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[54] DIRECT COMPRESSION VEHICLES AND METHOD THEREFOR

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[57] **ABSTRACT**

A granular, multicomponent direct compression vehicle is made by uniformly blending at least one compactible material with other materials, compacting the blend to a sheet, breaking the sheet up into particles of a desired size and, if necessary, screening. The resulting product when blended with an active material and, to the extent necessary, a lubricant, can be directly formed into a tablet.

11 Claims, No Drawings

DIRECT COMPRESSION VEHICLES AND METHOD THEREFOR

This invention relates to a multicomponent direct compression vehicle and to a method for its manufacture. More particularly, this invention relates to a particulate material, each granule of which comprises an intimate mixture of two or more substances and has substantially the same composition as the average composition of the bulk of the material, which particulate material is useful as a direct compression vehicle for the manufacture of tablets and the like, and to a method for the manufacture of such particulate material. This invention is particularly related to multicomponent direct compression vehicles having a sugar as the predominant component.

There are two general methods for forming tablets, i.e., compression of a dry particulate material and trituration, or molding of a moist material, of which the first technique is by far the most frequently employed. The compression technique may be further subdivided into three major categories, viz, direct compression, wet granulation and dry granulation. The direct compression technique is the most desirable, in that it employs the fewest steps and, in the case of the production of tablets containing sensitive or unstable actives, such as certain pharmaceuticals, minimizes the exposure to water or other conditions tending to adversely affect stability of the active. Unfortunately, however, it has been found that the direct compression technique is of limited applicability.

First, most active materials possess poor compression properties, and thus are unsuitable for this technique. In addition, many actives are required in such small amounts per unit dosage form that direct compression of the active alone is impractical, if not impossible. As a result, the active must be admixed with a direct compression vehicle, i.e., an inert composition which is compatible with the active and has good compressibility. In addition, the direct compression vehicle must have good flowability, good stability under normal ambient conditions, no adverse effect on tablet disintegration time, the ability to produce good tablet surfaces, and low cost.

To date, however, no material has been found which satisfies all of these criteria. For example, of the most popular of such compression aids, spray-dried lactose possesses poor stability and discolors on storing, dicalcium phosphate forms a tablet having poor strength, and microcrystalline cellulose is expensive.

In addition to active and compression vehicle, a tabletting formulation normally includes additives such as diluents, lubricants, flavors, colors, disintegration agents and the like. When the tabletting formulation includes a large number of components, direct compression techniques are even less useful because of the difficulty of assuring uniform mixing of the various components on dry blending. As a result, a pregranulation technique, normally wet granulation, has been found essential.

It is an object of the present invention to provide a new direct compression vehicle and a process for its production.

It is a further object of this invention to provide a multicomponent compression vehicle which may be combined with an active and, if desired, a lubricant, and the resulting dry mixture subjected to direct compression, and to a method for the production of such vehicle.

Other objects and advantages of this invention will be apparent to those skilled in the art in tablet manufacture upon review of the specification and claims.

In general the present invention relates to a method comprising mixing two or more components, compacting the resulting mixture to form a sheet, breaking up the sheet into particles of a desired size and, if desired, screening, and the product of such process.

At least one of the components charged to the process of this invention must be a compactible material. That is, at least one material must be capable of forming a coherent film which resists disintegration on handling. The material should be sufficiently compactible and employed in amounts such that at least about 75 percent, and preferably at least about 85 percent, of the mixture is converted to a compacted sheet, and

less than about 40 weight percent of the compacted mixture, and preferably less than about 20 weight percent, of the compacted mixture forms dust on granulation. By the term "dust" is meant particles having their largest cross-sectional dimension below about 325 mesh.

Suitable compactible materials, hereinafter referred to as "-compaction aids," are those which, after admixture with other components, permit compaction to a homogenous, grindable product which, after grinding to form a particulate product, is compressible. Illustrative compacting aids include high molecular weight ethyleneoxide polymers, i.e., polyethylene glycols having molecular weights in the range of from about 2,000 to about 10,000 such as the "Carbowaxes," especially Carbowax 6,000; glycerol monostearate; sorbitol; lactose; mannitol; microcrystalline cellulose such as "Avicel"; fatty acids such as palmitic; instantized gums such as those disclosed in U.S. Pat. Nos. 2,963,373 and 3,042,668; proteins; starch and hydrolyzed polysaccharide derivatives such as hydrolyzed cereal starch and dextrin; and certain sugar agglomerates.

