

PATENT SPECIFICATION

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(54) ASCORBIC ACID COMPOSITIONS

(71) We, TAKEDA YAKUHIN KOGYO KABUSHIKI KAISHA, also known as TAKEDA CHEMICAL INDUSTRIES LTD., of 27 Doshomachi 2-chome, Higashi-ku, Osaka, Japan, a corporation organised under the laws of Japan, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to the production of L-ascorbic acid granules with good fluidity and homogeneity, and to improvements in L-ascorbic acid-containing tablets (the tablets are briefly referred to as L-ascorbic acid tablets).

A high L-ascorbic acid content and a satisfactory product hardness or strength in practice have been very important requirements for L-ascorbic acid tablets. In the past, however, these two requirements were antagonistic to each other because, for the enhancement of the strength of the tablet, the addition of a large amount of adjuvant or excipient is necessary, which results in the necessity of imposing an upper limit on the L-ascorbic acid content of the tablet. This upper limit must be imposed on the L-ascorbic acid content, since otherwise the large amounts of the L-ascorbic acid component required in high potency tablets, for example, coupled with the large amount of adjuvant required, would make the tablets too large to be comfortably swallowed by a person.

U.S. Patent No. 3,453,368 is directed towards solving the aforementioned problems, but has not been entirely satisfactory. The U.S. Patent relates to a process for producing L-ascorbic acid tablets which comprises mixing 85 to 95 weight percent of L-ascorbic acid with 5 to 15 weight percent of modified starch or pregelatinized starch, followed by massing, crushing and drying in that order to yield L-ascorbic acid-containing granules; and then mixing the resulting granules with a lubricant and compressing the mixture into tablets (hereinafter briefly called a wet-granulation process).

However, it is difficult to provide granules of good fluidity and homogeneity by the wet granulation process and, as a result, L-ascorbic acid tablets which are compressed from such granules are far from satisfactory in their mechanical strength (i.e. their tensile strength or hardness).

We have sought to overcome the drawbacks of prior proposals and to provide an improved technique for preparing L-ascorbic acid granules which are suitable for tableting.

According to a first aspect of our invention, we provide L-ascorbic acid granules produced by spray-coating L-ascorbic acid powder, which passes through a 200-mesh screen, with a solution or suspension of a pharmaceutically acceptable binder under constant agitation in a fluidised-bed granulating apparatus until the amount of solid binder on the powder has reached from substantially 2 to substantially 4 weight percent relative to the L-ascorbic acid content.

According to a second aspect of our invention we provide a method of producing L-ascorbic acid granules, which comprises spray-coating L-ascorbic acid powder, which passes through a 200-mesh screen, with a solution or suspension of a pharmaceutically acceptable binder under constant agitation in a fluidised-bed granulating apparatus until the amount of solid binder on the powder has reached from substantially 2 to substantially 4 weight percent relative to the L-ascorbic acid content.

According to a preferred aspect of the present invention we provide L-ascorbic acid tablets produced from L-ascorbic acid granules as defined above and having the following characteristics:

- (a) L-Ascorbic acid content from substantially 100 to substantially 2000 mg per tablet, and its percentage in a tablet being from substantially 90 to substantially 97.1 percent by weight.
- (b) Amount of binder from substantially 2 to substantially 4 weight percent relative to L-ascorbic acid.

(c) Amount of lubricant; from substantially 1 to substantially 7 percent relative to L-ascorbic acid.

5 (d) Tensile strength; not less than 12.5 kg/cm².

10 The present invention provides L-ascorbic acid granules as a material suitable for the production of L-ascorbic acid tablets and also provides a process for producing such L-ascorbic acid granules. The invention further provides L-ascorbic acid tablets of high L-ascorbic acid content and high mechanical strength.

15 Further features and advantages of this invention appear from the following description of an embodiment of the present invention.

As a first step of the process, the L-ascorbic acid granules are prepared in the following manner. L-ascorbic acid powder which passes through a 200-mesh screen is spray-coated with a solution of a binder under continuously fluidising conditions.

