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(54) Title: NEW FURAZIDIN COMPOSITIONS AND METHODS OF THEIR MANUFACTURE

(57) Abstract: Furazidin composition in the form of suspension. A method of manufacturing the said composition where a phase I is obtained in such a way, that the suspending agent is dispersed in a part of purified water, then polyhydric alcohol or/and sugar, furazidin and possibly flavoring agents are added, the whole is homogenized, then a phase II is obtained in such a way that preservatives or/and the buffering mixture is dissolved in the remaining part of the purified water, then the phase II is added to the phase one. Furazidin composition in the form of powder or/and granules or/and coated granules. A method of manufacturing the said composition where a water or/and organic solution of the substance having binding properties is prepared, then furazidin is mixed with the substance having emulsifying properties and/or with the bulking agent, then the mixture is granulated. The obtained granules are calibrated and dried, and then possibly mixed with other excipients.

NEW FURAZIDIN COMPOSITIONS AND METHODS OF THEIR MANUFACTURE

TECHNICAL FIELD

The object of the present invention is an oral pharmaceutical composition comprising furazidin, a method of using it, and a method of manufacturing it.

BACKGROUND ART

Furazidin (Furaginum) is a derivative of nitrofuran, broad-spectrum chemotherapeutic agent. It acts against both Gram-positive and Gram-negative bacteria. It demonstrates bacteriostatic effect inter alia on *Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus faecalis, Salmonella, Shigella, Proteus, Klebsiella, Escherichia, Enterobacter*. Furazidin is used for treatment and prophylaxis of acute and chronic urinary tract infections.

Furazidin is administered in oral form – in the form of tablets. Tablets comprise corn starch, sucrose, colloidal silicon dioxide and stearic acid as excipients. The dosage form of a tablet is not very suitable for some groups of patients who have problems with swallowing e.g. children or elderly persons.

Patent specification RU2583945 discloses an agent containing as a hydrophilic mucoadhesive base a silicon-chitosan-containing glycerohydrogel obtained from a solution of silicon glicerolates Si(CHO) in glycerine CHO and weakly acidic aqueous solution of chitosan [(CHON)(CHON)] with deacetylation degree of 0.82 and molecular weight of 50-100 kDa, in molar ratio of initial substances: Si(CHO):CHO:[(CHON)(CHON)]:HO=1.0:6.0:0.2:76.8, and as medicinal additives furaginum and anaesthesin, with following ratio of components, wt%: furaginum -0.8-1.2; anesthesin - 0.8-1.2.

An article by Elzbieta Kuriata and Wieslaw Sawicki "Evaluation Of Cases With The Usage Of Commercially Available Tablets In The Pediatric Formula", Acta Poloniae Pharmaceutica - Drug Research, VOL. 72 NO. 3 PP. 551-558, 2015 reveals that lack of availability, of either the medicinal product intended to be used for children, or such in a dose which is fitting for the individual child's needs, results in physicians administering medicines meant for the adult. One of the medicines mentioned in the article is an antibacterial medicine containing furagin administered to children in the form of a tablet.

Use of furazidin was described by Paberza, M. et al.: „Some

aspects of the excretion of furagin with the urine of rabbits", Farmatsiya (Moscow, Russian Federation) (1980.06.30), 29(3), pp. 66-7, and by Hillers, S. et al.: „New chemical therapeutic preparation for the treatment of intestinal infections: furazidine (F-35)", Med. Nauka-Praktike (Riga: Akad. Nauk S.S.R.) Sbornik (1957), pp. 63-5.

Capsules comprising furazidin is sold at the market under commercial name Furamag. The filling of the capsules comprises furazidin, lactose monohydrate, maize starch and purified talc.

It has been found unexpectedly, that it is possible to deliver to those groups of patients a new oral dosage form which will be more suitable for them.

DISCLOSURE OF THE INVENTION

An oral pharmaceutical composition comprising furazidin according to the invention is in the form of suspension.

The composition comprises from 0,5% by weight to 20% by weight of furazidin.

The composition comprises at least one polyhydric alcohol or/and at least one sugar or their mixture in an amount from 5 to 80% by weight and water in an amount to 80% by weight.

The composition comprises at least one substance chosen from the group consisting of sorbitol, glycerol, mannitol, sucrose, glucose

or/and fructose.

The composition according comprises at least one suspending agent .

The composition comprises at least one suspending agent chosen from the group consisting of arabic gum, carbomer, xanthan gum, modified or/and unmodified starch, mixture of microcrystalline cellulose and croscarmellose sodium and/or their mixtures.

The composition comprises a suspending agent in an amount from 0,1% by weight to 10% by weight.

