
4	1	S. D.	S. D.	S. D.	D.	D.
5	0	P.	S. D.	S. D.	D.	D.
		Potato Starch				
1	2	L.	L.	L.	L.	L.
2	1	D.	D.	L.	L.	L.
3	1	S. D.	D.	D.	D.	D.
4	1	P.	S. D.	S. D.	D.	D.
5	0	P.	S. D.	S. D.	D.	D.

Table II again indicates that magnesium carbonate was most effective in preventing liquefaction. Drying to constant weight was of practically no advantage in the case of talc, lactose and the various starches. Drying was slightly beneficial for light and heavy magnesium oxides. Results on the capsules stored in closed vials were similar to the results on capsules stored in open containers as given in Table II.

It would be expected that the condition of the air as to temperature and humidity might have an effect on the stability of capsules in certain cases. The capsules of the previous experiment which had not shown liquefaction of the contents after two weeks were tested for stability at higher humidity by storage under a bell jar in which the air had previously been adjusted to a relative humidity of 75. The results showed that this humidity had no effect on the contents of the capsules in open beakers after three days. However, the gelatin capsules themselves became damp and soft. After reëxposure to the atmosphere the capsules regained their original condition after about a half day with the exception that the contents of the capsules containing light or heavy magnesium oxide became as hard as cement. There was no change in the capsules in closed vials.

In compounding prescriptions containing substances which tend to liquefy, it is usually considered best to mix one of the ingredients with an inert powder before mixing with the remaining substances or to mix each ingredient separately with some of the inert powder before combining the various ingredients. However, it has also been suggested (3) that the inert powder should be added to the liquefied material in a mortar. To determine the effect of variations in the method of compounding, prescription No. 1, with the addition of one gr. of magnesium carbonate per capsule, was compounded in several different ways as follows: (A) the salol and magnesium carbonate were triturated and the camphor added with light trituration, (B) same as A except that heavy trituration was employed, (C) the camphor and magnesium carbonate were triturated and the salol added with light trituration, (D) same as C except that heavy trituration was employed, (E) the camphor was triturated with part of the magnesium carbonate and the salol was triturated with the remainder of the magnesium carbonate and the two resulting powders were then mixed with light trituration, (F) same as E except that heavy trituration was employed, (G) the camphor, previously powdered with aid of a few drops of alcohol, was mixed with the magnesium carbonate and then the salol was added with light trituration, (H) the salol and camphor were triturated to form a pasty mass, the magnesium carbonate was added and the mixture triturated lightly, (I) same as H except that the pasty mass was added to the inert powder.

Table III.—Prescription No. 1. Effect of Variations in Method of Compounding. Capsules Stored in Open Containers

Method	Time in Days 0	1	2	4	14
A	P.	P.	P.	P.	P.
B	S. D.	S. D.	S. D.	S. D.	D.
C	P.	P.	P.	P.	P.
D	S. D.	S. D.	S. D.	S. D.	D.
E	P.	P.	P.	P.	P.
F	S. D.	S. D.	S. D.	S. D.	D.
G	P.	P.	P.	P.	P.
H	S. D.	S. D.	S. D.	S. D.	S. D.
I	S. D.	S. D.	S. D.	S. D.	S. D.

The results in Table III show that it is unwise to triturate the liquefiable ingredients before adding the inert powder. It is preferable to first mix one incompatible ingredient with the inert powder or each incompatible ingredient with a separate portion of the inert powder. The results also clearly indicate that light trituration may be used but that heavy trituration is objectionable.

Tests were made to determine whether camphor might be lost from the capsules on standing due to its volatility. Prescription No. 1 was compounded using one gr. of heavy magnesium oxide per capsule in one test and using the same proportion of lactose in another test. Each capsule was weighed accurately on an analytical balance. The capsules were then stored for three weeks in open containers and also in closed vials. Although the contents of the capsules liquefied in each case, there was no appreciable gain or loss in weight of the capsules in either type of container.

