Jan. 19, 1965 H. LOWEY 3,166,476

POWDER BASED TABLETS

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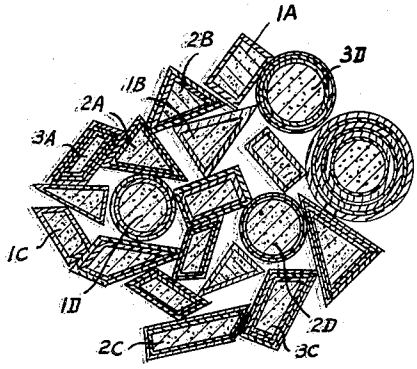


FIG. 1

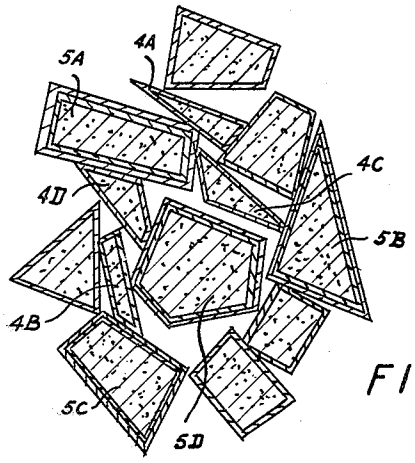


FIG. 2

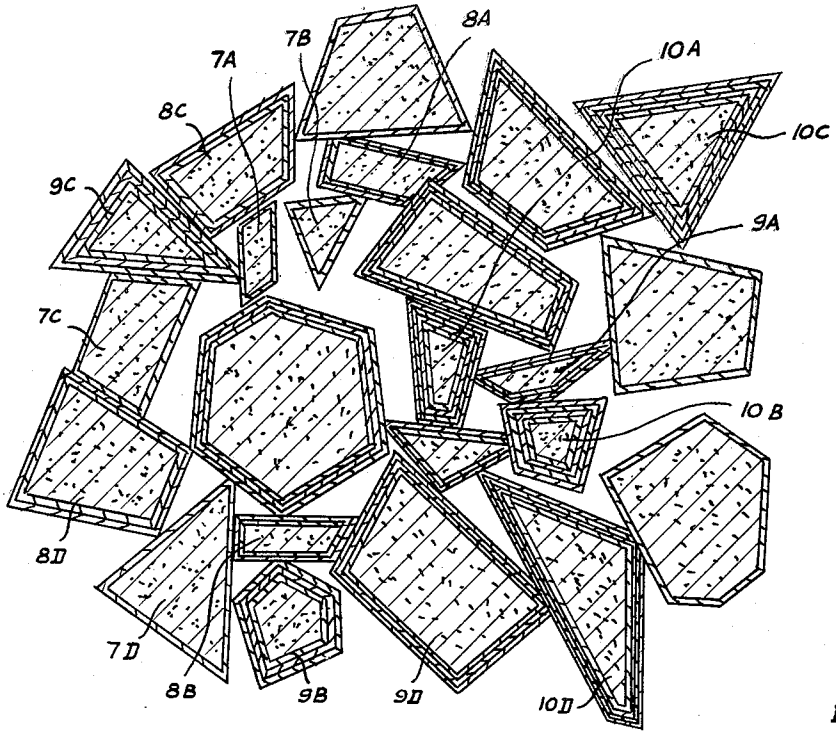


FIG. 3

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POWDER BASED TABLETS

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This invention relates to powder tablets and especially to tablets which are used in relatively large quantities of irregular powderized particles, such as aspirin or vitamins.

One of the objects of the invention is to facilitate the intake of such relatively large quantities by permitting the user to take once during a day or some other predetermined period, of relatively long duration, a relatively large amount and to cause this large amount to be effective over a relatively long period—for example, an entire day.

As a more specific object of the invention the finely powderized material of predetermined mesh is impregnated in several substantially equal batches with differently predetermined quantities of a delaying agent such as ethylcellulose whereupon these batches are mixed and compressed into form of relatively large tablets which can be taken at once and the corresponding components thereof will be released at predetermined times, for example every one hour in equal quantities.

Still another object of the invention is to provide the different batches, instead of with different coatings, and with the same amount of material coating but make these coatings differentially effective by providing in each batch differently sized irregular powder particles.

It has been found that differently sized powder particles are differently receptive to a coating because such coating will not surround the usually irregularly sized particles to an equal extent and therefore, differently sized particles will be coated differently by the same amount of action delaying coating and, as a result, will become effective medically after different periods.

