

which would pass through the digestive tract without disintegration. A considerable variation was noted in the time that was required for the pill and capsule to leave the stomach. In one subject, it was noted that the pill and capsule would remain in the stomach after a meal had passed through it. This condition seemed to be normal for this individual as the same results were obtained in three different experiments.

A formaldehyde concentration of 10 per cent and an immersion time of 5 seconds was considered to be the best method. This gave a disintegration in the upper intestine, which is usually desirable. If further penetration is desired, the 10- or 15-second immersion would be better.

We do not believe that the gelatin coating, formaldehyde treated, would be ideal for commercial products because of the mechanical difficulties which would develop. The method could be used successfully, however, by the pharmacist who may have an occasional call for a small number of specially prepared capsules. No extra equipment is necessary and the product, when dry, is not unsightly. The pharmacist must be careful that the capsules are well sealed or the contents are in some danger of becoming wet with the formaldehyde solution.

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A PROPOSED FORMULA FOR BELLADONNA OINTMENT.*

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Therapeutically, ointment of belladonna seems to have, for the most part, justified the claims made for it. Pharmaceutically, however, many complaints have been made about the present official formula. Chief among these are:

1. That it stains due to the presence of chlorophyll in the pilular extract.
2. It is difficult to rub the extract smooth previous to incorporation in the base. This may be due, in part, to the character and quality of the extract.
3. The finished product is too sticky.

Believing that it should be possible to prepare a satisfactory belladonna ointment free from the objections enumerated, prompted this study.

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PILULAR EXTRACT OF BELLADONNA IN VARIOUS OINTMENT BASES.

Nine ointments composed of the same amount of pilular extract of belladonna were prepared, using as many different bases with respect to composition or proportions of the various ingredients. The procedure consisted in rubbing the extract to a smooth paste with the alcohol and incorporating it in the fats, after the manner usually prescribed.

These ointments were prepared and studied under varying temperature conditions, for purposes of comparing consistency and keeping properties. For this study samples of the ointments were subjected to summer heat (room temperature), oven heat at 35° C. and to the electric refrigerator.

These ointments and their formulas are given in Table I following:

TABLE I.

Formula Amounts in Gm.	1. ^a	2. ^b	3. ^c	4.	5.	6.	7.	8.	9.
Extract belladonna pilular	10	10	10	10	10	10	10	10	10
Alcohol, dilute	5	5	10	5	5	5	5
Wool fat, anhydrous	30	30	20
Lard, benzoinated	55	..	60
Wax, yellow	..	5
Petrolatum	..	50
Purdue base ^d	85	85	85
Bibbins' base ^d	85
Lascoff base ^d	85
B. P. (1932) base ^d	85
Magnesium stearate ^e	5	..
Oleic acid	5

^a U. S. P. IX formula.

^b U. S. P. X formula.

^c B. P. (1914) formula.

^d See Table II for the composition of these bases.

^e A saturated solution in dilute alcohol used.

Comments.—Of the formulas in Table I, No. 1 had to be rejected because it was too thin. This may have been due, in part at least, to the quality of the lard. Formula No. 3 of about the same composition and consistency was also discarded early in the study. Number 5, made with the Bibbins' base was of good consistency but a little sticky. Compared to this, the Lascoff base made ointment No. 6 even more sticky than No. 5. This stickiness is attributed to the presence of proportionately larger amounts of wool fat in the bases, since formulas Nos. 4 and 7 were free from this objection. We do not regard stickiness, such as these showed, a serious fault.

The use of magnesium stearate in No. 8 did not indicate any improvement over the other formulas. In Formula 9, the oleic acid not being miscible with the extract, made it impossible to get a smooth ointment.

In Table II, following, is given the composition of the bases used in making four of the ointments in Table I. These have all been considered and tried by various members of the Revision Committee of the Pharmacopœia, XI (Sub.-Com. 13, Bull. 13).

TABLE II.

Constituents.	Purdue.	Bibbins.	Ointment Bases.	B. P. (1932).
			Lascoff.	
Wool fat	5	15	20	5
White wax	5	10	15	..
White petrolatum	90	75	65	85
Paraffin	10

Each is prepared by fusing the ingredients upon a water-bath and stirring, just enough, while cooling to insure thorough mixing.

