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PROCESS OF PREPARING PHARMACEUTICAL TABLET WITH ORANGE-PEEL-LIKE PROTECTIVE SUGAR COATING

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ABSTRACT OF THE DISCLOSURE

Described is a process for preparing a pharmaceutical form, which comprises heating tablets from 35 to 60° C. while rotating at from 5 to 30 r.p.m., spraying a protective sugar coating solution, in the presence of air under pressure, onto the tablets, whereby the tablets are given an orange-peel-like protective sugar coating. The ratio of sugar mixture solution to air is between 1:4 and 1:20, while the pressure of the sprayed air is from 0.5 to 2.5 atmospheres in the general circuit and 0.1 to 1.5 atmospheres in the liquid coating container. The temperature of the sprayed air is between 20 and 65° C., while the temperature of the sugar coating solution is between 15° and 80° C. The density of the sugar coating solution is between 1.15 and 1.37 at a temperature of 17.5° C.

Our invention relates to the new pharmaceutical form which we call a "farmoid" and to the process of its preparation. Farmoids constitute a new pharmaceutical form for oral administration in which a tablet containing the medicament is coated with a thin sugar film showing a wrinkled, orange-peel-like surface. This makes the farmoid completely different from both tablets and coated-tablets. Contrasted to tablets, the farmoid shows an outer sugar coating, which besides being an outer protective coating, also facilitates the ingestion of unpleasant tasting substances. Contrasted to coated-tablets, the farmoid shows a less thick sugar-coating, the surface of which is wrinkled instead of smooth.

The three procedures commonly used in the tablet coating art are:

Traditional tablet coating which consists in:

(a) applying a resinous material to the tablet for protecting it from moisture of the coat later applied;
(b) applying an under-coating material so that the tablet is as homogeneous as possible;
(c) applying numerous individual layers of syrup having various density with color optionally added; and
(d) finally polishing, with a suitable wax-like material, to give the coated tablet a pleasing appearance.

These operations, which may take from 2 to 4 days, result in a substantially lenticular sugar coated tablet having pleasing appearance and taste.

Tablet coating by paint which consists in using an appropriate resinous coating material with color optionally added. Upon completion of this operation, a coated form is obtained which completely differs from the traditional coated tablet, in that the original tablet form is maintained.

Coating by dry compression which consists in welding around the tablet a mixture of suitably granulated powders. Upon completion of this operation, a pharmaceutic form, which differs completely from the traditional coated tablet, and consisting practically of two tablets one inside the other, is obtained.

In the case of traditional coating, the time required for the complete process is dependent upon the fact that both

the under-coats and the syrups are put on, from aqueous solutions or suspensions. Between each coat, it is necessary to rotate the tablets in a coating pan, with air blowing over the tablets, in order to evaporate the moisture and form a hard, dry coat. Both the time required for the process, which requires a specialized labor, and the quantity of the material used, greatly increase the production cost of the coated tablet. 300 to 350 mg. of different excipients are used to surround each tablet which has a weight of 500 mg.

The coating by paint method requires a shorter time for the coated tablet preparation than the traditional coating method. In spite of this costs are equally high, because the special resins and the large volumes of inflammable solvents required need expensive equipment, both for safety and recovery of resins and solvents.

The coating process by dry compression besides requiring particular and expensive equipment, is also subject to the remarkable limitation that the active ingredients do not exceed a fixed ratio with respect to the excipient. Each new item also requires a preliminary and laborious setting-up of recipes for both the nucleus and the coating which not always are easy to weld.

Our invention has an object overcoming these difficulties and provides a method for coating an active substance tablet, using simple, low cost equipment while employing small quantities of the same raw materials used in traditional coating techniques.

Another object is to provide a distinctive coating. By distributing the coating mixture in finely subdivided form in the warm and in the presence of air at a ratio of coating mixture:air between 1:4 to 1:20, the pharmaceutical form obtained has the outer appearance wrinkled and orange-peel-like instead of smooth with coated tablets.

Farmoids, the new pharmaceutical form obtained according to the present invention, consist essentially of a tablet containing an average weight from 100 to 700 mg. of medicament around which from 30 to 200 mg. of excipients form the external coat.