20 Use is made of L-ascorbic acid powder which passes through a 200-mesh screen and preferably not less than 50 weight percent of which passes through a 325-mesh screen. By "mesh" is meant that of W. S. Tyler Standard, and the term "powder" includes both ground and unground finely divided material.

30 As the binder, there may be mentioned water-soluble binders such as pregelatinised starch (e.g. pregelatinised corn starch and pregelatinised white potato starch), pregelatinised modified starch (see Code of Federal Regulation (U.S.A.) §121.1031, a, b, c, d, e, f, g and h), water-soluble celluloses (e.g. hydroxypropyl-cellulose, hydroxymethyl-cellulose, hydroxypropylmethyl-cellulose and carboxymethyl-cellulose), polyvinylpyrrolidone, polyvinyl alcohol, dextrin, gum arabicum and gelatin, organic solvent-soluble binders, such as cellulose derivatives (e.g. cellulose acetate phthalate, hydroxypropylmethyl-cellulose phthalate and ethyl-cellulose).

45 As the solvent for preparing the solution or suspension for spray-coating, there may be mentioned, for example, water, alcohols, (e.g. methyl alcohol, ethyl alcohol and isopropyl alcohol), and acetone.

50 The concentration of the binder in the solution or suspension for spray-coating is optional but in practice ranges from substantially 1 to substantially 10 weight percent, and preferably from substantially 2 to substantially 8 weight percent.

55 The fluidised-bed granulating apparatus comprises a fluidised-bed drying device fitted with spray means to inject a mist of a binder in such a manner that the granulating and drying operations may be accomplished in a single apparatus. We mention, by way of example only, apparatus known under the names Glatt (trade mark; made by Glatt AG, West Germany), Aeromatic (trade mark;

made by Aeromatic AG, Switzerland), Calmic (trade mark; made by Calmic Engineering Co., England), Growmax (trade mark; made by Fuji Powder Co., Japan) and Flowcoater (trade mark; made by Freund Industries Co., Japan).

70 The granulating process continues until the proportion of the binder has reached from substantially 2 to substantially 4 weight percent relative to the L-ascorbic acid content.

As a second step of the process the resulting L-ascorbic acid granules are mixed with a lubricant and compressed into tablets.

The lubricant may be, for instance, a stearate (e.g. magnesium stearate, calcium stearate or stearic acid) or corn starch.

80 The amount and the kind of lubricant are optionally decided on the basis of various lubricating compounds which are known *per se*, but proportions of from substantially 1 to substantially 7 weight percent relative to L-ascorbic acid are recommended and, in particular, additions of a total of at least one weight percent (relative to L-ascorbic acid) of one or more stearates are most desired.

90 In accordance with the method of this invention, the L-ascorbic acid powder is homogeneously coated with a relatively small amount of binder, and the resulting L-ascorbic acid granules are substantially free from fine dusts of the raw materials, have good fluidity and are easy to mix with other components. The L-ascorbic acid component in the granules remains stable, since, whereas moisture is highly detrimental to L-ascorbic acid, the granules obtained by the present process can be coated with only a small amount of moisture-absorbing binder.

105 The granules obtained by the present method are differentiated from the granules obtained by the wet-granulating method in electron microscopic photographs.

110 Various features of the present granules combine to contribute to the improvement of the final L-ascorbic acid tablets. Thus, the tablets prepared from the resulting L-ascorbic acid granules are excellent in terms of L-ascorbic acid content and mechanical strength. In particular, the tablets can contain as high a content as from substantially 90 to substantially 97.1 weight percent per tablet of L-ascorbic acid while maintaining a tensile strength now lower than 12.5 kg/cm². In terms of L-ascorbic acid content per tablet the range is from substantially 100 to substantially 2000 mg., more preferably from substantially 400 to substantially 600 mg.

125 In terms of disintegration, the tablets are satisfactory in that the disintegration time of the tablets falls within the requirement of the standard in Japanese Pharmacopoeia, 8th Edition.

