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SOFT GELATIN CAPSULES

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4 Claims. (Cl. 167—83)

This invention relates to gelatin capsules and more particularly to soft gelatin capsules enclosing oleaginous compositions.

Soft gelatin capsules are known in the art. They are usually composed of gelatin, water, and a plasticizer, such as glycerin, and can be formed into various shapes and sizes.

The soft gelatin capsule of commerce is usually in the form of a continuous outer shell of the composed gelatin enclosing a fluid or semi-fluid fill. Dissolution of the shell or expression of the enclosed fill therefrom frees the fill for its intended use.

Since water has a marked affinity for gelatin and can exert thereby a deleterious action on the capsule shell, fills of an oleaginous type have been utilized to reduce the content of water in the fill. Even in the case of oleaginous-type fills, small amounts of water have caused defects in the yield and quality of capsules during preparation and storage. Similarly, defects have been encountered in capsules enclosing otherwise acceptable and useful oleaginous fills, for example, those including salts of strong acids and bases, such as sodium chloride; hygroscopic compounds, such as chloral hydrate; hydrochlorides, such as (o-methoxy-α-methylphenyl)-hydrazine hydrochloride; water soluble compounds, such as choline chloride; volatile solvents, such as alcohol; and non-volatile solvents, such as glycerin. The said defects greatly reduce the yield of quality-controlled capsules and impair the storage stability of the capsules; for example, through leaking, indenting, and shrinking of the capsules and the existence of excessively soft capsules and those with soft spots. Apparently, substances, such as the salts, hygroscopic compounds, hydrochlorides, water-soluble compounds, volatile and nonvolatile solvents, per se, have a deleterious action on the gelatin shell of the capsules, especially in the presence of water. The deleterious action of like substances is determined readily by a test run such as demonstrated in Tables I through VI.

It has now been discovered that, according to the present invention, oleaginous vehicles can be successfully filled into soft gelatin capsules by the use in the fill of an ingestible cellulosic compound, such as purified cellulose. The operability of an ingestible cellulosic compound is determined readily by a test run such as demonstrated in Example 1. As is known in the art, the oleaginous vehicles comprise fixed oils, such as corn oil and cottonseed oil; oily esters, such as isopropyl myristate; and the like. Oil-dispersible components, such as aluminum monostearate, white wax, and hydrogenated oils, can be incorporated into the oleaginous vehicles. For oral administration the vehicles and any added components must be ingestible. The invention is especially advantageous in the case of an oleaginous fill including an ingredient having a deleterious action on the gelatin, and especially an ingredient having such action in the presence of water.

The fill should be fluid enough for handling in the practical methods used in encapsulating flowing vehicles and compositions. An amount of the cellulosic compound up to about 20% by weight of the fill is feasible, and in some compositions higher amounts can be used. To provide best results any water included within the fill should usually be no more than about twice the amount of the cellulosic compound.

The mechanism of action of the said cellulosic compound in preventing the defects in yield and storage of the capsules is not completely understood. However, experimental data show that unexpectedly high yields of quality-controlled capsules are obtained from the compositions and process of the instant invention.

The heretofore unsolved problems are illustrated in the following tables, the percents of capsules accepted being those obtained after washing, drying and quality inspecting the capsules prepared by the known methods, the percents of ingredients being by weight.

TABLE I

Oleaginous Vehicle	Results of Quality Control Inspection, Percent of Capsules Accepted
Corn Oil, 85%; Water, 15%	67.79, Balance—collapsed shells.

TABLE II

Corn Oil, 84%; Compound A[1], 16%	27.08, Balance—Leakers.

TABLE III

Corn Oil, 93%; NaCl, 7%	0.00, All leakers.
Peanut Oil gel, 93%; NaCl, 7%	82.37, Balance—leakers.
Corn Oil, 87%; NaCl, 3%; Water, 10%	0.00, All leakers.

TABLE IV

Corn Oil, 90%; alcohol, 10%	37.50, Balance—leakers.