The composition comprises at least one flavoring agent or/and preservative. Preferably following substances are used as preservatives: benzoic acid; salts of benzoic acid e.g. sodium benzoate; esters of p-hydroxybenzoic acid e.g. methyl p-hydroxybenzoate, ethyl p-hydroxybenzoate, propyl p-hydroxybenzoate; sorbic acid; salts of sorbic acid e.g. potassium sorbate.

The composition comprises at least one buffering mixture. Preferably following buffering mixtures are used: citrate buffer, acetate buffer, phosphate buffer, oxalate buffer, citrate-phosphate

buffer.

The composition has pH between 2 and 9

A method of using the composition according to the invention consists in that the composition is administered to a mammal, including a human, in an amount providing a daily intake of furazidin from 25 to 600 mg. Daily dosage may be administered once, or may be divided into smaller dosages and may be taken several times a day, preferably from 2 to 4 times a day. A dosage for children shall be calculated using a ratio 5-7 mg/kg of child's body weight per day.

A method of manufacturing the composition according to the invention consists in that a phase I is obtained in such a way, that the suspending agent is dispersed in a part of purified water, then polyhydric alcohol or/and sugar, furazidin and possibly flavoring agents are added, the whole is homogenized, then a phase II is obtained in such a way that preservatives or/and the mixture of buffering mixtures is dissolved in the remaining part of the purified water, then the phase II is added to the phase one, the whole is homogenized and de-aerated.

A method of manufacturing the composition according to the

invention consists in that the suspending agent is dispersed in purified water, then polyhydric alcohol or/and sugar, and possibly flavoring substances, preservatives and buffering mixtures are dissolved, the whole is homogenized, and then furazidin is added, the whole is mixed and homogenized until a homogeneous suspension is obtained, and then it is de-aerated.

In the method according to the invention from 0,5% to 20% by weight of furazidin, polyhydric alcohol or/and at least one sugar or their mixture in an amount from 5 to 80% by weight and water in an amount to 80% by weight are used. The polyhydric alcohol or/and sugar is chosen from the group consisting of sorbitol, glycerol, mannitol, sucrose, glucose or/and fructose. The suspending agent is chosen from the group consisting of arabic gum, carbomer, xanthan gum, modified or/and unmodified starch, mixture of microcrystalline cellulose and croscarmellose sodium and/or their mixtures. The amount of suspending agent is from 0,1% by weight to 10% by weight. In the method at least one flavoring agent or/and preservative, and at least one buffer may be used. Preferably following preservative are used: benzoic acid; salts of benzoic acid e.g. sodium benzoate;

esters of p-hydroxybenzoic acid e.g. methyl p-hydroxybenzoate, ethyl p-hydroxybenzoate, propyl p-hydroxybenzoate; sorbic acid; salts of sorbic acid e.g. potassium sorbate. Preferably following buffering mixtures are used: citrate buffer, acetate buffer, phosphate buffer, oxalate buffer, citrate-phosphate buffer. The composition obtained by the method according to the invention has pH between 2 and 9.

A pharmaceutical composition comprising furazidin according to the invention is in the form of powder or/and granules or/and coated granules. The composition according to the invention may be directly administered to a patient. It may be used for preparation of oral suspension or/and a filling of hard capsule. It may be used for preparation of pellets or/and coated pellets or/and minitablets or/and coated minitablets, and they may constitute a filling of hard capsules. The composition according to the invention may be suspended in a dispersion phase what enables filling of soft capsule or/and hard capsule.

The composition has non-modified release characteristics.

The composition has modified release characteristics. The term “modified release” shall be understood as prolonged release, delayed

release, pulsatile release or accelerated release.

The composition comprises from 0.5% by weight to 95% by weight of furazidin.

The composition comprises at least one compound having binding or/and coating properties in an amount from 0.1% by weight to 30 % by weight.

The compound having binding or/and coating properties is chosen from the group consisting of saccharides, polyhydric alcohols, polymers of acrylic acid derivatives, polymers of methacrylic acid derivatives, polymers of vinyl alcohol derivatives, chemically modified cellulose derivatives, polyvinylpyrrolidones and/or polyethylene oxides. Saccharides used in the composition are e.g. sucrose or/and dextrins, polyhydric alcohols are e.g. sorbitol, mannitol, and chemically modified cellulose derivatives are e.g. hydroxypropyl cellulose, hydroxypropyl methylcellulose, cellulose phthalates or/and cellulose acetate. Polyvinylpyrrolidones used in the compositions are e.g. povidone K15/17 or/and povidone K25, whereas polyethylene oxides are e.g. PEG 400 or/and PEG 6000.