FLUIDEXTRACT OF BELLADONNA IN BELLADONNA OINTMENTS.

Since there is the problem of getting a smooth paste with the extract of belladonna and the alcohol, as prescribed in the official formula, it was thought that this trouble might be eliminated by starting with the proper amount of the fluid-extract as in the B. P. (1914). A number of ointments were therefore prepared, using fluidextract of belladonna root instead of the extract as officially prescribed. These are shown in Table III, in which the formulas are given.

TABLE III.

Formula Ingredients in Gm.	10.	11.	12.	13.	14.
Fluidextract belladonna root	30	30	30	30	30
Purdue base ¹	90	90	90	90	89
Magnesium stearate01	..
Oleic acid	1

¹ See Table II for formula.

Procedure.—The methods of making are somewhat different for each and will be given separately.

In No. 10, the fluidextract was evaporated, on a water-bath, to 10 Gm., cooled and incorporated in the base in the usual way. For No. 11, the fluidextract was evaporated as for No. 10, the base was then melted and added to the concentrated fluidextract and stirred until congealed. In Formula 12, the concentrated fluidextract was added to the melted base and the mixture stirred while congealing. In Formula 13, the magnesium stearate was added to the fluidextract previous to concentrating the latter. To this the melted base was added gradually with stirring until it congealed. For No. 14, the fluidextract and oleic acid were heated on the water-bath until reduced to 11 Gm. After the residue had cooled, the base was incorporated.

Comments.—In preparing this group of ointments, it was observed that when the concentrated fluidextract was incorporated in the cold base, as for ointment 10, droplets appeared in the finished product. These did not appear when the base was melted, previous to mixing it with the concentrated fluidextract, as was done with ointments 11 and 12.

The addition of magnesium stearate in ointment 13 did not seem to alter the appearance of the finished ointment. The use of oleic acid did not seem to cause the trouble in ointment 14 that it did in ointment 9, perhaps due to the use of heat in making the former.

The question as to whether the use of magnesium oleate and oleic acid in

these ointments affected the alkaloids present will have to be determined by further experimentation.

Finally there is this to be said for this group of ointments: 1, the question of getting a smooth ointment was entirely solved; 2, the low lanolin content of Purdue base yielded ointments free from the stickiness so often observed; 3, the use of belladonna root, instead of the highly colored extract, eliminated the undesirable staining properties of the present official ointment, and 4, the process of making is simple and comparatively easy.

OINTMENT OF BELLADONNA IN A CHOLESTERIN-CONTAINING BASE.

The presence of cholesterin in small amounts in petrolatum and other bases and base constituents such as wax, are reputed to greatly increase the water-holding property of the base. Two bases, Nos. 15 and 16, were, therefore, prepared each containing 1.5% cholesterin. The formulas were:

Number 15—Petrolatum, white	98.5 Gm.
Cholesterin	1.5 Gm.
Number 16—Petrolatum	93.75 Gm.
White wax	4.75 Gm.
Cholesterin	1.50 Gm.

Each was prepared by melting the ingredients upon a water-bath and stirring until cool.

When tested for their water-absorbing properties, Formula 15 easily took up 30 per cent of water which was not removed by melting the base upon a water-bath. It was found that Formula 16 took up somewhat more water, indicating that wax increases the water-holding property of such mixtures.

In view of the observations made with bases 15 and 16, it was decided to prepare an ointment of belladonna from fluidextract of belladonna root and base No. 16. The ointment which resulted was free from stickiness, of splendid consistency, had good spreading properties and was not difficult to prepare. When assayed according to the method of Deal, *J. A. O. A. C.*, 15 (1932), 442-446, the results were found to check favorably with those of an equivalent amount of the fluidextract as a control.

We, therefore, wish to suggest that we believe that the following formula for belladonna ointment would make a desirable preparation. It is free from most of the objectionable features of the present official formula. The proposed formula is as follows:

Fluidextract belladonna root	28.00 cc.
Cholesterin	1.50 Gm.
White wax	5.00 Gm.
White petrolatum	83.50 Gm.

Procedure.—Concentrate the fluidextract upon a water-bath to 10 Gm. Add to this the melted base, slowly and with stirring, until cool.