The following examples and tests are further illustrative of this invention. In the examples and tests, "part(s)" and "percent(s)"

are based on weight, unless otherwise specified.

The relationship between the hardness and the tensile strength of a tablet is shown by the following equation:

$$\sigma = \frac{2P}{\pi DT} \quad (\text{Kg/cm}^2)$$

wherein σ stands for tensile strength, P for hardness, D for diameter, T for thickness and π for the circular constant, respectively.

For practical use, tablets having not less than 12.5 kg/cm² of tensile strength are satisfactory.

Example 1.

(a) 97 parts of ground powdery L-ascorbic acid, which passed through a 200-mesh screen, 4.5 weight percent of which was held back by a 250-mesh screen but 82.8 weight percent of which passed through a 325-mesh screen, were sprayed under constant agitation in a fluidised-bed granulator with a paste which had been prepared by gelatinising a 5.0 weight percent aqueous suspension of corn starch at 85°C. and cooling to 50°C., until the coating amount of starch had reached 3 parts, followed by drying *in situ*. The product was then comminuted in a Fitz-mill (cf. Remington's Pharmaceutical Science, Osol and Hoover; Mack Publ. Co. 1975) equipped with a 1.0 mm-screen to obtain L-ascorbic acid granules.

(b)-1 To 515 parts of the granules prepared as above there were added 5 parts of magnesium stearate and 15 parts of corn starch, and, after mixing, the composition was compressed to form a 535 mg. tablet.

L-Ascorbic acid content: 93.5 weight percent
Hardness: 12.1 kg.
Tensile strength: 18.4 kg/cm²

(b)-2 To 515 parts of the granules prepared as above (a), there were added 5 parts of magnesium stearate, and, after mixing, the composition was compressed to form a 520 mg. tablet.

L-ascorbic acid content: 96.2 weight percent
Hardness: 11.5 kg.
Tensile strength: 17.5 kg/cm²

(b)-3 To 515 parts of the granules prepared as above (a), there were added 5 parts of magnesium stearate and 30 parts of corn starch, and, after mixing, the composition was compressed to form a 550 mg. tablet.

L-Ascorbic acid content: 90.9 weight percent
Hardness: 11.8 kg.
Tensile strength: 18.0 kg/cm².

Example 2.

(a) 98 parts of ground powdery L-ascorbic

acid which passed through a 200-mesh screen, 4.5 weight percent of which remained over a 250-mesh screen but 82.8 weight percent of which passed through a 325-mesh screen, were sprayed under constant agitation in a fluidised-bed granulator with a paste which had been prepared by gelatinising a 2.5 weight percent aqueous suspension of white potato starch at 85°C. and cooling to 50°C., until the coating amount of white potato starch had reached 2 parts, followed by drying *in situ*. The product was then comminuted in a Fitz-mill equipped with a 1.5 mm-screen to obtain ascorbic acid granules.

(b) To 510 parts of the granules prepared as above there were added 5 parts of magnesium stearate and 15 parts of corn starch, and, after mixing, the composition was compressed to form a 530 mg. tablet.

L-Ascorbic acid content: 94.3 weight percent
Hardness: 10.0 kg.
Tensile strength: 15.2 kg/cm².

Example 3.

(a) 96 parts of ground powdery L-ascorbic acid which passed through a 200-mesh screen, 4.5 weight percent of which was held back by a 250-mesh screen but 82.8 weight percent of which passed through a 325-mesh screen were sprayed under constant agitation in a fluidised-bed granulator with an aqueous solution of 5.0 weight percent of hydroxypropylmethylcellulose until the coating amount of hydroxypropylmethylcellulose had reached 4 parts, followed by drying *in situ* to obtain L-ascorbic acid-containing granules.

(b) To 520 parts of the granules prepared as above there were added 5 parts of magnesium stearate and 15 parts of corn starch, and, after mixing, the composition was compressed to form a 540 mg. tablet.