Prescription No. 2

℞ Camphor	gr. i
Salol	grs. iii
Aspirin	grs. ii
Caffeine citrate	gr. i

M. ft. of such doses, capsules no. xii.

On compounding the prescription as written, a damp powder results, gradually becoming semi-liquid. To overcome the formation of a pasty mass, it was recommended (4) that half of the citrated caffeine be replaced by half its weight of caffeine base (in order to adjust the strength), and that one gr. of heavy magnesium oxide to the capsule be added, the latter to be combined with each ingredient separately before mixing all to form a uniform powder.

Table IV.—Prescription No. 2. With Inert Powders

Capsules Stored in Open Containers

Inert Powder, Grs.	Size of Capsule	Time in Days 0	1	2	4	14
Heavy Magnesium Oxide						
1	1	D.	L.	L.	C. M.	C. M.
2	0	P.	L.	C. M.	C. M.	C. M.
3	00	P.	C. M.	C. M.	C. M.	C. M.
4	00	P.	C. M.	C. M.	C. M.	C. M.
5	00	P.	C. M.	C. M.	C. M.	C. M.
Light Magnesium Oxide						
1	0	P.	L.	L.	C. M.	C. M.
2	00	P.	P.	D.	D.	C. M.
3	00	P.	P.	S. D.	S. D.	C. M.
4	0[a]	P.	P.	P.	P.	C. M.
5	0[a]	P.	P.	P.	P.	C. M.
Magnesium Carbonate						
1	0	P.	D.	D.	L.	L.
2	0[a]	P.	S. D.	S. D.	S. D.	L.
3	0[a]	P.	P.	P.	P.	P.
4[a]	0	P.	P.	P.	P.	P.
5[a]	0	P.	P.	P.	P.	P.

[a] Double the number of capsules were made.

Table IV.—(*Continued*)

Talc						
5	00	P.	L.	L.	L.	L.
Lactose						
5	00	P.	L.	L.	L.	L.
Dried Corn Starch						
5	00	P.	L.	L.	L.	L.
Dried Wheat Starch						
5	00	P.	L.	L.	L.	L.
Dried Potato Starch						
5	00	P.	L.	L.	L.	L.

On combining the ingredients as advised and placing individual doses in No. 1 capsules, the contents liquefied within a day. After standing four days the ingredients developed into a mass of cement-like hardness. Similar results were obtained when using 2 grs. of the inert powder per capsule and placing individual doses in No. 0 capsules. Using 3, 4 and 5 grs. of the inert powder, respectively, per individual dose and using No. 00 capsules, liquefaction did not occur, but the ingredients developed into a mass of cement-like hardness.

Tests were carried out in which prescription No. 2 was filled, with the addition of inert powders. The temperature was between 75° and 78° F. In each case the camphor was triturated with the inert powder and the aspirin, citrated caffeine and salol were added in the order named, after which the final mixture was triturated lightly.

The results show that magnesium carbonate was most efficient as an inert powder. Although as much as 3 grs. of the inert powder per capsule was required to prevent liquefaction, it did not change the ingredients into a mass of cement-like hardness. Both light and heavy magnesium oxides were equally as efficient as magnesium carbonate in preventing liquefaction but the capsules containing these inert powders developed into a cement-like mass after standing two weeks. Talc, lactose and the various dried starches did not prevent liquefaction even when using 5 grs. of the inert powder per capsule. In all capsules where liquefaction or a soft mass developed, the ingredients shrunk considerably.

The appearance of the capsules placed in closed containers was similar to those placed in open beakers and neither type of container had any distinct advantage over the other.

