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DIGITALIS CAPSULE

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This invention relates to digitalis capsules, and more particularly to such capsules formed from gelatin and enclosing a specific dosage of digitalis drug.

Among the objects of this invention are the provision of capsules of the indicated type which remain stable over extended periods of time; the provision of such capsules which may be stored under normal conditions for extended periods of time, and still retain their initial potency; the provision of capsules of the indicated type which may be administered in the usual manner, and which are effective without substantial loss of time; the provision of such capsules which are effective on the human organism as quickly as the present commercial forms of digitalis; and the provision of capsules of the class indicated which are easy and inexpensively prepared from widely available materials. Other objects will be in part obvious and in part pointed out hereinafter.

The invention accordingly comprises the elements and combinations of elements, steps and sequence of steps, features of construction and manipulation, and arrangements of parts which will be exemplified in the structures and methods hereinafter described, and the scope of the application of which will be indicated in the following claims.

Digitalis is a valuable medicinal widely employed in the treatment of certain forms of heart affections. As is true of many drugs, digitalis is toxic in dosages substantially above the therapeutic dose. It is therefore important that the potency of a given quantity of drug be established and known to the physician administering it.

Digitalis is customarily marketed, either in the form of a tincture, or in the form of tablets formed from the powder of dried digitalis leaves. The tincture so formed is, however, subject to deterioration with the passage of time. The same is true of the tablets unless thoroughly dry and stored in air-tight containers. As a result, these tablets or the tincture cannot be stored under normal conditions for any extensive period. The tincture is customarily made up fresh at frequent intervals, in order to insure administration of the proper dosage. Moreover, as the United States Pharmacopoeia states, the digitalis leaves themselves must be preserved "thoroughly dried, in air tight containers" to minimize loss of effectiveness. Such expedients, although expensive, are essential to maintain the potency of the tincture or tablets subsequently formed from the digitalis leaves. The tincture and tableted

powder must not only be made up fresh a short time before use and/or rigidly protected after preparation, but the principal ingredient, the digitalis leaves, must likewise be rigidly protected.

According to the present invention a digitalis preparation is provided which may be stored over extended periods of time, and which will show substantially no deterioration after an extended storage. The preparation of the present invention may be kept on drug store shelves, or under otherwise normal storage conditions until required. A physician who prescribes a given dosage of digitalis may be certain that the composition of the present invention will provide such a dosage, although it has been stored over an extended period.

Digitalis is, in accordance with the present invention, prepared in the form of plasticized gelatin capsules. These capsules are of the customary type, namely, a plasticized gelatin outer layer enclosing a given dosage of the medicinal ingredient. The digitalis itself is suspended in a bland inert vehicle which is liquid over at least part of the temperature range between 40 and 65° C. The vehicle must not be hydrophilic, and it must be of suitable specific gravity to retain the digitalis particles suspended during capsulation. This vehicle is preferably digestible.

It has been found that mineral oil, cotton seed oil, mixtures of edible vegetable oils, either hydrogenated or unhydrogenated, or similar edible fatty acid glycerides are quite suitable as suspending agents for use in the present invention. The preferred vehicle is a mixture of hydrogenated and unhydrogenated fatty acid glycerides.

The digitalis leaf, preferably finely divided, such as to 80–100 mesh, and dried to a moisture content of not more than 10% and preferably of not more than 4 to 5%, is suspended in a suitable proportion of a vehicle of the class indicated. The proportion of vehicle and digitalis may be varied over relatively wide ranges, but the vehicle must be present in sufficient proportion to surround the digitalis particles. The viscosity of the mixture should be such that the drug does not sediment during capsulation. The particles of digitalis are uniformly dispersed in the vehicle, preferably a mixture of vegetable oil and hydrogenated oil, and the product may be diluted with additional quantities of oil to form the desired dosage. Thus a given capsule size may contain one-half grain, one grain, one and one-half grains etc., of active units, dependent upon particular manufacturing convenience.