L-Ascorbic acid content: 92.6 weight percent
Hardness: 15.5 kg.
Tensile strength: 23.6 kg/cm²

Example 4.

(a) 97 parts of ground, powdery L-ascorbic acid which passed through a 200-mesh screen, 4.5 weight percent of which was held back by a 250-mesh screen but 82.8 weight percent of which passed through a 325-mesh screen, were sprayed under constant agitation in a fluidised-bed granulator with an alcoholic solution of 4.0 weight percent of ethylcellulose until the coating amount of ethylcellulose had reached 3 parts, followed by drying *in situ* to obtain L-ascorbic acid-containing granules.

Example 5.

(a) L-Ascorbic acid granules were obtained in the same manner as in Example 4 (a), but with the use of hydroxypropylmethylcellulose instead of ethyl cellulose.

(b) 515 parts of the granules prepared as

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above (a) were compressed in a similar manner to Example 1, (b)-1 to form a 535 mg. tablet.

L-Ascorbic acid content: 93.5 weight percent
Hardness: 12.2 kg.

5 Tensile strength: 18.6 kg/cm²

Example 6.

(a) 97 parts of ground powdery L-ascorbic acid which passed through a 200-mesh screen, 4.5 weight percent of which was held back by a 250-mesh screen but 82.8 weight percent of which passed through a 325-mesh screen, were sprayed under constant agitation in a fluidised-bed granulator with a paste which had been prepared by gelatinising a 3.0 weight percent aqueous suspension of hydroxypropyl starch (described in the Code of Federal Regulation § 121.1031) at 70°C and thereafter cooling to 50°C, until the coating amount of hydroxypropyl starch had reached 3 parts; this was followed by drying *in situ*. The product was then comminuted in a Fitz-mill provided with a 1.5 mm-screen to obtain L-ascorbic acid granules.

(b) To 515 parts of the granules prepared as above there were added 5 parts of magnesium stearate and 15 parts of corn starch, and, after mixing, the composition was compressed to form a 535 mg. tablet.

30 L-Ascorbic acid content: 93.5 weight percent
Hardness: 12.3 kg.
Tensile strength: 18.7 kg/cm²

Example 7.

(a) 96 parts of ground powdery L-ascorbic acid which passed through a 200-mesh screen, 4.5 weight percent of which was held back by a 250-mesh screen but 82.8 weight percent of which passed through a 325-mesh screen, were sprayed under constant agitation in a fluidised-bed granulator with a paste which had been prepared by gelatinising a 5.0 weight percent aqueous suspension of corn starch at 85°C and cooling to 50°C, until the coating amount of starch had reached 4 parts, followed by drying *in situ*. The product was then comminuted in a Fitz-mill equipped with a 1.5 mm-screen to obtain L-ascorbic acid granules.

(b) To 520 parts of the granules prepared as above there were added 5 parts of calcium stearate and 15 parts of corn starch, and, after mixing, the composition was compressed to form a 545 mg. tablet.

L-Ascorbic acid content: 92.6 weight percent
Hardness: 15.7 kg.
Tensile strength: 23.9 kg/cm².

Example 8.

55 (a) 96 parts of ground powdery L-ascorbic acid which passed through a 200-mesh screen, 4.5 weight percent of which was held back by a 250-mesh screen but 82.8 weight percent of

which passed through a 325-mesh screen, were sprayed under constant agitation in a fluidised-bed granulator with a paste which had been prepared by gelatinising an 8 weight percent aqueous suspension of pregelatinised modified starch, STA-RX 1500 (A. E. Staley Mfg. Co., U.S.A.) at 85°C and cooling to 50°C, until the coating amount of the starch had reached 4 parts, followed by drying *in situ*. The product was then comminuted in a Fitz-mill equipped with a 1.5 mm-screen to obtain L-ascorbic acid granules.

(b) To 520 parts of the granules prepared as above there were added 5 parts of calcium stearate and 1.5 parts of corn starch, and, after mixing, the composition was compressed to form a 540 mg. tablet.

