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[54] LAMINATED TABLETS

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[63] Continuation-in-part of Ser. No. 01,023, Jan. 6, 1970, abandoned.

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[56]

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[57]

ABSTRACT

Laminated, pan-coated tablets are described wherein the various medicament layers are separated by a layer containing 10–50 percent of a silica gel having a specified pore size. This silica gel layer not only substantially reduces the processing time but also aids in preventing migration of the ingredients and in accelerating dissolution.

6 Claims, No Drawings

LAMINATED TABLETS

This application is a continuation-in-part of our copending application, Ser. No. 1,023, filed Jan. 6, 1970 now abandoned.

Numerous pharmaceutical formulations can be advantageously administered in a dosage unit tablet form wherein at least one medicament is present in a series of layers surrounding a core. This core can either be pharmacologically inert or can itself contain active substances, which even may be pharmaceutically incompatible with active ingredients in the surrounding layers.

Such laminated tablets are useful for various purposes, such as achieving differential release in rate and/or situs. One can prepare by this means tablets of the repeat-action type wherein one dose of the medicament is in the core or in an interior layer and another dose is in a more exterior layer separated by an enteric coating as described, for example, in U.S. Pat. No. 2,991,226. Another use is to provide an outer layer which is soluble in the mouth for sublingual absorption while the inner layer is intended for release after the tablet is swallowed. Still another important application of laminated coating is in tableting a formulation involving pharmaceutically incompatible medicaments, as for example, aspirin and phenylephrine.

The preparation of such tablets has heretofore been a tedious and lengthy procedure. A core is formed from the medicaments and suitable excipients in known manner by direct compression or alternatively, by first forming a wet or dry granulation and then compressing the granulation. If an inert core is desired, non-pareil seeds or the like can be directly used. Many coats of the solution of active ingredients must be laid down on the core to obtain the desired thickness with acceptable uniformity. Following the application of each coat in conventional coating pans, a dusting powder is generally applied to prevent the tablets from sticking to one another and to help build up the thickness of the tablet coat. Typical of such dusting powders are starch, talc, terra alba, pulverized gum acacia and the like. After dusting powder is absorbed on the tablet, heat is applied, usually in the form of dry hot air. This drying is the most time-consuming operation in the overall process and is particularly onerous in the case of those medicaments which have poor drying characteristics such as phenylephrine and diethylpropion. Then various conventional grossing, coloring and polishing coats may be optionally applied in known manner to impart pharmaceutical elegance.

We now have discovered that the art of laminated tablets can be significantly advanced if one applies between each of the medicament-containing layers, a thin layer containing about 10 to 50 percent by weight of a silica gel having an average pore diameter of from about 90–400 angstrom units.

This silica gel layer dramatically reduces the drying time. Moreover, it protects against the migration of ingredients from one layer into a different layer or into the core or onto the surface of the tablet. Similarly, it protects against migration of any materials from the core into the layers. Still further, by means of a wicking action, it results in more rapid and complete disintegration of the coating under the conditions desired for disintegration.

This silica gel-containing coat can be applied to the tablet either as a powder or in slurry form. It is preferred that this silica gel-containing coat additionally be applied directly to the tablet core. This further protects against any tendency of the laminated medicaments to migrate into or out of the core.

In a preferred embodiment, the silica gels of this invention have an average pore diameter within the range of 125–300 angstrom Units. Examples of commercially available silica gels within this range are Syloid 74 (average pore diameter believed to be about 150 A.) and Syloid 244 (average pore diameter believed to be about 250 A.), both of which are available from W. R. Grace and Company.

The following example of the preparation of decongestant-type cold tablets illustrates a preferred embodiment of this invention.

EXAMPLE

One thousand cores are prepared in a standard manner by first mixing 162 grams of phenacetin, 32 grams of caffeine and 40 grams of starch and forming a wet granulation thereof with 50 ml. of a 10 percent gelatin solution. The mixture is passed through a screen, dried in the oven and rescreened. An additional 15 grams of starch and 4 grams of calcium stearate (lubricant) is then added along with 230 grams of aspirin and the mixture is compressed into cores in the conventional manner. These cores are placed in a conventional coating pan and coated in the following manner. First, they are coated with Composition A composed of 51.2 percent sugar, 12.8 percent acacia, and 36.0 percent water. The moist coated cores are then dusted prior to hot air drying with Powder B composed of 25 percent by weight of a silica gel having an average pore diameter of 250 Angstrom units (Syloid 244) and 75 percent by weight of terra alba (dehydrated calcium sulfate).

The dusted cores are dried by hot air in the conventional manner. The dried cores are then coated with Suspension C which contains 2 grams of chlorpheniramine maleate and 10 grams of L-phenylephrine base suspended in 50 ml. of Composition A. Dusting Powder B is applied and the coated cores are hot-air dried. This serial application of Suspension C and Dusting Powder B followed by hot-air drying is repeated five times. Then follows a sequence of applying a coat of Composition A followed by dusting with Powder B and hot-air drying and this sequence is repeated. Three coats are then applied of a grossing composition composed of 20 percent Powder B, 3 percent titanium dioxide, 3 percent corn starch, 48 percent sugar and 26 percent water. The tablets are then given a white color by coating with a 3 percent titanium dioxide suspension in sugar syrup.

The above coating operation can be satisfactorily performed in one day. If the specified silica gel is omitted, the coating operation on the moist core requires about 4 days. In addition, the specified silica gel in the above-produced tablets helps prevent the pharmaceutically incompatible aspirin and 1-phenylephrine ingredients from migrating toward each other and additionally accelerates the dissolution of the tablet when ingested.

Numerous variations of the above-described tablets will be apparent to one skilled in the art within the spirit of this invention.

What is claimed is:

1. A laminated, pan-coated tablet comprising a medicament-containing or inert compressed tablet core surrounded by a plurality of pan-coated medicament-containing subcoating layers comprised of active ingredients having poor drying characteristics and aqueous syrups requiring thorough drying prior to successive pan-coating operations, and having absorbed upon and between said medicament-containing subcoating layers, a dusting powder absorbent layer serving to prevent the moist syrup-coated tablets from sticking to one another, and to help build up tablet thickness, containing about 10–50 percent by weight of a silica gel having an average pore diameter of from about 90–400 angstrom units, said silica gel absorbent serving to (1) reduce the drying time of the moist pan-subcoated layered tablets, (2) accelerate the dissolution of the tablet when ingested, by means of a wicking

action resulting in more rapid and complete disintegration of the subcoating, and (3) prevent the medicaments of each subcoating layer from migrating toward each other, into the core, or onto the surface of the tablet.

2. A tablet according to claim 1 wherein said core contains at least one pharmacologically active ingredient.

3. A tablet according to claim 1 wherein said core contains a material incompatible with at least one material in the surrounding layers.

4. A tablet according to claim 1 wherein a layer of said silica gel surrounds said core before the first of said medicament-containing layers.

5. A tablet according to claim 1 wherein said silica gel has an average pore diameter of from about 125 to 300 angstrom units.

6. A tablet according to claim 1 where at least one of said medicament-containing layers comprises phenylephrine.

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