The potency of the digitalis drug itself and of the finished capsules is determined in the usual way by biological assay.

The digitalis is suspended in the vehicle by a suitable mixing operation which must, however, avoid the introduction of air or moisture; that is, an emulsion is not formed. A uniform dispersion of the digitalis particles is, however, made. No special precautions other than those indicated are necessary, and any mixing apparatus customarily employed may be used for this purpose.

A suitable quantity of the digitalis preparation formed as described, is then formed into a gelatin capsule in the customary manner. The usual temperatures for capsulation may be employed, which in general are from 40-65° C. The digitalis suspension in the inert vehicle is as indicated, fluid at these temperatures, and therefore is easily made into gelatin capsules.

Gelatin capsules formed in accordance with the present invention and having digitalis suspended in an inert bland water-free vehicle of the type indicated have been tested, both promptly after manufacture and after storage under normal drug store storage conditions for an extended period of time.

It has been found that capsules prepared in accordance with the instant invention present the drug in a ready assimilable form. It has been found that, the digitalis is effective as quickly after administration as is the case when the customary tincture or tableted digitalis are administered.

In order to test the time required for the digitalis to become effective, precisely equal amounts of the drug prepared from the same lot of digitalis powder were made into three dosage forms, namely, gelatin capsules in accordance with the present invention, a tincture, and digitalis tablets in which the material was merely tableted. The latter two were made in accordance with standard pharmacal practice. Equal dosages of each were given orally to guinea pigs and cats, in sufficient quantity to be toxic. The length of time required for death was in each instance similar. As the time required for the toxic effect to become lethal shows that the rate of absorption was the same, the digitalis preparation of the present invention is effective as promptly as the customary forms for presenting digitalis.

Digitalis capsules which had been stored over a period as long as a year, were tested for potency, and for absorption rate. It was found in each instance that no appreciable decrease, either in potency or absorption rate, had occurred, although these capsules were stored under customary drug store storage conditions. The tincture or tab-

leted digitalis particles show marked deterioration under these conditions, unless rigidly protected both from moisture and air. In fact, it has been found that even temporarily opening and closing a given container of powdered digitalis a limited number of times, such as is necessary in withdrawing a portion of the drug for the preparation of a tincture or infusion thereof, is sufficient to cause marked deterioration in the remainder. This deterioration occurs even though an air-tight and moisture-proof container is employed, and even though the drug has been previously thoroughly dried, as required by the Pharmacopoeia. No such precautions are required with the gelatin capsules of the present invention. They may be stored in open containers in contact with air, yet suffer no appreciable deterioration.

In view of the above, it will be seen that the several objects of the invention are achieved and other advantageous results attained.

As many changes could be made in the above methods and products without departing from the scope of the invention, it is intended that all matter contained in the above description shall be interpreted as illustrative and not in a limiting sense.

What is claimed is:

1. A digitalis capsule comprising an outer layer of gelatin enclosing digitalis leaf suspended in an inert, water-free viscous oil vehicle, said digitalis leaf containing not substantially in excess of 10% moisture.
2. A stable digitalis capsule comprising a gelatin outer layer enclosing digitalis leaf suspended in an inert, water-free, viscous, digestible oil vehicle, said digitalis leaf containing not substantially in excess of 10% moisture.
3. A gelatin capsule comprising an outer layer of gelatin and a central portion comprising digitalis leaf suspended in an inert, water-free, oil vehicle which is fluid at a capsulating temperature, said digitalis leaf containing not substantially in excess of 10% moisture.
4. A gelatin capsule comprising an outer layer of gelatin and a central portion comprising digitalis leaf suspended in a mixture of hydrogenated and unhydrogenated vegetable oils, said digitalis leaf containing not substantially in excess of 10% moisture.
5. A gelatin capsule comprising an outer layer of gelatin and a central portion comprising powdered digitalis leaf suspended in an inert, water-free, oil vehicle which is fluid at a capsulating temperature, said digitalis leaf containing not substantially in excess of 10% moisture.

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