One suitable sugar agglomerate is one comprising generally spherical, firm porous agglomerates of sugar particles in a cementum or matrix of a noncrystalline sugar. These agglomerates are dry (from about 0.1 about 3 percent moisture), free-flowing particles having particle sizes within the range of from about 325 to about 12 mesh, and are obtained by:

1. Spraying a particulate solid sugar with an aqueous solution of binder;
2. Providing the resulting mixture with sufficient high-intensity agitation to uniformly intermingle the sugar and binder and to build up agglomerates of a desired size:
3. "Snowballing" the agglomerates to impart a general spherical shape thereto and to firm or densify the agglomerate;
4. Drying; and, if necessary
5. Separating over- and under-sized agglomerates.

The particulate sugar can be a mono-, di- or tri- saccharide, such as arabinose, xylose, ribose, fructose, mannose, galactose, glucose, sucrose, maltose, lactose and the like, including mixtures of two or more of such sugars, with sucrose being preferred. The particulate sugar can be obtained synthetically or it can be a refined natural product such as corn syrup solids, molasses solids, honey solids, maple syrup solids and the like. The particle size of the sugar is not narrowly critical, so long as it is small enough to permit formation of agglomerates of the desired size. For most purposes, ordinary 6X powdered sugar, of which most (95–99 percent) passes through a 200-mesh screen, is suitable, If the agglomerate is to be employed in the production of a chewable tablet, however, the particulate solid sugar should be more finely divided to avoid grittiness. For this use, the sugar should have substantially no particles, i.e., not more than about 1percent, having sizes greater than about 40 microns, and at least 50percent of the particles should have sizes below about 25 microns. Preferred are sugars having an average particle size of about 15 microns.

The second component which is employed to form the agglomerate is an aqueous solution or dispersion of a polyhydroxy compound as a binder. Illustrative polyhydroxy compounds include propylene glycol, glycerol, erythritol, arabitol, xylitol, adonitol, mannitol, dulcitol, sorbitol, sugars, such as arabinose, xylose, ribose, glucose, mannose, levulose, fructose, sucrose, maltose and lactose, dextrin and the like, with polyols of the formula $HOCH_2(CHOH)_xCH_2OH$, wherein x is 1 to 4, and sugars being preferred. The aqueous binder composition can be a solution or dispersion of a pure compound, or can comprise two or more polyhydroxy binders. The aqueous medium can be obtained synthetically, or it can be a refined natural product, such as corn syrup, molasses, honey, maple syrup and the like. Invert syrup is preferred.

The concentration of binder in the aqueous medium is not narrowly critical, provided that it is not so high as to cause crystallization or provide solutions so viscous as to prevent spraying and intimate intermingling and uniform distribution

of binder and solids. Thus, the concentration will depend upon the solubility of the binder. For example, glucose ordinarily cannot be employed in amounts greater than about 48 percent, whereas propylene glycol, glycerol, mannitol and sorbitol can be present in amounts up to about 80 percent. When invert sugar is the binder, concentrations of from about 50 to about 80 percent are employed, with concentrations of from about 70 to about 74 percent being preferred. Other than this, the amount of water in the aqueous medium should be so correlated with the desired ratio of binder to sugar that agglomeration occurs. Thus the amount of water should be insufficient to form a paste, and yet sufficient to minimize the presence of powder, or unagglomerated sugar. In general it has been found that the mixture of sugar and aqueous binder should contain from about 2 to about 6 percent water, with amounts of about 4 percent water being preferred.

The initial contact of the solids and liquid is effected by spraying the aqueous medium onto the dry solids at a rate such that there is employed from about 0.1 to about 30 parts of binding agent per 100 parts of solid.

The mixing is ordinarily conducted at about room temperature (65°–75° F.). Higher and lower temperatures can be employed, if desired, provided the properties of the aqueous medium and the agglomerate product are not adversely affected. In particular, the temperature of the aqueous medium may be varied to achieve a desired viscosity for spraying. However, if the temperature is too low, e.g., below about 50° F., the aqueous medium is ordinarily too viscous to be easily sprayed; and if the temperature is too high, e.g., above about 200° F., water may evaporate too rapidly to permit adequate control of the characteristics of the binding solution. In addition, the use of elevated temperatures during processing tends to result in a discolored product, and also may cause dissolution of the dry ingredient and thus adversely affect particle size and quality.