The composition comprises at least one compound having

emulsifying properties in an amount from 0.1% by weight to 45% by weight chosen from the group consisting of phospholipids, polyoxyethylene sorbitan derivatives, fatty acids and/or fatty alcohols. Phospholipids used in the compositions are soya lecithin or/and sunflower lecithin, and sorbitan derivatives are e.g. sorbitan sesquioleate. Fatty acids used in the composition are e.g. oleic acid, fatty alcohols are e.g. oleic alcohol.

The composition comprises at least one compound chosen from the group of surfactants (e.g. sodium lauryl sulfate) in an amount from 0.1% by weight to 15% by weight.

The composition comprises at least one bulking agent in an amount from 5% by weight to 99% by weight. Bulking agents used are e.g. starch, gelatinized starch, microcrystalline cellulose, lactose, glucose, mannitol, sorbitol, talc, dextrins or/and their mixture.

The composition comprises at least one lubricant in an amount from 0.1% by weight to 10% by weight. Lubricants used are e.g. stearic acid, magnesium stearate, talc or/and their mixture.

The composition comprises at least one substance chosen from the group consisting of sweetening agents, flavoring agents and

buffering agents in an amount from 0.01% by weight to 25% by weight. The composition may comprise just one of these agents or any of their mixtures. Sweetening agents used are e.g. sucrose, acesulfame K, sodium saccharin or/and sucralose. Flavoring agents comprised in the composition are e.g. orange, cherry, lemon or/and banana flavor, and buffering agents are e.g. sodium dihydrogen phosphate, sodium hydrogen phosphate, citric acid or/and sodium citrate.

The object of the present invention is also a method of manufacturing the composition as defined above which consists in that a water or/and organic solution of the substance having binding properties is prepared, then furazidin is mixed with the substance having emulsifying properties and/or with the bulking agent, then the mixture of furazidin with the substance having emulsifying properties and/or with the bulking agent is granulated with addition of the binding substance solution, after granulation the obtained granules are calibrated and dried, and then they are mixed with a bulking agent and/or a lubricant and/or a surfactant and/or a sweetening agent and/or a flavouring agent and/or a buffering agent. The composition obtained by this method is in the form of granules.

The water or/and the organic solution of the substance having binding and/or coating properties used in the method has concentration from 5% by weight to 90% by weight.

Granules directly after drying or after drying and calibration, and before mixing with other substances is coated with coating agents.

The object of the present invention is also a method of manufacturing the composition as defined above in the form of a powder. The method consists in that furazidin is mixed with a bulking agent or/and a binding agent or/and an emulsifying agent or/and a surfactant or/and a lubricant or/and a sweetening agent or/and a flavoring agent or/and a buffering agent.

BEST MODE OF CARRYING OUT THE INVENTION

The following examples illustrate the invention without setting or delineating its limits.

Example 1

Quantitative-qualitative composition of the formulation is depicted below.

No.	Name of the ingredient	%
		wt/wt
1	Furazidin	0,5
2	Sorbitol 70% non-crystallising	5

3	Glycerol	5
4	Xanthan gum	10
5	banana flavor	1,5
6	Sodium benzoate	1
7	Potassium sorbate	1
8	Purified water	76
	SUM:	100

Description of technological process: Phase I: Xanthan gum was dispersed in the part of purified water. Sorbitol and Glycerol were added. Phase II: In a separate vessel Sodium benzoate and Potassium sorbate were dissolved in the remaining part of purified water. Furazidin and flavor were added to Phase I. Homogenization was performed at speed from 100 to 6 000 rpm not less than for 5 min. Phase II was added. Homogenization was performed, and then the whole was stirred until de-aeration.

Example 2

Quantitative-qualitative composition of the formulation is depicted below.

No.	Name of the ingredient	%
		wt/wt
1	Furazidin	2,5
2	Sorbitol 70% non-crystallising	5
3	Glycerol	80
4	Xanthan gum.	0,5
5	banana flavor	2,5
6	Sodium benzoate	0,02
7	Potassium sorbate	0,1

8	Purified water	9,38
	SUM:	100

Description of technological process: Phase I: Xanthan gum was dispersed in the part of purified water. Sorbitol and Glycerol were added. Phase II: In a separate vessel Sodium benzoate and Potassium sorbate were dissolved in the remaining part of purified water. Furazidin and flavor were added to Phase I. Homogenization was performed at speed from 100 to 6 000 rpm not less than for 5 min. Phase II was added. Homogenization was performed, and then the whole was stirred until de-aeration.

Example 3

Quantitative-qualitative composition of the formulation is depicted below.

