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**PROCESS OF PREPARING PHARMACEUTICAL
TABLET WITH ORANGE-PEEL-LIKE PROTEC-
TIVE SUGAR COATING**

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6 Claims

ABSTRACT OF THE DISCLOSURE

Described is a process for preparing a pharmaceutical 15
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 pres-
sure, onto the tablets, whereby the tablets are given an
orange-peel-like protective sugar coating. The ratio of 20
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 atmos-
pheres in the liquid coating container. The temperature 25
of the sprayed air is between 20 and 65° C., while the tem-
perature 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 30
which we call a "farmoid" and to the process of its prep-
aration. 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 35
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, 40
also facilitates the ingestion of unpleasant tasting sub-
stances. 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 coat- 45
ing art are:

Traditional tablet coating which consists in:

- (a) applying a resinous material to the tablet for pro- 50
tecting 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 55
give the coated tablet a pleasing appearance.

These operations, which may take from 2 to 4 days, 60
result in a substantially lenticular sugar coated tablet hav-
ing pleasing appearance and taste.

Tablet coating by paint which consists in using an ap- 65
propriate 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 70
around the tablet a mixture of suitably granulated pow-
ders. 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

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the under-coats and the syrups are put on, from aqueous
solutions or suspensions. Between each coat, it is neces-
sary 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 quan-
tity of the material used, greatly increase the production
cost of the coated tablet. 300 to 350 mg. of different ex-
cipients 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 coat-
ing 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 re-
quiring particular and expensive equipment, is also sub-
ject 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 tradi-
tional 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 ac- 35
cording 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 ex-
cipients form the external coat.

The process comprises coating the tablets with a pro- 40
tective resinous material; heating the tablets at a tem-
perature 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 be- 45
cause 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; 55
- (2) less excipients are wasted because by spraying a
perfectly continuous coat is obtained employing a rela-
tively 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 di-
rect 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:

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

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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:

| | |
|--------------------|-----|
| 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 equip-

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ment 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-

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

| | | |
|---|-------------|----|
| | G. | |
| Vitamins B ₁₂ ----- | 0.100 | |
| Folic acid ----- | 0.010 | 5 |
| Titanium dioxide ----- | 0.500 | |
| Ethyl alcohol 95° C. ----- | 5.000 | |
| Polyvinyl alcohol ----- | 0.500 | |
| Saccharose ----- | 50.000 | |
| Distilled water to ----- | 100.000 | 10 |
| Then the operation may be followed by spraying on the following solution: | | |
| Erythrosine extra yellowish (F.D. and C. Red No. 3) ----- | G. 0.150 | |
| Arabic gum ----- | 2.000 | 15 |
| 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

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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.

References Cited

UNITED STATES PATENTS

| | | | | |
|----|-----------|---------|------------------|----------|
| 20 | 3,096,248 | 7/1963 | Rudzki. | |
| | 3,106,492 | 10/1963 | Macdonald et al. | |
| | 3,331,696 | 7/1967 | Rieckmann et al. | 167—82.7 |
| | 3,361,631 | 1/1968 | Weinstein. | |
| | 3,379,554 | 4/1968 | Brindamour. | |

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