

1

2,940,901

COATED MEDICAMENTS

Gordon D. Hiatt and John Emerson, Rochester, N.Y.,
assignors to Eastman Kodak Company, Rochester,
N.Y., a corporation of New Jersey

No Drawing. Filed Feb. 3, 1958, Ser. No. 712,619

5 Claims. (Cl. 167—82)

This application relates to medicament tablets having a coating selected from certain cellulose derivatives.

Pharmaceutical preparations or medicines which are solids are commonly dispensed in the form of compressed units referred to as pills or tablets. These tablets are prepared by processing the medicament in powder form in tablet compressing machines of any suitable type. It has been customary to coat the compressed pharmaceutical tablets thus obtained by tumbling them in a coating pan which involves the successive applications of sugar syrup, sometimes with fillers such as chalk or the like, while the tablets are being tumbled in the coating pan. This procedure results in building up a continuous coating of sugar upon the surface of the tablets, making those tablets easy to handle and readily administered. This overcoating gives the tablets a smooth surface which is easily polished, and prevents chipping of the tablets during handling. The application of such coatings, however, to the pharmaceutical tablets is time consuming because the water employed as a solvent for the sugar to form the coating composition must be evaporated. Tablets so coated are water susceptible and are subject to spoilage whenever wet accidentally.

One object of our invention is to provide a coating for medicament tablets which can be applied thereto from a solution of a cellulose derivative in a low-boiling solvent, susceptible to rapid evaporation, whereby a smooth surface is formed on the tablets. Another object of our invention is to provide coated medicaments in which the coating thereof is resistant to water. A further object of our invention is to provide a cellulose derivative coating for medicaments, which coating will disintegrate in the presence of dilute aqueous acid such as is encountered in the stomach. Other objects of our invention will appear herein.

The above objects are met by coating medicament tablets such as of aspirin, acetanilide, dried yeast, compounded vitamins, mineral salts such as bismuth subnitrate, calcium carbonate, ferrous lactate, magnesium oxide or potassium iodide, or any solid medicament or medicament compounded to a solid form with a solution of an alkyl amino acylate of a cellulose derivative, for example, cellulose acetate diethyl amino acetate. Cellulose derivatives of this type are dissolved in volatile organic solvents such as acetone or a low-boiling chlorinated hydrocarbon and applied to medicament tablets. Upon subjecting the tablets to drying conditions such as a current of warm air or a vacuum treatment, the coating quickly loses solvent and there results tablets having a smooth, water-resistant surface which is also resistant to the ordinary handling to which medicament tablets are subjected. Tablets coated in this fashion remain unchanged in water, but the coating thereon readily disintegrates in dilute aqueous acid such as gastric juice which permits the release of the medicament shortly after its entrance into the stomach.

Our invention also includes the use of alkyl amino

2

acetates of cellulose derivatives as a binder in the preparation of medicament products. For instance, some of the solution of the cellulose alkyl amino acetate compound may be milled or kneaded with medicament in solid form to form a mass of fairly uniform composition which is then given form or shape such as by extrusion and then dried.

The amino acetates of cellulose derivatives which are useful are the dimethyl amino acetates, the monomethyl amino acetates, the diethyl amino acetates, the dinormal propyl and diisopropyl amino acetates, the dibutyl amino acetates, the morpholine acetates, and the piperidine acetates of cellulose derivatives. As a matter of fact, the derivatives of any of the amines having not more than 8 carbon atoms are useful. The cellulose derivatives to which these amino acetate groups may be imparted to obtain compounds useful for coating medicament tablets are cellulose, cellulose acetate, cellulose acetate propionate, cellulose acetate butyrate, ethyl cellulose, and hydroxyethyl cellulose. The amount of substitution should be such that in the making of the cellulose derivatives there should be at least $4\frac{1}{2}$ –25% of chlorine in the compound when in the chloroacetate stage of preparation. It is desirable for best results, when the higher amines are supplied that the substitution be well above the minimum given. The following example shows the preparation of cellulose compounds useful for coating medicament tablets in accordance with our invention. This procedure may be followed by the preparation of the cellulose compounds which have been mentioned above as useful for this purpose:

A hydrolyzed cellulose acetate was treated with chloroacetic acid to give a cellulose acetate chloroacetate having a chlorine content of 8.4%. This cellulose acetate chloroacetate was reacted with diethyl amine whereby the chlorine was replaced with diethyl amino groups. The cellulose acetate diethyl amino acetate obtained had a nitrogen content of 2.4% nitrogen.

The preparation of compounds of this type is not our invention, but is the invention of John W. Mench and Brazelton Fulkerson and is described in their application Serial No. 619,681, filed Nov. 1, 1956, now Patent No. 2,861,068. That disclosure may be referred to for details of the method of preparing compounds useful for coating medicaments to form products in accordance with our invention.

The cellulose acetate diethyl amino acetate formed as described above was dissolved in acetone to give a solution of 15% concentration. This solution was added portionwise to compressed sodium chloride tablets, which tablets were tumbled to distribute the solution thereon. At intervals an air jet was applied to remove the acetone from the tablets. The application of the coating of cellulose acetate diethyl amino acetate to the tablets took less than one hour. The tablets thus coated when immersed in water did not change form after two hours immersion. However, these tablets when treated with dilute aqueous hydrochloric acid simulating gastric juice disintegrates the coating and allows release of the salt to the solution. Our invention is applicable to any solid medicament tablets in which the medicament is intended for release in the stomach when administered in medication procedures.

Another method of operation is to use the cellulose derivative amino acylate as a binder with a medicament capable of plasticizing or softening the binder, especially when the composition is heated. Other medicaments can be added to this two component mixture whether they soften the binder or not. They may actually be the main therapeutic agent and are enclosed by the plasticized binder composition which, for example, may be cellulose acetate diethylamino acetate and acetyl salicylic acid or aspirin.

3

We claim:

1. A medicament composition comprising tablets of a solid form medicament compounded with an alkyl amino acetate of a cellulose derivative the alkyl amino groups of which have no more than 8 carbon atoms.

2. Medicament tablets containing thereon a coating of an alkyl amino acetate of a cellulose compound the alkyl amino groups of which have no more than 8 carbon atoms.

3. A medicament composition comprising tablets of a solid medicament having thereon a coating of cellulose acetate diethyl amino acetate.

4. Sodium chloride tablets containing a coating of cellulose acetate diethyl amino acetate.

5. A method of preparing a medicament composition which comprises tumbling compressed units of medica-

4

ment with a solution of an alkyl amino acetate of a cellulose compound the alkyl amino groups of which have no more than 8 carbon atoms in a volatile solvent and followed by removal of the volatile solvent from the composition.

References Cited in the file of this patent

UNITED STATES PATENTS

2,072,870	Dreyfus	Mar. 9, 1937
2,136,296	Hardy	Nov. 8, 1938
2,233,475	Dreyfus	Mar. 4, 1941
2,512,960	Morgan	June 27, 1950
2,518,203	Thompson	Aug. 8, 1950

FOREIGN PATENTS

344,380	Great Britain	Mar. 2, 1931
---------	---------------	--------------