Simultaneously with the spraying, the mixture is agitated to effect thorough and uniform intermingling of the sugar and binder and to effect agglomeration. High-intensity mixing, such as is obtained with a Patterson-Kelley Blender or a Lodige mixer is essential to achieve the necessary thorough, uniform mixing and agglomeration.

The agitation is continued until agglomerates of the desired size are formed. Ordinarily, agglomeration is continued until agglomerates above about 325 mesh are formed, and is terminated before significant amounts of agglomerates larger than about 12 mesh are formed. The size of the agglomerate is also affected by the ratio of aqueous binder to particulate sugar, with larger agglomerates being formed when a greater proportion of liquid medium is present.

The agglomerates typically have a narrow size distribution. That is, high yields, normally 80 percent or more, of the agglomerates fall within a few screen sizes. For example, when operating to produce a 20- to 80-mesh agglomerate, at least 80 percent, and in some instances at least 90 percent, of the agglomerated product will fall within this range.

Simultaneously with and/or subsequent to agglomeration, the agglomerates are "snowballed," i.e., subjected to a tumbling or rolling operation, to impart a general spherical shape thereto. In addition, the agglomerates are firmed or densified whereby the bulk density is increased to about 50 to 100 percent over that of the dry particulate sugar, and normally in the range of from about 30 to about 50 pounds per cubic foot.

Finally, and when necessary, the agglomerates are dried to a moisture content of less than about 3 percent, and preferably less than about 1.5 percent. Although complete drying is theoretically possible, the moisture content of the product is ordinarily at least about 0.1 to 0.2 percent. The temperature at which drying occurs is not narrowly critical in all cases, but ordinarily the temperature of the agglomerate should not exceed about 140° F. To achieve such drying, the product is preferably contacted with hot air at a temperature not exceeding 190° F. A preferred drying technique is the use of a fluid bed dryer. In this manner, very fine particles, i.e., dust, are separated from the product.

If desired, the dried product may be screened to remove oversized and undersized particles. Oversized particles are discarded or can be reduced to smaller size. Undersized particles may be recycled.

A second class of compacting aids comprises a product comprising a dry (moisture content of less than about 4 percent), free-flowing, particulate composition comprising an inert edible diluent dispersed in a matrix of a hydrophilic, hydratable, high polymer, such as the products of U.S. Pat. Nos. 2,963,373 and 3,042,668.

The diluent can be any normally solid material, i.e., any material which is solid under conditions of normal atmospheric pressures and temperatures, provided it is inert, edible and permissible in the tablet formed from the direct compression vehicle. Thus it can be either soluble or insoluble in water. If insoluble, however, it must be capable of reduction to a size which is useful in the practice of this invention, i.e., a size below about 200 mesh and preferably below about 10 microns.

Preferred diluents include normally saccharine materials, i.e., a mono- or disaccharide such as glucose, mannose, galactose, fructose, arabinose, xylose, sucrose, maltose, and lactose; as well as certain polyols of the formula $HOCH_2(CHOH)_xCH_2OH$, wherein x is 1 to 4, such as glycerol, erythritol, arabitol, xylitol, adonitol, mannitol, dulcitol and sorbitol. In addition, certain salts may be employed, including sodium chloride, sodium citrate, calcium carbonate, calcium sulphate and tricalcium phosphate. The diluent may be one or a mixture of two or more of the aforesaid substances. In the event the diluent is a sugar, it may be of synthetic or natural origin, and may be supplied to the mixing step in the form of a solution or syrup, such as molasses, affination syrup, invert syrup and the like.

The hydratable polymer includes hydrophilic polysaccharides, hydrocolloids or proteinaceous materials which, although not soluble in water, are hydrated upon admixture with water, and when substantially fully hydrated form a clear aqueous sol of swollen polymer and water. Illustrative examples of these high polymers include starch, agar, locust bean gum, carrageen, dextrin, cereal flour and the like.