Still another object of the invention is to affect the surface of such particles in a different manner prior to coating by the action-delaying coating, for example, by passing the powder particles over differently shaped, for example differentially roughened, metallic surfaces thus making them more or less receptive to receive action delaying coatings.

Still further an object of the invention is to prepare the surface of powdered particle batches by different agents affecting such surface, for example by alcohol or water, or non-wetting agents such as gelatine or other viscous material so as to change the receptivity of the surface of the powder particles in a predetermined manner so as to make them more or less or differentially receptive to the action delaying coating.

An object of the invention, furthermore, is to apply different action delaying coatings to different batches of powdered particles of the material to be tableted so as to produce in these batches different action delaying characteristics.

Still further an object of the invention is to use action delaying agents of different concentration and to apply them to different batches of medically active powders which are to be mixed thereafter, and to be applied simultaneously in the form of tablets or portions containing components of the same material which are to be medically active at predetermined intervals after intake.

As a further object of the invention any of the aforementioned steps may be combined, for example differently sized particles which are to be coated with differently concentrated action delaying agents so as to obtain a further differentiation in their action delaying effects without departing from the scope of this disclosure.

These and other objects of the invention will be more fully apparent from the drawings annexed herewith in

which FIG. 1 represents in cross-section a tablet showing powder particles at an enlarged scale of the same size and applied with cellulose coatings of different effectivity as far as action delay is concerned.

FIGS. 2 and 3 respectively show a modification, applied to a salicylamide tablet in which differently sized particles are applied with the same or different coatings to produce the desired action delaying differences.

In FIG. 1, part of an aspirin tablet or capsule is shown in cross section containing powder particles of substantially the same mesh and consisting of a mixture of irregular and regular shapes, the latter being preferably spherical are shown to be coated, respectively, with different action delaying coatings adapted not to react with the active or base ingredient of the material, for example methyl cellulose.

Thus, particles 1A to 1D are coated with one thickness or quantity of coating material consisting of one or several layers represented in FIG. 1 as a single layer and corresponding for example to a two-hour release time, i.e., the average time of passage through the stomach.

Particles 2A to 2D are provided with a different, for example a much thicker coating such as to be effective for example after three hours. Particles 3A to 3C are to be effective after 4 hours, and further particles may be provided (although they are not shown in FIG. 1) to be effective after further predetermined time intervals.

The mixture of irregular and regular shapes has the advantage that it is possible to provide certain drugs or active ingredients in the form of base coatings on regularly shaped carriers or kernels especially spherical granules which are more accurately releasable and also releasable in more accurate quantities than the drugs or active ingredients provided on or in particles of irregular shapes.

FIG. 2 shows a combination of particles compressible, like the particles shown in FIG. 1, into a tablet, consisting of irregular particles of several mesh numbers. For example, particles for 4A, 4B, 4C, 4D, may consist of particles of a number 80 mesh and provided with one predetermined thickness of coating which again as in the example shown in FIG. 1 may consist of one or a great number of coatings to assure better adherence and elasticity.

This thickness of coating may correspond to an action delay of two hours. Another batch of particles included in the tablet and schematically indicated as 5A, 5B, 5C and 5D may consist of larger particles corresponding to a mesh number of say, 60 and may be provided with twice the thickness or twice the amount of coating as provided for particles 4A to 4D. This thickness may correspond to an action delay of 6 hours.

In such a tablet further particles may be provided of other different mesh numbers carrying different coatings to effect release at different, yet predetermined time intervals.

In the example shown in FIG. 3 particles of the same mesh number are shown to be provided with different coatings and mixed with particles of other meshes, each mesh number being provided with different coatings.

This is in order to compensate for or equalize the difference in release effect caused by the difference in particle size which may affect the amount and aherence of the coating to differently sized or shaped particles.

As shown in FIG. 3, particles of four different mesh numbers corresponding for example to mesh numbers 80, 60, 40 and 20 are shown at 7A, 8A, 9A, and 10A respectively. Each of these particles is provided with one thickness of coating corresponding for example to a two hour action delay.

Another set of particles of different but the same mesh numbers are shown at 7A, 8A, 9A, 10A, 7B, 8B, 9B, and 10B, respectively and provided with a different thickness

of coating for example with twice the thickness as that provided for particles of the type 7A, 8A, 9A, 10A, and corresponding to a release time or an action delay of 4 hours.