L-Ascorbic acid content: 92.6 weight percent
Hardness: 13.6 kg.
Tensile strength: 20.7 kg/cm²

Example 9.

(a) 98 parts of ground powdery L-ascorbic acid which passed through a 200-mesh screen, 4.5 weight percent of which was held back by a 250-mesh screen but 82.8 weight percent of which passed through a 325-mesh screen, were sprayed under constant agitation in a fluidised-bed granulator with a paste which had been prepared by gelatinising a 5.0 weight percent aqueous suspension of corn starch at 85°C and cooling to 50°C, until the coating amount of starch had reached 2 parts, followed by drying *in situ*. The product was then comminuted in a Fitz-mill equipped with a 1.0 mm-screen to yield L-ascorbic acid granules.

(b) To 510 parts of the granules prepared as above there were added 5 parts of magnesium stearate, and, after mixing, the composition was compressed to form a 515 mg. tablet.

L-Ascorbic acid content: 97.1 weight percent
Hardness: 8.9 kg.
Tensile strength: 13.6 kg/cm²

Test 1.

(A) Method

(i)—1 Preparation of granules

(a) Granules obtained by the present invention (ground powder was employed)

Granule (1)—granules obtained by Example 3 (a) (granules containing about 96% of L-ascorbic acid).

Granule (2)—granules obtained by Example 1 (a) (granules containing substantially 97% of L-ascorbic acid).

Granule (3)—granules obtained by Example 9 (a) (granules containing substantially 98% of L-ascorbic acid).

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(b) Granules obtained by the wet-granulation method (ground powder was employed)

5 Powdered L-ascorbic acid, which passed through a 200-mesh screen, 4.5 percent of which was held back by a 250-mesh screen and 82.8 percent of which passed through a 325-mesh screen, and pregelatinised starch, Amicol (trade mark) C (made by Nippon

10 Starch Refining Co., Japan) were charged into the Pony Mixer (cf. Colloidal Dispersions, Fisher, John Wiley & Sons Inc. 1953) and thoroughly mixed therein, 10 percent of water was then added followed by massing (i.e. forming a soft mass or granules). The resulting

15 moistened powder is forced through a 3.0 mm-screen, dried overnight at 40°C., and then comminuted in a Fitz-mill equipped with a 1.5 mm-screen.

Granule (4)—granules which contain substantially 90 percent of L-ascorbic acid. 20

Granule (5)—granules which contain substantially 95 percent of L-ascorbic acid. 25

Granule (6)—granules which contain substantially 97 percent of L-ascorbic acid.

(i)—2 Preparation of tablets

The following tableting granules were compressed in a rotary tablet machine (RTM-S36-2S, made by Kikusui Seisakusho Co., Japan) with 11.5 mm flat-faced, bevelled edged punches and die to obtain 600 mg. tablets. 30 35

Tablets	Granules used	Calcium stearate	Silicon dioxide	Com starch
(1)	Granule (2)	1.0%	—	5.0%
(2)	Granule (1)	1.0%	—	3.0%
(3)	Granule (2)	1.0%	—	3.0%
(4)	Granule (3)	1.0%	—	3.0%
(5)	Granule (3)	1.0%	—	—
(6)	Granule (4)	1.0%	1.0%	3.0%
(7)	Granule (4)	1.0%	—	3.0%
(8)	Granule (5)	1.0%	1.0%	3.0%
(9)	Granule (5)	1.0%	—	3.0%
(10)	Granule (6)	1.0%	1.0%	3.0%

(ii) Tests of strength of tablets

40 Tablets (1) to (10) were compressed diametrically in a physical testing instrument (Autograph (trade mark) IS-5000, made by Shimazu Seisakusho Co., Japan) to measure their crushing strength (see page 124 of Y. Yamaguchi and Y. Nishimatsu: Introduction to Rock Mechanics, University Press of Tokyo

45 (1967)).