The polymer, diluent and water are admixed in any convenient manner and in proportions such that there is obtained a substantially clear fluid mixture comprising an aqueous solution or dispersion of diluent dispersed throughout the swollen hydrated polymer. The precise conditions and proportions will vary widely, depending upon the polymer employed, and the amount of and the additive employed. The amount of water necessary to hydrate the hydrophilic polymer is either known or is readily determined by the simple experiment of adding water is known amount to a known amount of dry polymer until a clear sol is obtained. In general, at least about 8 parts of water are required per part of starch or dextrin, at least about 25 parts of water are required per part of locust bean gum, and at least about 33 parts of water are required per part of agar or carrageen. The foregoing amounts of water yields a product of optimum properties, but lesser amounts of water, for example as low as 50 percent or more of the above values, can be employed.

When the diluent is insoluble in water, no additional water is required. When, however, the diluent is water-soluble, enough additional water must be employed to dissolve the additive, For example, if sucrose is added to a clear, fully hydrated starch the resulting mixture becomes more fluid because the sucrose has a greater affinity for water than starch, and thus removes some of the water of hydration. If, however, in addition, there is added at least 0.5 part of water per part sucrose to ensure solution of the sucrose, the starch remains fully hydrated and the sucrose remains in solution. Although greater quantities of water can be employed, if desired, they are unnecessary and in fact disadvantageous in increasing the heat load for drying and may preclude the use of certain drying techniques, such as drum drying, which require a relatively viscous liquid.

The ratio of water-soluble additive to hydratable polymer can vary widely, depending upon the particular materials employed and the characteristics desired in the product direct compression vehicle. In general, however, ratios of from about 0.25 to about 250 parts of additive per part of polymer, preferably from about 2 to about 50 parts additive per part of polymer, are useful. Ratios of from about 20 to about 30 parts additive per part of polymer are most preferred.

Drying of the resulting dispersion may be effected by a variety of techniques, such as spray drying, belt drying, tray drying, drum drying and the like. In a preferred technique, the dispersion is dried by deposition on a heated surface to effect evaporation and convert the dispersion into a dry, hot, plastic film, removing the firm from the heated surface and attenuating the film while simultaneously cooling it, to convert the plastic film to a brittle or frangible condition. After the film has been thus cooled, it is fragmented and ground to a desired particle size and the ground product is employed.

A preferred way to practice the method of this invention is through the use of a heated drum dryer and a cooled rotary takeoff reel located a slight distance therefrom with a current of cooling air passing therefrom.

In such a process the dispersion of the aqueous solution of a saccharine material and the high polymer is prepared and introduced into the nip between a pair of steam-heated oppositely rotating drums at a rate to effect rapid evaporation of the water, but without permitting the resultant dehydrated product which contains not more than 4 percent moisture, and which forms a relatively thick plastic film on the surfaces of the drums, to reach a temperature at which destructive decomposition would begin. Thus the temperature of the dehydrated material should not exceed about 350° F., and the operating conditions of the drums should be adjusted accordingly. At the line of transfer to the reel, which is rotating with a peripheral speed greater than that of the drum, the hot dehydrated film is removed by a doctor blade from its associated drum and transferred to the reel across a current of cooling air, having a 60°–80° F. temperature, which effects an initial cooling of the dehydrated material to near room temperature of about 70° F. to about 95° F. and the cooling air at the line of removal of the film from the reel aids both its removal therefrom and a final cooling to a brittle or frangible state. The frangible film then drops away from the reel as a brittle sheet or fragments onto a conveyor for transport to a storage bin or to a comminuting device for reduction to the desired particle size for direct tabletting.

If only one takeoff reel is used, it will, of course, be necessary to provide a scraper or other means on the opposite drum to prevent passage of the hot dehydrated film therearound and force it over onto the other drum.

Although in the foregoing description of the method mention has been made of a two-drum dryer with either a single or two takeoff reels, it will be appreciated that a single drum dryer with a single takeoff reel can be used with equal effectiveness.

A particularly preferred product is obtained when a mixture of the above-described spherical agglomerates and flakes is employed as the compacting aid. Tablets made from the direct compression vehicles of this invention employing the spherical agglomerate alone tend to have poor color stability, and tablets made from the vehicles of this invention employing the flake material have poor strength characteristics when magnesium stearate is employed as a lubricant during tabletting.

When both materials are employed, however, the tablets produced from the resulting vehicle possess both good strength and color stability. The weight ratio of spherical agglomerate to flake can obviously vary widely depending upon the composition of these materials as well as the composition and properties of the remaining components and the compaction properties desired in the directly compressible vehicle. In general, however, this ratio is in the range of from about 50:1 to 1:1, preferably from 20:1 to 30:1, and most preferably about 25:1.