To determine the effect of variations in the method of compounding, prescription No. 2, with the addition of three grs. of magnesium carbonate per capsule, was compounded in several different ways as follows: (A) the salol and magnesium carbonate were triturated first and the camphor, citrated caffeine and aspirin were added in the order named,

the entire mixture being triturated lightly, (B) same as A except that the final mixture was triturated with pressure, (C) the camphor and magnesium carbonate were triturated first and the citrated caffeine, aspirin and salol were added in the order named, the final mixture being triturated lightly, (D) same as C except that the final mixture was triturated with pressure, (E) part of the magnesium carbonate was mixed with the camphor and the remainder of the magnesium carbonate was mixed with the salol; the resulting powders were mixed lightly and the citrated caffeine and aspirin were added after which the entire mixture was triturated lightly, (F) same as E except that the entire mixture was triturated with pressure, (G) the camphor, previously powdered with the aid of a few drops of alcohol, was mixed with the magnesium carbonate and the citrated caffeine, aspirin and salol were added in the order named and the final mixture was triturated lightly, (H) the ingredients were triturated until the mixture liquefied, the magnesium carbonate was added and the entire mixture was triturated, (I) same as H except that the liquid mixture was added to the magnesium carbonate.

Table V.—Prescription No. 2. Effect of Variations in Method of Compounding

Capsules Stored in Open Containers

Method	Time in Days 0	1	2	4	14
A	P.	P.	P.	P.	P.
B	S. D.	D.	D.	D.	D.
C	P.	P.	P.	P.	P.
D	S. D.	D.	D.	D.	D.
E	P.	P.	P.	P.	P.
F	S. D.	D.	D.	D.	D.
G	P.	P.	P.	P.	P.
H	S. D.	S. D.	S. D.	S. D.	S. D.
I	S. D.	S. D.	S. D.	S. D.	S. D.

The results in Table V clearly indicate that it is preferable to first mix one incompatible ingredient with the inert powder or each incompatible ingredient with a separate portion of inert powder. It is shown that heavy trituration is objectionable. The results on capsules stored in closed vials were similar to those on capsules placed in open containers.

Prescription No. 3

℞ Acetophenetidin	gr. i
Acetylsalicylic acid	gr. ii
Quinine ethylcarbonate	gr. ii

M. ft. caps. No. 1. Disp. tales no. xii.

On mixing acetylsalicylic acid and quinine ethylcarbonate a dry powder resulted. However, the ingredients developed into a mass of cement-like hardness within a day. After standing two weeks, the ingredients shrank to one-half of the original size and remained in a hardened condition. A mixture of acetophenetidin and quinine ethylcarbonate remained dry after standing two weeks. There was no hardening of the contents. On compounding the prescription as written a dry powder resulted and individual doses were put in No. 1 capsules. The ingredients developed into a cement-like mass within a day and, after standing two weeks, the contents shrank and remained in a hardened condition.

Prescription No. 3 was filled with the addition of inert powders at a temperature of 75° to 78° F. In each case the quinine ethylcarbonate was triturated with the inert powder and then the acetylsalicylic acid and acetophenetidin were added in the order named.

Table VI.—Prescription No. 3. With Inert Powders

Capsules Stored in Open Containers

Inert Powder, Grs.	Size of Capsule	Time in Days 0	1	2	4	14
		Heavy Magnesium Oxide				
1	0	P.	P.	P.	P.	P.
		Light Magnesium Oxide				
1	0	P.	P.	P.	P.	P.
		Talc				
1	0	P.	C. M.	C. M.	C. M.	C. M.
		Lactose				
1	0	P.	C. M.	C. M.	C. M.	C. M.
		Magnesium Carbonate				
1	0	P.	P.	P.	C. M.	C. M.
		Dried Corn Starch				
1	0	P.	C. M.	C. M.	C. M.	C. M.
3	0	P.	C. M.	C. M.	C. M.	C. M.
		Dried Wheat Starch				
1	0	P.	C. M.	C. M.	C. M.	C. M.
		Dried Potato Starch				
1	0	P.	C. M.	C. M.	C. M.	C. M.

Table VI shows that best results were obtained with light and heavy magnesium oxides, which in this particular case did not form cement-like masses. The other inert powders prevented liquefaction but the ingredients formed into hard, solid bodies. Similar results were obtained for capsules stored in closed vials.