TABLE V

Corn Oil, 90%; glycerol, 10%	0.00, All spotted.
Corn Oil, 88%; glycerol, 12%	0.00, All spotted.

TABLE VI

Corn Oil, 93%; chloral hydrate, 7%	90.22, Balance—leakers.

[1] Compound A is (o-methoxy-α-methylphenyl) hydrazine hydrochloride.

The above data show the deleterious effects of these oleaginous compositions on the yield and physical condition of the capsules.

The capsules and methods of the instant invention are set forth in the following tables, the percents being expressed as in Tables I through VI.

TABLE VII

Oleaginous Vehicle	Results of Quality Control Inspection, Percent of Capsules Accepted
Corn Oil, 83%; purified cellulose, 6%; water, 11%---	92.07.

TABLE VIII

Corn Oil, 89.1%; purified cellulose, 2%; Compound A[1], 8.9%.	99.25.
Corn Oil, 86.1%; purified cellulose, 5%; Compound A, 8.9%.	99.76.
Corn Oil, 81.1%; purified cellulose, 10%; Compound A, 8.9%.	99.68.
Isopropyl myristate, 84%; purified cellulose, 10%; Compound A, 16%.	99.84.
Corn Oil, 74%; crystalline cellulose, 10%; Compound A, 16%.	99.36.

TABLE IX

Corn Oil, 83%; purified cellulose, 10%; NaCl, 7%---	96.60.
Peanut Oil gel, 78%; purified cellulose, 15%; NaCl, 7%.	96.47.
Corn Oil, 77%; purified cellulose, 10%; NaCl, 3%; water, 10%.	97.36.

TABLE X

Corn Oil, 80%; purified cellulose, 10%; alcohol, 10%.	99.28.

TABLE XI

Corn Oil, 80%; purified cellulose, 10%; glycerin, 10%.	97.68, No soft spots.
Corn Oil, 76%; purified cellulose, 12%; glycerin, 12%.	99.44, No spotting or shrinking.

TABLE XII

Corn Oil, 74%; purified cellulose, 10%; chloral hydrate, 16%.	97.84.
Corn Oil, 81%; purified cellulose, 10%; chloral hydrate, 7%; water, 2%.	95.67.

[1] Compound A is (o-methoxy-α-methylphenyl) hydrazine hydrochloride.

The above data show the superiority, greatly improved yields and acceptable physical characteristics of the capsules and methods of the instant invention.

In the manner and process of making the invention, an oleaginous composition is prepared by mixing and blending the components thereof into a homogeneous whole, using the known techniques for preparing oleaginous vehicles for encapsulation into soft gelatin capsules. The order of addition of components to the oleaginous vehicle is not critical. The oleaginous fill is thereafter encapsulated by the known techniques.

The invention is used to provide increased yields of accepted soft gelatin capsules, especially ingestible soft gelatin capsules.

The following examples set forth the best mode contemplated by the inventor of carrying out his invention.

EXAMPLE 1

Capsules Enclosing an Oleaginous Composition Comprising Water

400 cms. of an oleaginous composition is prepared from the following ingredients:

	Grams
Purified water, U.S.P	60
Corn oil	300
Purified cellulose,[1] powdered	40

[1] Solka-Floc, Brown Company.

The corn oil is stirred with a high-speed stirrer, and the water is added gradually during the stirring. The purified cellulose is powdered and homogeneously incorporated into the oil-water mixture during continued stirring.

The composition is encapsulated into 2.65 minim soft gelatin capsules by the known techniques. 99.6 percent of the capsules are found acceptable by the quality control inspectors.

EXAMPLE 2

Capsules Enclosing an Oleaginous Composition Comprising a Hydrochloride

300 gms. of an oleaginous composition is prepared from the following ingredients:

	Grams
(o - Methoxy-α-methylphenyl)-hydrazine hydrochloride	48
Isopropyl myristate	222
Purified cellulose	30

The isopropyl myristate is stirred with a high-speed stirrer, and the (o-methoxy-α-methylphenyl)-hydrazine hydrochloride is added gradually during the stirring. The purified cellulose is incorporated into the mix and the whole is thoroughly stirred to obtain a homogeneous composition.

