

Contributed and Selected

FORMALDEHYZED CAPSULES.*

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It is a matter of common knowledge that formaldehyde hardens gelatin solution, and in the course of a short time renders it insoluble in water. Within a few years there have appeared articles in pharmaceutical journals stating that gelatin capsules treated with formaldehyde were suitable for use as enteric capsules, i. e., as capsules which would pass through the stomach unchanged but would dissolve in the intestines. In most instances, the writers have given no specific formula for treating the capsules, nor have they stated the strength of formaldehyde which should be used or the length of time that the capsules should be treated.

One writer, however, directed that the capsules should be immersed in a ten percent solution of formaldehyde for five minutes.

The value of this treatment will be pointed out later.

Gelatin capsules and pearls containing medicaments, which have been treated with formaldehyde, have appeared on the market, and claim to be enteric. Whether there is very much demand for these the writer does not know, but they attracted the attention of medical men, and have received some endorsement.

It has seemed worth while, therefore, to test the method and to find the conditions most suitable for producing desirable results in treating gelatin capsules; so a little more than three years ago a series of experiments were made for this purpose.

It was quickly found that strong solutions of formaldehyde were not suitable because they produced a capsule which would not dissolve in a weakly alkaline solution within 24 hours.

The treated capsules were tested by immersing them in 0.3 percent hydrochloric acid containing a little pepsin, and kept at a temperature of 37° to 38° C. The aim was to produce a capsule which would remain unbroken in this acid solution for at least three hours, but which would dissolve or disintegrate in a 0.5 percent solution of monohydrated sodium carbonate within three to five hours, at a temperature of 37° to 38° C.

Since the experiments were made mostly on filled capsules of the elastic or soft variety, the treatment consisted in immersing the capsules in formaldehyde solution of definite strength for a definite period of time, then draining and drying them without washing.

Ten percent solutions of formaldehyde were employed for the first experi-

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ments, and immersion was made for periods varying from 30 minutes to one minute.

All capsules so treated proved to be insoluble in either the artificial gastric or intestinal juice, and were unsuited for enteric purposes. Weaker solutions gave better results, and after preliminary tests covering several weeks of time, an aqueous solution containing one percent of (absolute) formaldehyde was found to be the most suitable strength for the purpose. A further series of tests showed that the time that the capsules remain in such a solution is an important factor. It was soon learned that if the capsules were allowed to remain in the solution more than six minutes, they would not dissolve, nor soften sufficiently to break, in the alkaline solution in three hours.

It was next learned that the action of the formaldehyde on the gelatin is slow and that it continues after the capsules have dried. Thus-treated capsules which tested satisfactorily the day after they were made, were found to be very unsatisfactory a week later. That is they dissolved in the first test in the alkaline solution within two or three hours, but remained intact in it for three to five hours in the second test.

Experiments were therefore made in which the capsules were immersed for 5, 4½, 4, 3½, 3, 2½, 2, 1½ and 1 minutes respectively.

On testing the next day it was found that all of these dissolved in the acid solution within one hour, and were therefore not enteric; but a month later the same capsules all resisted the acid solution for three or more hours, and those which had been treated more than 3½ minutes resisted the alkaline solution for 3 hours, while those treated 3 minutes or less broke or dissolved in the alkaline solution within three hours.

Two months later the tests were again repeated, and none of them were soluble in the alkaline solution in three hours, though a few broke.

These experiments showed that for the above treatments the action of the capsules could be relied upon for short periods of time, but they were useless for enteric purposes until a few days after treatment, and also after about two months' time.

Alcoholic solutions of formaldehyde were then tried, but did not prove satisfactory, the capsules breaking up and dissolving in the acid solution almost as quickly as the untreated capsules, even after five minutes' treatment in a 5 percent formaldehyde solution.

Another series of experiments was then made with 1 percent aqueous formaldehyde solution, the capsules being macerated for 60 seconds, 45 seconds, 30 seconds and 15 seconds respectively. Tested three days after treatment, all of these dissolved in the acid solution. After standing two weeks those which had been treated 15 and 30 seconds partly broke in acid solution within three hours, while the others resisted for three hours. All dissolved in the alkaline solution within one-half to two hours. Monthly tests on these during the first five months showed them all to be satisfactory for enteric use after the first month.

At the end of a year, those treated for 15, 30 and 45 seconds were still satisfactory, resisting the acid solution for three hours but dissolving in the alkaline

solution within three hours; the others were not soluble in the alkaline solution in three and one-half hours.

This seemed to prove that treatment of the capsules for 30 seconds by a one percent formaldehyde solution, at ordinary temperature, produces a satisfactory enteric capsule. But two years later, or three years after the capsules were so treated, they were found to be entirely insoluble in either the acid or alkaline liquids after nineteen hours. In the alkaline solution the capsules swelled and softened, but none broke. Those treated for 15 seconds acted similarly.

The inevitable conclusion is that the treatment of gelatin capsules with formaldehyde solution for enteric purposes has only a limited value.

For general prescription practice its value is limited by the fact that the capsules either do not become enteric for several days after treatment, or else become insoluble and unfit for use after three or four days.

If it be practical to prepare the capsules two weeks in advance of their use, then all that is needed is to immerse them in a one percent aqueous formaldehyde solution for 30 seconds, drain them quickly and dry them, then store for two weeks before using. Capsules so treated should not be employed after about a year, because they become wholly insoluble.

Within these limits the capsules have proved satisfactory both by tests *in vitro* and by chemical use. But it should not be forgotten that on long standing the capsules become wholly unfit for use.

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THE EXTEMPORANEOUS PREPARATION OF CAMPHOR LINIMENT.

ROBERT WOOD TERRY.

Having noticed the article entitled, "A Medley," by George M. Beringer, Jr., in the August issue of the Journal, I would like to call your attention to a very simple and rapid method of preparing camphor liniment.

Mr. Beringer recommends the purchase of an almond grater to reduce the camphor to fine granules to which the oil is added and the mixture placed on a water-bath, when after fifteen minutes the camphor will be in solution, this being more rapid than by the official method in which coarser particles of camphor are used, the assumption being, presumably, that the more surface of the camphor exposed to the solvent action of the oil, the more rapid the solution; therefore, why not carry out this theory to its limit of practical application?

The following method I have used for three years and have prepared camphor liniment in less than ten minutes by this method: Place the camphor in a mortar and add sufficient chloroform or ether to reduce the camphor to an extremely fine powder, being sure no small lumps remain, and allow this to stand a minute with an occasional stir to facilitate the spontaneous evaporation of the solvent; then, add a small quantity of the oil and triturate until a thoroughly homogeneous mass