To ascertain whether tight packing of the ingredients in capsules had any part in developing the contents into a cement-like mass, the prescription was filled using 1 gr. of magnesium carbonate per capsule and individual doses were placed in some capsules tightly and in others loosely. After standing four days, the contents of the tightly packed capsules were of cement-like hardness while the contents of the loosely packed capsules remained in the same condition as when filled.

Prescription No. 4

℞ Phenyl salicylate	gr. xxxvi
Acetophenetidin	
Quinine hydrochloride aa	gr. xxiv
Camphor	gr. x
Mild mercurous chloride	gr. iss

M. Fiat cap. no. xxiv.

This prescription when compounded as written develops into a pasty mass.

Prescription No. 4 was filled with the addition of inert powders, the temperature being 78° to 80° F. In each case the camphor was triturated with the inert powder and the mild mercurous chloride, quinine hydrochloride, acetophenetidin and phenyl salicylate were added in the order named; the final mixture was triturated lightly.

Table VII.—Prescription No. 4. With Inert Powders

Capsules Stored in Open Containers

Inert Powder, Grs.	Size of Capsule	Time in Days 0	1	2	4	14
		Heavy Magnesium Oxide				
1	1	S. D.	C. M.	C. M.	C. M.	C. M.
2	0	P.	C. M.	C. M.	C. M.	C. M.
3	0	P.	C. M.	C. M.	C. M.	C. M.
		Light Magnesium Oxide				
1	0	P.	C. M.	C. M.	C. M.	C. M.
2	0	P.	P.	P.	P.	P.
3	00	P.	P.	P.	P.	P.
		Magnesium Carbonate				
1	0	P.	D.	D.	L.	L.
2	0	P.	P.	P.	P.	P.
3	00	P.	P.	P.	P.	P.
		Talc				
5	0	P.	D.	L.	L.	L.
		Lactose				
5	0	S. D.	L.	L.	L.	L.
		Dried Corn Starch				
5	0	S. D.	L.	L.	L.	L.
		Dried Wheat Starch				
5	0	S. D.	L.	L.	L.	L.
		Dried Potato Starch				
5	0	S. D.	L.	L.	L.	L.

Table VII shows that magnesium carbonate and light magnesium oxide gave the best results. Talc, lactose and the various dried starches did not prevent liquefaction. Heavy magnesium oxide prevented liquefaction but the contents of the capsules became cement-like masses. Similar results were obtained for capsules kept in closed vials.

Prescription No. 5

℞ Phenyl salicylate	ʒii
Acetylsalicylic acid	ʒ i
Antipyrine	ʒi
Strychnine sulfate	gr. 1/4

Mix and make capsules No. 24.
Label: One every four hours.

As this prescription contains several liquefiable combinations, some tests were first made on pairs of ingredients. On mixing acetylsalicylic acid and antipyrine, a damp powder resulted which liquefied in capsules within a day. A mixture of acetylsalicylic acid and phenyl salicylate in capsules gave a slightly damp powder after standing for one week. Capsules containing phenyl salicylate and antipyrine liquefied after standing for one week.

Prescription No. 5 was filled with the addition of inert powders, the temperature being 78° to 80° F. In each case the antipyrine was first powdered and the inert powder added; the strychnine sulfate, phenyl salicylate and acetylsalicylic acid were then added in the order named and the final mixture was triturated lightly.

Table VIII.—Prescription No. 5. With Inert Powders

Capsules Stored in Open Containers

Inert Powder, Grs.	Size of Capsule	Time in Days 0	1	2	4	14
		Heavy Magnesium Oxide				
1	0	P.	C. M.	C. M.	C. M.	C. M.
2	00	P.	C. M.	C. M.	C. M.	C. M.
		Light Magnesium Oxide				
1	0	P.	P.	P.	P.	P.
		Magnesium Carbonate				
1	0	P.	L.	L.	L.	L.
2	00	P.	P.	P.	S. D.	L.
3[a]	0	P.	P.	P.	P.	P.
		Talc				
5	00	P.	S. D.	L.	L.	L.
		Lactose				
5	00	S. D.	L.	L.	L.	L.
		Dried Corn Starch				
5	00	P.	L.	L.	L.	L.
		Dried Wheat Starch				
5	00	P.	L.	L.	L.	L
		Dried Potato Starch				
5	00	P.	L.	L.	L.	L.