(iii) Disintegration test

This was done according to the general test 31 disintegration test of Japanese Pharmacopoeia 8th Edition with the exception that in the present test the attached disk was not used and water was used as a solvent. 50

The requirement of the Japanese Pharmacopoeia is that the disintegration time of the tablet should be not longer than 30 minutes.

(B) Results

Tablet number	L-Ascorbic acid content (%)	Troubles in tableting	Hardness (kg)	Tensile strength (kg/cm ²)	Disintegration (minutes)
(1)	substantially 90.9	No	12.2	16.9	5.1
(2)	substantially 92.3	No	16.0	22.2	28.0
(3)	substantially 93.2	No	12.5	17.3	9.7
(4)	substantially 94.1	No	9.6	13.3	4.1
(5)	substantially 97.1	No	9.1	12.6	4.3
(6)	substantially 86.4	not free following, Sticking	6.0	8.3	26.0
(7)	substantially 87.3	Sticking	5.7	7.9	26.1
(8)	substantially 91.4	Sticking	4.9	6.8	3.3
(9)	substantially 90.5	Sticking Lamination	4.1	5.7	3.5
(10)	substantially 93.2	Sticking, Lamination	2.8	3.9	0.6

From the above tests, the tablets in accordance with the process of this invention are shown to be advantageous in terms of the combination of tableting difficulty, tensile strength, hardness and disintegration time.

WHAT WE CLAIM IS:—

1. L-Ascorbic acid granules produced by spray-coating L-ascorbic acid powder, which passes through a 200-mesh screen, with a solution or suspension of a pharmaceutically acceptable binder under constant agitation in a fluidised-bed granulating apparatus until the amount of solid binder on the powder has reached from substantially 2 to substantially 4 weight percent relative to the L-ascorbic acid content.

2. A method of producing L-ascorbic acid granules, which comprises spray-coating L-ascorbic acid powder, which passes through a 200-mesh screen, with a solution or suspension of a pharmaceutically acceptable binder under constant agitation in a fluidised-bed granulating apparatus until the amount of solid binder on the powder has reached from substantially 2 to substantially 4 weight percent relative to the L-ascorbic acid content.

3. A method according to claim 2, wherein not less than 50 weight percent of the L-ascorbic acid passes through a 325-mesh screen.

4. A method according to claim 2 or 3, wherein the concentration of the binder in the solution or suspension is from substantially 1 to substantially 10 weight percent.

5. L-Ascorbic acid tablets produced from L-ascorbic acid granules according to claim 1 and having the following characteristics:

(a) L-Ascorbic acid content: from substantially 100 to substantially 2000 mg. per tablet, and its percentage in a tablet being from substantially 90 to substantially 97.1 percent by weight.

(b) Amount of a binder: from substantially 2 to substantially 4 weight percent relative to L-ascorbic acid.

(c) Amount of lubricant: from substantially 1 to substantially 7 weight percent relative to L-ascorbic acid.

(d) Tensile strength: not less than 12.5 kg/cm².

6. L-Ascorbic acid tablets according to claim 5, wherein the lubricant is a stearate.

7. L-Ascorbic acid tablets according to claim 6, wherein the stearate is magnesium stearate, calcium stearate or stearic acid.

8. A process for producing granular L-ascorbic acid with improved tableting qualities characterised in that said process comprises spray-coating L-ascorbic acid powder, which passes through a 200-mesh screen, with a

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(B) Results

Tablet number	L-Ascorbic acid content (%)	Troubles in tableting	Hardness (kg)	Tensile strength (kg/cm ²)	Disintegration (minutes)
(1)	substantially 90.9	No	12.2	16.9	5.1
(2)	substantially 92.3	No	16.0	22.2	28.0
(3)	substantially 93.2	No	12.5	17.3	9.7
(4)	substantially 94.1	No	9.6	13.3	4.1
(5)	substantially 97.1	No	9.1	12.6	4.3
(6)	substantially 86.4	not free following, Sticking	6.0	8.3	26.0
(7)	substantially 87.3	Sticking	5.7	7.9	26.1
(8)	substantially 91.4	Sticking	4.9	6.8	3.3
(9)	substantially 90.5	Sticking Lamination	4.1	5.7	3.5
(10)	substantially 93.2	Sticking, Lamination	2.8	3.9	0.6

From the above tests, the tablets in accordance with the process of this invention are shown to be advantageous in terms of the combination of tableting difficulty, tensile strength, hardness and disintegration time.