The remaining components which are charged to the mixing step of the process of this invention are those commonly employed in tablets, other than the active material. By the term "active material" is meant any material intended for ingestion having a beneficial or desirable effect on the user. Suitable active materials include therapeutic materials, such as anesthetics, antibiotics, antitussives, vitamins, aspirin, antacids, and the like; foodstuffs such as cocoa, dried oats, fruit flakes, and the like; edible dyes and other food additives; and so on. Illustrative additional components include flavors, colors, diluents, materials to impart the desired texture, hardness, lubricity and disintegration rate in use of the ultimate tablet and the like. The process of this invention is of particular importance when granular sugar, especially sucrose, is employed as a diluent.

The proportions of the several components in the mixture to be compacted is not critical, provided that the desired degree of compaction is achieved, and the granular product has the desired properties. In general, there should be at least 10 weight percent of one or more compaction aids, with amounts in the range of about 70 to about 95 percent being most usual. In some instances, as where glycerol monostearate is employed, the compaction aid may be present in amounts as low as about 3 percent.

Particularly preferred direct compression vehicles within the scope of the present invention are those wherein a sugar, especially sucrose, is employed in admixture with one of the above-mentioned compaction aids. In such compositions, the sugar comprises from about 50 to about 90 percent of the direct compression vehicle.

Although not essential to the process of this invention, it is desirable that the compacting aid and the remaining components have substantially similar particle sizes to minimize segregation by size on handling before compacting and compacted product. As a general rule, the particle sizes of the components should not vary more than ±50 percent from the mean particle size of the entire mixture. It should be noted, however, that at small mean particle sizes, deviations of larger than 50 percent may be tolerated because at lower overall dimensions, small absolute variations in particle size represent larger percentages of the mean size.

The various components are then mixed by suitable means, such as ribbons blenders, Lodige mixers, Patterson-Kelley mixers and the like to produce a uniform blend of the several particulate components.

The resulting blend is fed to a compactor, such as a Compacting Rolls made by Komarek-Greaves Co., or a Chilsonator made by Fitzpatrick Co., which converts the particulate mixture into a compact, nonfriable sheet. The degree of compaction will vary widely, depending upon the nature and proportions of the compacting aid and the remaining components, but it is essential that the sheet does not disintegrate under slight pressure. More particularly, the sheet should not, upon granulation, form more than about 40, preferably about 20, percent dust upon granulation.

The next step of the process of this invention is granulation, i.e., reduction of the compacted sheet to particles of a desired average size, preferably within the range of from about 16 to about 325. This size reduction is effected with conventional equipment, such as Fitzmills and the like, and may be accomplished in one or more steps.

The final, and optional, step of the process of this invention for producing a directly compressible vehicle is screening of the particulate product to a desired size range. Illustrative size ranges include 16 to 100 mesh; 100 to 200 mesh; and 200 to 325 mesh. The particular mesh size will vary depending upon the particular active with which the vehicle of this invention is to be blended and formed into a tablet. In general, the size range should approximate that of the active to ensure a uniform blend of vehicle and active in the tabletting mixture and the tablet produced therefrom.

The vehicle is a g free-flowing granular material and imparts improved flow characteristics to the active material and other

components of the blend, thereby assuring ease of tabletting. The uniform granular direct compression vehicle of this invention is employed by blending with the active material and, if necessary, a lubricant, and compressed in conventional manner to form a tablet or wafer.

The following examples are illustrative. Unless otherwise specified, all parts and percentages are by weight. In the examples, the following products were employed:

Flake A—a flake containing 34 percent starch, 27 percent sucrose and 39percent invert (sucrose and invert dispersed throughout a starch matrix) prepared by mixing 3,750 parts water, 350 parts starch and 284 parts powdered sucrose, cooking the resulting mixture at 180° F. to hydrate the starch and dissolve the sucrose, and adding 571 parts of a 70 percent invert syrup, followed by drum drying to about 2 percent moisture and granulating to about one-half inch.

Flake B—a flake product containing about 25 percent invert and 50 percent sucrose dispersed in a matrix of 25 percent starch produced in a manner similar to Flake A.

Flake C—a flake product containing about 45 percent invert and 30 percent sucrose dispersed in a matrix of 25 percent starch produced in a manner similar to Flake A.

Flake D—a flake product containing about 25 percent starch and 75 percent sucrose produced in a manner similar to Flake A.