Similarly a third set of differently sized particles may be provided in a tablet or capsule as indicated schematically at 7C and 10C, each provided with another type of thickness for example with a still larger thickness as that provided for particles 7B to 10B and corresponding to an action delay of say 6 hours.

Obviously in this way any number of sets of particles of different meshes and of any number of meshes may be provided with different coatings to produce predeterminedly desired action delays in an accurate manner without involving the use of accurately shaped granules or carriers and permitting the direct use of relatively inexpensive bulk material and simple powderizing process. In specific examples, the invention has been applied to bulk type materials such as aspirin, salicylamide and vitamin C.

Care should be taken that the medically active ingredient or bulk material does not react with the active delaying coating material.

Powderization or particularization of the material to the required mesh was achieved by the so called slugging process, i.e., a process in which the material is first compressed into relatively large tablets and then broken up by impact to the required size represented by sieves arranged in the slugging equipment or ball mill in otherwise well known manner.

In a specific example, salicylamide is reduced to batches of powdered particles of 80, 70, 60, 50, 30 and 20 mesh, and each of these batches was coated in rotating pans with 85% alcohol solution of ethyl cellulose, starting with a percentage in weight of 10% for the 80 mesh particles and representing an action delaying interval of 1 hour. The 70 mesh particles are coated with a similar solution but representing 11% of the weight of the particles and corresponding to a 2 hour action delay. The 60 mesh particles were coated with an ethyl cellulose solution representing 12% of its weight and corresponding to a 3 hour action delay.

Similarly the 50, 60, 40, 30 and 20% mesh batches are coated with 85% alcohol solutions of ethyl cellulose of 13, 14, 15, 16 and 17% weight of the particles, and correspond to action delaying intervals of 4, 5, 6, 7 hours respectively.

Similar quantities and similar solutions were used with powder particles consisting of vitamin C.

In the production of aspirin tablets having an action delay extending over several hours, ethyl cellulose solutions cannot be used because they react with the aspirin powder, and here methyl cellulose solutions or other action delaying coatings of otherwise well known structure can be used in quantities similar to those mentioned above and with similar effects, without departing from the scope of this invention.

The invention is not limited to the medically active ingredients illustrated and described above nor to any particular coating solutions and preparations, above but may be applied in any form or manner whatsoever, without departing from the scope of this disclosure.

I claim:

1. A time delay medicament comprising a multiplicity of powderized therapeutic particles of different sizes and shapes substantially equal proportions of which have been impregnated with a time delay material and the impregnated powderized particles compressed into tablets, the particles being pre-treated to alter their surface receptivity prior to impregnation by a mechanical agent.

2. A time delay medicament comprising a multiplicity of powderized therapeutic particles of different sizes and shapes substantially equal proportions of which have been impregnated with a time delay material and the impregnated powderized particles compressed into tablets, the particles being pre-treated to alter their surface receptivity prior to impregnation by passing the particles over differentially roughened metallic surfaces.

3. A time delay medicament comprising a multiplicity of powderized therapeutic particles of different sizes and shapes substantially equal proportions of which have been impregnated with a time delay material and the impregnated powderized particles compressed into tablets the particles being pre-treated to alter their surface receptivity prior to impregnation by subjecting the surface of the particles to the action of a chemical agent selected from the group consisting of water, alcohol and gelatine.

4. A process for the production of a time delay medicament which comprises screening powderized medicament particles the surface receptivity of which is increased into separate batches of various mesh sizes and regular and irregular shape, separately coating each such batch with a different thickness of coating material which is thickest for the smallest mesh size and thinnest for the largest mesh size and proportionally thick for intermediate mesh sizes by applying thereto the same amount of a similar coating material, mixing the separately coated batches and compressing the resulting mixture into tablets.

5. A time delay medicament comprising a multiplicity of powderized therapeutic particles of different sizes and shapes substantially equal proportions of which have been impregnated with a time delay material and the impregnated powderized particles compressed into tablets, the particles being pre-treated to alter their surface receptivity prior to impregnation by a chemical agent.

References Cited by the Examiner

UNITED STATES PATENTS

2,738,303	5/56	Blythe	167—82
2,793,979	5/57	Svedres	167—82
2,853,420	9/58	Lowey	167—82
3,078,216	2/63	Greif	167—82

FOREIGN PATENTS

109,438	1/40	Australia.

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