WHAT WE CLAIM IS:—

1. L-Ascorbic acid granules produced by spray-coating L-ascorbic acid powder, which passes through a 200-mesh screen, with a solution or suspension of a pharmaceutically acceptable binder under constant agitation in a fluidised-bed granulating apparatus until the amount of solid binder on the powder has reached from substantially 2 to substantially 4 weight percent relative to the L-ascorbic acid content.

2. A method of producing L-ascorbic acid granules, which comprises spray-coating L-ascorbic acid powder, which passes through a 200-mesh screen, with a solution or suspension of a pharmaceutically acceptable binder under constant agitation in a fluidised-bed granulating apparatus until the amount of solid binder on the powder has reached from substantially 2 to substantially 4 weight percent relative to the L-ascorbic acid content.

3. A method according to claim 2, wherein not less than 50 weight percent of the L-ascorbic acid passes through a 325-mesh screen.

4. A method according to claim 2 or 3, wherein the concentration of the binder in the solution or suspension is from substantially 1 to substantially 10 weight percent.

5. L-Ascorbic acid tablets produced from L-ascorbic acid granules according to claim 1 and having the following characteristics:

(a) L-Ascorbic acid content: from substantially 100 to substantially 2000 mg. per tablet, and its percentage in a tablet being from substantially 90 to substantially 97.1 percent by weight.

(b) Amount of a binder: from substantially 2 to substantially 4 weight percent relative to L-ascorbic acid.

(c) Amount of lubricant; from substantially 1 to substantially 7 weight percent relative to L-ascorbic acid.

(d) Tensile strength: not less than 12.5 kg/cm².

6. L-Ascorbic acid tablets according to claim 5, wherein the lubricant is a stearate.

7. L-Ascorbic acid tablets according to claim 6, wherein the stearate is magnesium stearate, calcium stearate or stearic acid.

8. A process for producing granular L-ascorbic acid with improved tableting qualities characterised in that said process comprises spray-coating L-ascorbic acid powder, which passes through a 200-mesh screen, with a



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- 5 solution or suspension containing substantially 1 to substantially 10 weight percent of a binder while said powdery L-ascorbic acid is constantly agitated in fluidised-bed granulating apparatus until the amount of the binder has reached substantially 2 to substantially 4 weight percent relative to L-ascorbic acid.
- 10 9. A process for producing a pharmaceutical product in tablet form which contains a high amount of L-ascorbic acid, characterised in that said process comprises spray-coating L-ascorbic acid powder, which passes through a 200-mesh screen, with a solution or suspension containing substantially 1 to substantially
- 15 10 weight percent of a binder while said powdery L-ascorbic acid is constantly agitated in fluidised-bed granulating apparatus until the amount of the binder has reached substantially 2 to substantially 4 weight percent relative to
- 20 L-ascorbic acid, and compressing the resultant granular L-ascorbic acid mixed with a lubricant into tablets.
10. L-Ascorbic acid granules substantially as herein described with reference to any of the specific examples. 25
11. L-Ascorbic acid tablets substantially as herein described with reference to any of the specific examples.
12. A method of producing L-Ascorbic granules substantially as herein described with reference to any of the specific examples. 30
13. A method of producing L-Ascorbic tablets substantially as herein described with reference to any of the specific examples.
14. L-Ascorbic granules or tablets made by a method or process as claimed in any of Claims 2 to 4, 8, 9, 12 and 13. 35
- ELKINGTON & FIFE,
Chartered Patent Agents,
High Holborn House,
52/54 High Holborn,
London, WC1V 6SH.
Agents for the Applicants.