[a] Double the number of capsules were made.

The results in Table VIII show that light magnesium oxide was most effective in preventing liquefaction. Magnesium carbonate was efficient when

3 grs. of the inert powder per capsule were used. Heavy magnesium oxide prevented liquefaction, but capsules containing this inert powder developed the contents into a mass of cement-like hardness. Talc, lactose and the various dried starches did not prevent liquefaction even when using 5 grs. of the inert powder per capsule. Similar results were obtained on capsules stored in closed vials.

An experiment was carried out to determine whether pressure, such as applying weight on a thin layer of the mixed ingredients or packing the powders tightly in capsules would have any effect in hastening liquefaction. Prescription No. 5 was filled using 1 gr. of magnesium carbonate per capsule and the resulting powder was placed on a glass plate. A portion of the powder was spread out in a thin layer and a 1000 Gm. weight was placed over it. The other portion was also treated in the same way except that no weight was placed over it. Likewise, capsules were filled in which the ingredients were packed tightly in No. 0 capsules and packed loosely in No. 00 capsules. The capsules and spread powders were examined at one-hour intervals.

Table IX.—Prescription No. 5. Effect of Pressure

Time Intervals in Hours	Powder with Weight over It	Powder without Weight	Powder in 0 Capsules	Powder in 00 Capsules
0	P.	P.	P.	P.
1	S. D.	P.	S. D.	P.
2	S. D.	P.	S. D.	P.
3	D.	P.	D.	P.
4	D.	S. D.	D.	S. D.
5	D.	S. D.	D.	S. D.
6	L.	S. D.	L.	D.
10	L.	D.	L.	D.
12	L.	D.	L.	D.
13	L.	D.	L.	L.
14	L.	L.	L.	L.

The results in Table IX show that the application of pressure on the powder hastened liquefaction.

Prescription No. 6

℞ Acid Acetylsalicylic	℥ ii
Amidopyrine	℥ ii
Citrated Caffeine	℥ ss

Div. cap. no. xviii.

This prescription (5) yields a dry powder but after a few days the contents of the capsules become damp. When the citrated caffeine was replaced by half its weight of caffeine base a dry powder was obtained and individual doses were put in No. 00 capsules; the contents of the capsules became damp after one week.

Prescription No. 6 was filled with the addition of inert powders, the temperature being between 78° and 80° F. In each case the acetylsalicylic acid was triturated with the inert powder, the amidopyrine and citrated caffeine were added in the order named and the mixture was triturated lightly. Due to the fact that the addition of the inert powder increased the bulk, each dose was placed in two capsules rather than in one.

Table X.—Prescription No. 6. With Inert Powders

Capsules Stored in Open Containers

Inert Powder, Grs.	Time in Days 0	1	2	4	14
		Heavy Magnesium Oxide			
1	P.	S. D.	D.	C. M.	C. M.
2	P.	C. M.	C. M.	C. M.	C. M.
3	P.	C. M.	C. M.	C. M.	C. M.
		Light Magnesium Oxide			
1	P.	P.	P.	P.	D.
2	P.	P.	P.	P.	P.
3	P.	P.	P.	P.	P.
		Talc			
1	P.	D.	D.	D.	D.
2	P.	S. D.	D.	D.	D.
3	P.	S. D.	S. D.	S. D.	D.
		Lactose			
1	P.	D.	D.	D.	D.
2	P.	S. D.	D.	D.	D.
3	P.	S. D.	S. D.	S. D.	D.
		Magnesium Carbonate			
1	P.	P.	P.	P.	D.
2	P.	P.	P.	P.	P.
3	P.	P.	P.	P.	P.
		Dried Corn Starch			
1	P.	D.	D.	D.	D.
2	P.	S. D.	D.	D.	D.
3	P.	S. D.	S. D.	S. D.	D.
		Dried Wheat Starch			
1	P.	D.	D.	D.	D.
2	P.	S. D.	D.	D.	D.
3	P.	S. D.	S. D.	S. D.	D.
		Dried Potato Starch			
1	P.	D.	D.	D.	D.
2	P.	S. D.	D.	D.	D.
3	P.	S. D.	S. D.	S. D.	D.