The composition is encapsulated into 2.65 minim soft gelatin capsules by the known techniques. 99.84 percent of the capsules are found acceptable by the quality control inspectors.

EXAMPLE 3

Capsules Enclosing an Oleaginous Composition Comprising a Volatile Solvent

400 gms. of an oleaginous composition is prepared from the following ingredients:

	Grams
Alcohol, U.S.P	40
Corn oil	320
Purified cellulose	40

The corn oil is stirred vigorously and the alcohol is added gradually during the stirring. Then the purified cellulose is added and the whole is stirred continuously into a homogeneous mixture.

The composition is encapsulated into 2.65 minim soft gelatin capsules by the known techniques. 99.28 percent of the capsules are found acceptable by the quality control inspectors.

EXAMPLE 4

Capsules Enclosing an Oleaginous Composition Comprising a Nonvolatile Solvent

400 gms. of an oleaginous composition is prepared from the following ingredients:

	Grams
Glycerin, U.S.P	40
Cottonseed oil	320
Purified cellulose	40

The cottonseed oil is stirred with a high-speed stirrer, and the glycerin is added gradually thereto. Next the purified cellulose is added during continuous stirring to obtain a homogeneous mixture.

The composition is encapsulated into 2.65 minim soft gelatin capsules by the known techniques. 97.68 percent of the capsules are found acceptable by the quality control inspectors. The capsules do not show soft spots or shrinking.

EXAMPLE 5

Capsules Enclosing an Oleaginous Composition Comprising a Hygroscopic Compound

300 gms. of an oleaginous composition is prepared from the following ingredients:

	Grams
Chloral hydrate	48
Corn oil	222
Purified cellulose	30

The corn oil is stirred vigorously, and the chloral hydrate is added gradually to form a good solution. There-

after the purified cellulose is added during continuous stirring to form a homogeneous mixture.

The composition is encapsulated into 2.65 minim soft gelatin capsules by the known techniques. 97.84 percent of the capsules are found acceptable by the quality control inspectors.

EXAMPLE 6

Capsules Enclosing an Oleaginous Composition Comprising a Salt and Water

400 gms. of an oleaginous composition is prepared from the following ingredients:

	Grams
Sodium chloride, powder	12
Purified water, U.S.P	40
Corn oil	308
Purified cellulose	40

The corn oil is stirred vigorously, and during the continuous stirring there is added the solution of the sodium chloride in the water. The purified cellulose is then added during continuous stirring to obtain a homogeneous mixture.

The composition is encapsulated into 2.65 minim soft gelatin capsules by the known techniques. 97.36 percent

of the capsules are found acceptable by the quality control inspectors.

What is claimed is:

1. A filled soft gelatin capsule wherein the fill comprises a fluid oleaginous vehicle and powdered ingestible cellulose.

2. A filled soft gelatin capsule wherein the fill comprises a fluid oleaginous vehicle, powdered ingestible cellulose, and an ingredient having a deleterious action on gelatin.

3. A filled soft gelatin capsule wherein the fill comprises a fluid oleaginous vehicle and up to about 20% by weight of the fill of powdered ingestible cellulose.

4. A filled soft gelatin capsule wherein the fill comprises a fluid oleaginous vehicle, up to about 20% by weight of the fill of powdered ingestible cellulose and an ingredient having a deleterious action on gelatin.

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UNITED STATES PATENT OFFICE

CERTIFICATE OF CORRECTION

Patent No. 3,126,321 March 24, 1964

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It is hereby certified that error appears in the above numbered patent requiring correction and that the said Letters Patent should read as corrected below.

Column 3, TABLE VIII, line 7 thereof, for "84%" read -- 74% --; same column 3, line 64, for "400 cms." read -- 400 Gms. --.

Signed and sealed this 28th day of July 1964.

(SEAL)

Attest:

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