The process comprises coating the tablets with a protective resinous material; heating the tablets at a temperature from 35° C. to 60° C. in a coating-pan rotating at 5 to 30 r.p.m.; and spraying, on the protected tablets, the solution or suspension for coating; said solution is maintained at a temperature of from 15° to 80° C.

Farmoids have the advantages of coated tablets because of the protection from outside, sweet taste of the coat and agreeable outer aspect. Furthermore they show other advantages over coated tablets:

(1) quicker preparation because of the single coating operation of the tablet. The average time necessary to prepare one lot of coated tablets is reduced from 30 hours to an average time of 2 hours for one lot of farmoids;
(2) less excipients are wasted because by spraying a perfectly continuous coat is obtained employing a relatively small quantity of coating mixture. Of course, the total saving of excipients depends upon the weight and the form of the starting tablet, but in general it is about 30–35%;
(3) less volume as direct consequence of (2);
(4) lower production and forwarding costs both as direct consequence of the advantages illustrated in (1), (2) and (3), and because the coating process may be carried out by a non-highly specialized staff.

In greater detail, the process of the present invention may be carried out as follows:

Into a coating pan are put from 2 to 80 kg. of tablets (according to the capacity of the pan itself), to which a

film of protective resinous substance has been first applied. The coating pan is adjusted to a rotary speed, which depends upon the diameter of the pan itself and may be between 5 and 30 r.p.m. At the same time, heating is carried out by warm air, gas, vapor, infrared or other suitable heating sources. The heating is regulated so that the temperature of the tablets is between 35° and 60° C. The pan is also provided with an appropriate aspiration system to remove the excess of spray over that required for the coating process. As the heated tablets, rotate, a coating mixture, at a temperature of 15 to 80° C., is sprayed over the tablets in the presence of sprayed air, at a temperature of 20 to 65° C. Farmoids so obtained may be optionally polished with a polishing solution, such as natural or synthetic gums and resins like benzoin, lac gum or carnauba wax dispersed or dissolved in suitable solvents.

The equipment used for spraying the coating mixture comprises the following elements:

(a) a paint spray gun having external or internal mixer nozzles provided with a spray head to produce a rather large spray pattern. The pressure at which the liquid is sprayed is 0.5–2.5 atmospheres. For higher quantities of tablets, two or more spray-guns may be used;
(b) a cup for paints under pressure from 0.1 to 1.5 atmospheres provided with a pressure regulator and a stirrer which is necessary, if the coating mixture contains substances insoluble in suspensions;
(c) a heating system which may be embodied into the cup or inserted between the cup and spray-gun. This system regulates the temperature of the coating mixture and of the air so that the required temperature is reached.

The spraying mixture consists essentially of a sugar solution having a density of between 1.15 and 1.37 at a temperature of 17.5° C. Sorbital or saccharose may be employed as the sugar. The sugar solution may be suitably charged with an inert excipient, such as calcium carbonate, titanium dioxide, starch, talc, natural gum, etc. Among coloring substances, which may be used in the practice of this invention, are any of the non-toxic dyes, which have been certified for use, in particular indigo carmine (F.D. and C. Blue No. 2), sunset yellow (F.D. and C. Yellow No. 6) erythrosine extra yellowish (F.D. and C Red No. 3), tartrazine yellow (F.D. and C. No. 5), amaranth red (F.D. and C. Red No. 2). The coating mixture may also be loaded with pharmaceutical substances which must be kept separated from the components of the tablet. Sometimes it is opportune also to add a plasticizing agent such as polyvinyl alcohol, polyethylene glycol or a surface-active agent such as a polyoxyethylene ester of sorbitol, etc. Small quantities of water-miscible solvents, preferably ethyl alcohol and acetone, may be added. The coating liquid is sprayed onto the tablets by means of the spray-gun in the form of a mist, in which the ratio of liquid:air is between 1:4 and 1:20.