Table X indicates that light magnesium oxide and magnesium carbonate prevented the formation of a damp powder. The contents of the capsules containing heavy magnesium oxide assumed a cement-like hardness. Talc, lactose and the various dried starches were ineffective. Similar results were obtained with capsules stored in closed vials.

Prescription No. 7

℞ Acetylsalicylic acid	gr. v
Methenamine	gr. v

Ft. caps. d. t. d. xii. no.

In filling this prescription a damp powder resulted; after one day the contents of the capsules liquefied and on longer standing a yellowish green color developed.

Prescription No. 7 was filled with the addition of inert powders. The temperature at the time of compounding was from 78° to 80° F. In each case the methenamine was mixed with the inert powder and the acetylsalicylic acid added, the final mixture being triturated lightly.

Table XI.—Prescription No. 7. With Inert Powders

Capsules Stored in Open Containers

Inert Powder, Grs.	Time in Days 0	1	2	4	14
		Heavy Magnesium Oxide			
1	P.	L.	L.	L.	C. M.
3	P.	D.	D.	C. M.	C. M.
5	P.	S. D.	C. M.	C. M.	C. M.
		Light Magnesium Oxide			
1	P.	L.	L.	C. M.	C. M.
3	P.	D.	L.	C. M.	C. M.
5	P.	P.	D.	C. M.	C. M.
		Talc			
1	P.	L.	L.	L.	L.
3	P.	L.	L.	L.	L.
5	P.	L.	L.	L.	L.
		Lactose			
1	S. D.	L.	L.	L.	L.
3	P.	L.	L.	L.	L.
5	P.	L.	L.	L.	L.
		Magnesium Carbonate			
1	P.	L.	L.	L.	L.
3	P.	D.	L.	L.	L.
5	P.	P.	L.	L.	L.
		Dried Corn Starch			
1	P.	L.	L.	L.	L.
3	P.	L.	L.	L.	L.
5	P.	L.	L.	L.	L.
		Dried Wheat Starch			
1	P.	L.	L.	L.	L.
3	P.	L.	L.	L.	L.
5	P.	L.	L.	L.	L.
		Dried Potato Starch			
1	P.	L.	L.	L.	L.
3	P.	L.	L.	L.	L.
5	P.	L.	L.	L.	L.

Capsules Stored in Closed Vials

		Heavy Magnesium Oxide			
1	P.	D.	C. M.	C. M.	C. M.
3	P.	P.	C. M.	C. M.	C. M.
5	P.	C. M.	C. M.	C. M.	C. M.
		Light Magnesium Oxide			
1	P.	D.	C. M.	C. M.	C. M.
3	P.	P.	P.	P.	S. D.
5	P.	P.	P.	P.	P.
		Talc			
1	P.	D.	D.	C. M.	C. M.
3	P.	P.	C. M.	C. M.	C. M.
5	P.	C. M.	C. M.	C. M.	C. M.
		Lactose			
1	S. D.	D.	D.	C. M.	C. M.
3	P.	P.	C. M.	C. M.	C. M.
5	P.	C. M.	C. M.	C. M.	C. M.
		Magnesium Carbonate			
1	P.	P.	P.	S. D.	L.
3	P.	P.	P.	P.	S. D.
5	P.	P.	P.	P.	P.
		Dried Corn Starch			
1	P.	D.	D.	C. M.	C. M.
3	P.	P.	C. M.	C. M.	C. M.
5	P.	C. M.	C. M.	C. M.	C. M.
		Dried Wheat Starch			
1	P.	D.	D.	C. M.	C. M.
3	P.	P.	C. M.	C. M.	C. M.
5	P.	C. M.	C. M.	C. M.	C. M.
		Dried Potato Starch			
1	P.	D.	D.	C. M.	C. M.
3	P.	P.	C. M.	C. M.	C. M.
5	P.	C. M.	C. M.	C. M.	C. M.