Agglomerate A—a product comprising generally spherical agglomerates of about 8.5 percent invert, 91.5 percent sucrose and less than 1 percent water prepared by spraying a 72° Brix full invert syrup on sucrose in a Patterson-Kelley blender, drying and screening to a fraction having a size of from 20 to 80 mesh.

Agglomerate B—a product comprising generally spherical, uniform agglomerates containing about 2.5 percent invert, 97.5 percent sucrose and less than about 1 percent moisture produced in a manner similar to Agglomerate A, except that the syrup comprised 20 percent invert and 52 percent sucrose.

Unless otherwise specified, all parts and percentages are by weight.

EXAMPLE 1

A dry blend of 50 parts of Flake C and 50 parts of powdered sugar was fed to a Chilsonator operated at a roll speed of 15 r.p.m. and hydraulic pressure of 200 p.s.i. The resulting compacted sheet was fed to a Fitzmill equipped with a 2A screen and number 225 K blades operating at 2,200 r.p.m. The resulting particulate product was screened to provide +30-mesh; 30 to 60-mesh; 60 to 80-mesh and -80-mesh fractions as follows:

Particle Size, mesh	Parts by Weight of Total
+30	9.2
30–60	66.8
60–80	15.0
−80	6.4

The thus obtained product was employed to produce 13/32-inch, 0.5-gram tablets at 3,000 and 9,000 p.s.i. and only slight capping was observed.

EXAMPLE 2

Employing procedures similar to those described in example 1, except that the initial blend comprised 10 parts of Flake B and 30 parts of sucrose, there was produced a compacted granular product having the following particle size distribution:

Particle Size	Parts by Weight of Total
+30 mesh	3.8
30–60 mesh	75.4
60–80 mesh	12.0
−80 mesh	5.2

The thus obtained product could be used as a direct compression vehicle.

EXAMPLE 3

A mixture of 1,125 parts of Agglomerate B, 37 parts of Flake A, 5 parts of magnesium stearate and 83 parts sugar was charged at a rate of 3,000 parts per hour to a Chilsonator at a roll speed of 16 r.p.m. and a hydraulic pressure of 1,200 p.s.i., and the resulting compacted sheet was fed to a Fitzmill equipped with 225 K blades and a No. 1 screen operating at 1,590 r.p.m. The resulting granular product contained 3.95 percent invert, 0.5 percent magnesium stearate, 0.35 percent moisture, 0.7 percent starch and 94 percent sucrose and had the following sieve analyses:

Particle Size	Parts by Weight
+20 mesh	0
20–40 mesh	2.8
40–100 mesh	14.8
100–200 mesh	21.0
−200 mesh	61.4

EXAMPLE 4

A mixture of 250 parts of the −200 mesh fraction of example 3, 930 parts of Agglomerate A, 30 parts of Flake A and 40 parts of sucrose was blended, pulverized by a Mikro pulverizer to a particle size of less than about 800 mesh (95 percent through 200 mesh), and fed to a Chilsonator under essentially the conditions described in example 3. The product, after granulation on the Fitzmill, was screened through 40-, 100- and 200-mesh screens to yield three products (coarse—plus 40 mesh; medium—40 to 100 mesh; fine—100 to 200 mesh). The yields and analyses of these products, based upon the dry blend fed to the Chilsonator, is as follows:

Product	Coarse	Medium	Fine
Yield, %	21.6	16.8	26.4
Density, g./cc.	0.796	0.811	0.756
Sieve Analyses			
30 20 mesh	0.8%	Tr	Tr
20–40 mesh	93.3%	0.2%	Tr
40–60 mesh	Tr	60.5%	Tr
60–80 mesh	Tr	22.3%	8.8%
80–100 mesh	Tr	8.0%	41.3%
100–140 mesh	Tr	5.2	25.6
140–200 mesh	Tr	1.0	20.3
31 200 mesh	Tr	Tr	

EXAMPLE 5

Employing procedures and equipment similar to these described in example 4, a blend of 25 parts of a particulate composition containing 90 percent tricalcium phosphate and 10 percent locust bean gum made as described in U.S. Pat. No. 3,420,668 and 75 parts sugar was fed to the Chilsonator at a roll pressure of 1,400 p.s.i. The +200 mesh portion of the granulated product comprised 0.4 percent of a +40-mesh fraction; 1.9 percent of a 40- to 100-mesh fraction and 97.7 percent of a 100- to 200-mesh fraction.