The present invention is further illustrated, without intent to limit it, by the following examples:

Example 1

25 kg. of tablets having an average weight of 500 mg. are placed into a copper pan with inside diameter of 84 cm. and provided with a suitable aspiration system. The tablets are conventionally prepared. The tablets are rounded, rather hard and surrounded by a protective film of natural gums or artificial resins. The pan is rotated at a speed of 9 r.p.m., and at the same time heated by gas to a tablet temperature of about 50° C. Onto the heated tablet the following solution is sprayed:

	G.
Saccharose	67
Distilled water to	100

To obtain a good vaporization, the coating solution is heated at about 80° C., the air at 20° C. and the equipment is adjusted to provide a pressure of 2 atm. in the general circuit, and 0.6 atm. in the cup containing the solution itself. Spraying is continued without interruption until the desired coat is obtained. The average weight of the tablets, after such a treatment, is increased by about 30%. The time required for the whole process is about 1 hour and 30 minutes. Finally the farmoids may be polished by one of the systems used for the polishing of coated tablets, e.g. applying lac gum and carnauba wax.

Example 2

Operating as described in Example 1, a paint having the following composition is employed:

	G.
Arabic gum	1.0
Calcium carbonate	5.0
Titanium dioxide	0.5
Saccharose	60.0
Distilled water to	100.0

Example 3

Operating as described in Example 1, a paint having the following composition is employed:

	G.
Tartrazine yellow (F.D. and C. No. 5)	0.150
Titanium dioxide	2.000
Polyoxyethylenesorbitol monooleate	0.500
Saccharose	65.000
Distilled water to	100.000

Example 4

10 kg. of tables, previously coated with the usual protective film of natural gum or artificial resin, are placed into a stainless steel pan having an inside diameter of 63 cm., and provided with an aspiration system. The tablets have an average weight of 350 mg. The pan is rotated at 24 r.p.m., and at the same time the tablets are heated by a 1000 watt infrared ray lamp. The heating is such as to obtain a tablet temperature of about 40° C. Nebulization of a coating paint of the following composition then starts:

	G.
Erythrosine extra yellowish (F.D. and C. Red No. 3)	0.100
Saccharose	65.000
Distilled water to	100.000

The temperature of the solution is kept at about 40° C., the temperature of the air at 50° C., and the equipment is adjusted to give a pressure of 1.5 atm. in the general circuit and 0.1 atm. in the cup containing the coating mixture. Nebulization is continued without interruption until the desired coat is obtained. The time required for the whole process is about 1 hour and 10 minutes, while the average weight increases by about 25%. The farmoids may be finally polished like coated tablets.

Example 5

Operating as described in Example 4, a paint with the following composition is employed:

	G.
Talc	3.0
Starch	2.0
Titanium dioxide	1.5
Polyoxyethylenesorbitol monolaurate	0.4
Polyethylene glycol "4000"	1.0
Saccharose	55.0
Distilled water to	100.0

Example 6

Operating as described in Example 4, a solution or suspension of a medicament having the following compo-

sition is sprayed on the tablet together with the coating paint:

	G.
Vitamins B_{12}	0.100
Folic acid	0.010
Titanium dioxide	0.500
Ethyl alcohol 95° C.	5.000
Polyvinyl alcohol	0.500
Saccharose	50.000
Distilled water to	100.000

Then the operation may be followed by spraying on the following solution:

	G.
Erythrosine extra yellowish (F.D. and C. Red No. 3)	0.150
Arabic gum	2.000
Saccharose	60.000
Distilled water to	100.000

All pressures are gauge pressure.

Obviously, many modifications and variations of the present invention are possible in the light of the above teachings. It is therefore to be understood that the invention may be practiced otherwise than as specifically described.

We claim:

1. A process for preparing a pharmaceutical form, which comprises heating tablets from 35 to 60° C. in a coating pan rotating at from 5 to 30 r.p.m., spraying a protective sugar coating solution onto the tablets in the presence of air, the ratio of sugar mixture solution to air being between 1:4 and 1:20, under pressure, whereby the tablets are given an orange-peel-like protective sugar coating.

2. The process of claim **1**, wherein the pressure of the air sprayed onto said tablet is from 0.5 to 2.5 atmospheres in said pan and is 0.1 to 1.5 atmospheres in the liquid coating solution.

3. The process of claim **1**, wherein the temperature of the sprayed air is between 20 and 65° C.

4. The process of claim **3**, wherein the temperature of the sugar coating solution is between 15° and 80° C.

5. The process of claim **4**, wherein the density of the sugar coating solution is between 1.15 and 1.37 at a temperature of 17.5° C.

6. The process of claim **5**, wherein the tablets are given a protective resinous coating prior to the sugar coating.

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