Table XI shows that in this prescription the results were different according to whether the capsules were stored in open containers or in closed vials. In capsules stored in open containers light and heavy magnesium oxides caused the formation of cement-like masses and capsules containing light magnesium oxide assumed an orange color which was most intense when one or two grains of the inert powder were used. With other powders the contents liquefied.

In capsules stored in closed vials the use of talc, lactose, heavy magnesium oxide and the various starches caused formation of cement-like masses. Magnesium carbonate and light magnesium oxide in the proportion of three grains per capsule prevented liquefaction when the capsules were stored in closed vials.

DISCUSSION OF RESULTS

Inert powders which are light and fluffy appear to be most efficient in preventing liquefaction due to formation of a eutectic mixture. The results with various prescriptions indicate that magnesium carbon-

ate and light magnesium oxide are most effective while heavy magnesium oxide is less effective and talc, lactose and various starches are comparatively inefficient in preventing liquefaction. The probable explanation of the results is that powders which are light and fluffy are more effective in holding apart the particles of the substances which tend to liquefy on contact. When a light, fluffy powder is used it is somewhat more difficult to fill the capsules since the resulting powder packs less readily and has a tendency to fall out of the body of the capsule during the filling.

In some instances the use of light or heavy magnesium oxide caused the contents of the capsule to change into a hard, cement-like mass. Tests on some of the hardened masses showed that they did not disintegrate in water in four days; in 0.5 per cent solution of hydrochloric acid the solid mass was reduced slightly in size but retained its form. Since insoluble masses of this kind would probably pass through the alimentary tract without disintegrating it is important that the pharmacist take precautions to prevent their formation. In most cases cement-like masses did not form when magnesium carbonate was used as the inert powder.

SUMMARY

Experiments were carried out with various prescriptions for capsules to determine the relative efficiency of various inert powders in preventing liquefaction due to formation of a eutectic mixture. Inert powders which are light and fluffy appear to be most efficient. Magnesium carbonate and light magnesium oxide proved most effective, heavy magnesium oxide ranked next, and talc, lactose and various starches were least effective. In some cases, particularly with light and heavy magnesium oxide, the contents of the capsules assumed a cement-like hardness.

As to the various methods of compounding, the results show that it is better to first mix one incompatible ingredient with the inert powder or to mix each incompatible ingredient with a separate portion of the inert powder. Heavy trituration hastens liquefaction. Likewise the use of too small a capsule hastens liquefaction due to the tightness of packing.

Apparently exposure of the filled capsules to the air usually has little or no effect when the liquefaction is due to formation of a eutectic mixture.

In most cases the use of about two grs. of magnesium carbonate or light magnesium oxide per capsule stabilized the capsules over a period of two weeks.

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The Status of Phenol in Ointment of Phenol, U. S. P.*

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To meet the United States Pharmacopœial requirements, Ointment of Phenol must contain not less than 1.8 per cent nor more than 2.2 per cent of C_6H_5OH. As is noted, a tolerance of 0.4 per cent is allowed to take care of possible error in weighing, questionable strength of the phenol used and probable loss during manufacture of the ointment. The purpose of this investigation was to determine whether or not various samples made by different individuals actually met the requirements as designated in the United States Pharmacopœia in respect to the content of phenol.

G. R. Page (1) of England, working on the British Pharmacopœia (1932) Ointment of

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