EXAMPLE 6

Employing procedures and equipment similar to those described in example 4, a blend of 25 parts microcrystalline cellulose and 75 parts sucrose was pulverized and fed to the Chilsonator at a roll pressure of 1,200 p.s.i. The +200-mesh product comprised 0.3 percent +40-mesh fraction, 15.5 percent 40–100-mesh fraction and 84.5 percent 100–200-mesh fraction.

EXAMPLE 7

Employing procedures and equipment similar to those described in example 4, a blend of 10 parts of Carbowax 6,000 and 90 parts sucrose was pulverized and fed to the Chilsonator at a roll pressure of 1,200 p.s.i. The +200-mesh product comprised 3.9 percent +40-mesh fraction; 45.6 percent 40–100-mesh fraction and 50.5 percent 100–200-mesh fraction.

EXAMPLE 8

Employing procedures and equipment similar to those of example 4, a dry blend of 30 parts sorbitol and 70 parts sugar was pulverized and fed to the Chilsonator at a roll pressure of 1,200 p.s.i. to yield a +200-mesh product comprising 2.1 percent +40-mesh fraction, 76.4 percent of a 40–100-mesh fraction and 21.5 percent of a 100–200-mesh fraction.

EXAMPLE 9

Employing procedures and equipment similar to those of example 4, a dry blend of 75 parts dextrose and 25 parts sorbitol was fed to the Chilsonator to yield a +200-mesh product comprising 10.4 percent of a +40-mesh fraction, 66.3 percent of a 40–100-mesh fraction and 22.2 percent of a 100–200-mesh fraction.

EXAMPLE 10

Employing procedures and apparatus similar to those of example 4, a blend of 1 part of Flake D and 2 parts sucrose was fed to the Chilsonator at a roll pressure of 1,100 p.s.i. to yield a +200-mesh product comprising 3.6 percent of a +40-mesh fraction, 60 percent of a 40–100-mesh fraction and 36.4 percent of a 100–200-mesh fraction.

EXAMPLE 11

Employing procedures and apparatus similar to those of example 4, a blend of 50 parts corn starch, and 50 parts sucrose were fed to the Chilsonator to yield a +200-mesh product comprising 8.4 percent of a +40-mesh fraction, 68 percent of a 40–100-mesh fraction and 22.6 percent of a 100–200-mesh fraction.

EXAMPLE 12

Employing procedures and apparatus similar to those of example 4, a blend of 15 parts of a flake comprising 5 percent agar, 3½ percent starch and 91½ percent sucrose made as described in U.S. Pat. No. 2,963,373 and 85 parts sucrose was fed to the Chilsonator at 1,200 p.s.i. roll pressure to yield a +200-mesh fraction comprising 9.2 percent of a +40-mesh fraction, 72 percent of a 40–100-mesh fraction, and 18.8 percent of a 100–200-mesh fraction.

EXAMPLE 13

Employing procedures and apparatus similar to those of example 4, a blend of 10 parts of a flake product produced by drum drying a mixture of 833 parts of water, 9 parts agar, 9 parts locust bean gum, 12 parts tapioca flour (starch) and 200 parts sucrose, and 20 parts sucrose were fed to the Chilsonator at 1,200 p.s.i. roll pressure to yield a +200-mesh product comprising 4.6 percent of a +40-mesh product, 78.4 percent of a 40–100-mesh product and 17 percent of a 100–200-mesh product.

Each of the direct compression vehicles of the foregoing examples can be blended in accordance with the following recipes and compressed to form tablets and wafers.

A. CONFECTIONERY TABLETS OR WAFERS

1. LEMON FLAVORED confectionery tablet:
   - 100.0 pts. direct compression vehicle
   - 1.0 pt. citric acid, dry
   - 0.25 pt. encapsulated lemon flavor
   - 0.10 pt. yellow color No. 5
   - 1.0 pt. magnesium stearate

2. GRAPE FLAVORED tablet:
   - 50.0 pts. direct compression vehicle
   - 50.0 pts. 6X powdered sugar
   - 2.0 pts. tartaric acid
   - 0.25 pt. grape flavor
   - 0.05 pt. grape color
   - 0.5 pt. calcium stearate

3. CHERRY FLAVORED confectionery tablet:
   - 100.0 pts. direct compression vehicle
   - 2.0 pts. fumaric acid
   - 0.2 pt. cherry flavor
   - 0.1 pt. red color
   - 1.0 pt. magnesium stearate

B. PHARMACEUTICAL FORMULATIONS

1.	50.0 pts.	direct compression vehicle
	37.5 pts.	aluminum hydroxide
	1.0 pt.	magnesium stearate
2.	100.0 pts.	direct compression vehicle
	25.0 pts.	calcium carbonate
	5.0 pts.	magnesium carbonate
	1 drop	peppermint oil
	2.0 pts.	magnesium stearate
3.	100.0 pts.	direct compression vehicle
	25.0 pts.	acetyl salicylic acid
	15.0 pts.	corn starch
	2.0 pts.	magnesium stearate
	90.0 pts.	direct compression vehicle
	10.0 pts.	vitamin C in dry form
	2.0 pts.	magnesium stearate

Other active ingredients of use in blends with the agglomerate are: sodium bicarbonate, acetanilid, phenacetin, and magnesium trisilicate.

C. SPECIALTY PRODUCTS

1. INVERTASE SUGAR TABLET

96.4 pts.	direct compression vehicle
3.6 pts.	liquid triple strength invertase (K=0.9)
1.0 pt.	magnesium stearate

After blending, the mixture is tabletted to form a cocoa-sugar tablet.

2. COCOA-SUGAR TABLET

90.0 pts.	direct compression vehicle
10.0 pts.	high fat cocoa
0.2 pts.	dendritic salt
1.0 pt.	magnesium stearate

After blending, the mixture is tabletted to form a cocoa-sugar tablet.

3. SUGAR-SYNTHETIC SWEETENER TABLET

450.0 pts.	direct compression vehicle
7.16 pts.	calcium cyclamate
0.8 pt.	sodium saccharin
5.0 pts.	calcium stearate

4. HIGHLY CONCENTRATED COLOR TABLET

90.0 pts.	direct compression vehicle
10.0 pts.	dried yellow FD & C No. 6
10.0 pts.	sodium benzoate

5. YEAST FOOD TABLET

34.0 pts.	calcium sulfate ($2H_20$)
23.0 pts.	flour
9.0 pts.	ammonium chloride
0.25 pt.	potassium bromate
17.75 pts.	sodium dihydrogen phosphate
16.0 pts.	salt
900.0 pts.	direct compression vehicle
10.0 pts.	magnesium stearate

What is claimed is:

1. A method for producing a direct compression vehicle for tablets comprising forming a dry mixture of a plurality of tablet components, at least one of which is a compaction aid selected from the group consisting of a polyethylene glycol having a molecular weight in the range of from about 2,000 to about 10,000, glycerol monostearate, sorbitol, lactose, mannitol, microcrystalline cellulose, fatty acids, instantized gums, proteins, starch, hydrolyzed polysaccharide derivatives, a free-flowing particulate generally spherical, firm, agglomerate of sugar particles in a matrix of noncrystalline sugar, or a free-flowing particulate composition comprising an inert, edible diluent dispersed in a matrix of a hydrophilic, hydratable, high polymer, said mixture being free of active material, compacting said mixture to form a compact, nonfriable sheet, and breaking up said sheet to form particles thereof.

2. The granular product of the method of claim 1.

3. A method according to claim 1 wherein at least about 75 percent of said mixture is formed into said sheet, and less than about 40 percent of said sheet is converted to dust upon said breaking up.

4. A method according to claim 3 wherein said compaction aid comprises from about 70 to about 95 percent of said mixture.

5. The method according to claim 1, including the steps of blending the product thereof with an active material and directly compressing the resulting blend to form a tablet.

6. The tablet of the method of claim 5.

7. A method according to claim 1 wherein said compaction aid is selected from the group consisting of said generally spherical sugar agglomerate and said particulate composition comprising an inert, edible diluent dispersed in a matrix of a hydrophilic, hydratable polymer.

8. A method according to claim 7 wherein said compaction aid is a mixture of said agglomerate and said particulate composition.

9. A method according to claim 8 wherein the weight ratio of agglomerate to particulate composition is in the range of from about 50:1 to about 1:1.

10. The granular product of the method of claim 9.

11. A tablet obtained by blending the product of claim 10 with an active material and directly compressing the resulting blend to form a tablet.

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