No.	Name of the ingredient	%
		wt/wt
1	Furazidin	5
2	Sorbitol 70% non crystallising	40
3	Glycerol	40
4	Arabic gum	5
5	banana flavor	1,5
6	Sodium benzoate	0,5
7	Potassium sorbate	0,5
8	Purified water	7,5
	SUM:	100

Description of technological process: Phase I: Xanthan gum was dispersed in the part of purified water. Sorbitol and Glycerol were added. Phase II: In a separate vessel Sodium benzoate and Potassium sorbate were dissolved in the remaining part of purified water. Furazidin and flavor were added to Phase I. Homogenization was performed at speed from 100 to 6 000 rpm not less than for 5 min. Phase II was added. Homogenization was performed, and then the whole was stirred until de-aeration.

Example 4

Quantitative-qualitative composition of the formulation is depicted below.

No.	Name of the ingredient	%
		wt/wt
1	Furazidin	1,5
2	Sucrose	6,5
3	Glycerol	13
4	Carbomer	0,35
5	NaOH	0,07
6	banana flavor	0,1
7	Sodium benzoate	0,01
8	Potassium sorbate	0,1
9	Purified water	78,37
SUM:		100

Description of technological process: Phase I: Carbomer was dispersed in the part of purified water. NaOH was added. Stirring was

performed for n.m.n 10 min. Sucrose and Glycerol were added. Phase II: In a separate vessel Sodium benzoate and Potassium sorbate were dissolved in the remaining part of purified water. Furazidin and flavor were added to Phase I. Homogenization was performed at speed from 100 to 6 000 rpm not less than for 5 min. Phase II was added. Homogenization was performed. The whole was stirred until de-aeration.

Example 5

Quantitative-qualitative composition of the formulation is depicted below.

No.	Name of the ingredient	%
		wt/wt
1	Furazidin	1,5
2	Sucrose	30
3	Carbomer	0,35
4	NaOH	0,07
5	banana flavor	1,5
6	Sodium benzoate	1
7	Potassium sorbate	1
8	Purified water	64,58
SUM:		100

Description of technological process: Phase I: Carbomer was dispersed in the part of purified water. NaOH was added. Stirring was performed for not less than 10 min. Sucrose was added. Phase II: In a

separate vessel Sodium benzoate and Potassium sorbate were dissolved in the remaining part of purified water. Furazidin and flavor were added to Phase I. Homogenization was performed at speed from 100 to 6 000 rpm not less than for 5 min. Phase II was added. Homogenization was performed. The whole was stirred until de-aeration.

Example 6

Quantitative-qualitative composition of the formulation is depicted below.

No.	Name of the ingredient	% wt/wt
1	Furazidin	0,5
2	Sorbitol 70% non-crystallising	5
3	Glycerol	5
4	Xanthan gum	10
5	Citric acid	5,38
6	Sodium citrate	4,71
7	banana flavor	1,5
8	Sodium benzoate	1
9	Potassium sorbate	1
10	Purified water	65,91
SUM:		100

Description of technological process: Phase I: Xanthan gum was dispersed in the part of purified water. Sorbitol and Glycerol were added. Phase II: In a separate vessel Citric acid, Sodium citrate,

Sodium benzoate and Potassium sorbate were dissolved in the remaining part of purified water. Furazidin and flavor were added to Phase I. Homogenization was performed at speed from 100 to 6 000 rpm not less than for 5 min. Phase II was added. Homogenization was performed. The whole was stirred until de-aeration.

Example 7

Quantitative-qualitative composition of the formulation is depicted below.

No.	Name of the ingredient	% wt/wt
1	Furazidin	1,5
2	Sorbitol 70% non-crystallising	40
3	Glycerol	15
4	Mixture of cellulose and croscarmellose	10
5	banana flavor	1,5
6	Sodium benzoate	1
7	Potassium sorbate	1
8	Purified water	30
SUM:		100

Mixture of cellulose and croscarmellose was suspended in purified water. Under stirring Sorbitol and Glycerol were added. The flavor, Sodium benzoate and Potassium sorbate were added. Homogenization was performed at speed from 100 to 6 000 rpm not less than for 5 min. Furazidin was added. The whole was stirred and homogenized

until homogeneous dispersion was formed.

Example 8

Quantitative-qualitative composition of the formulation is depicted below.

No.	Name of the ingredient	% wt/wt
1	Furazidin	3
2	Sucrose	40
3	Mixture of cellulose and croscarmellose	10
4	banana flavor	1,5
5	Sodium benzoate	1
6	Potassium sorbate	1
7	Purified water	43,5
SUM:		100

Mixture of cellulose and croscarmellose was suspended in purified water. Under stirring Sucrose was added. The flavor, Sodium benzoate and Potassium sorbate were added. Homogenization was performed at speed from 100 to 6 000 rpm not less than for 5 min. Furazidin was added. The whole was stirred and homogenized until homogeneous dispersion was formed.

Example 9

Quantitative-qualitative composition of the formulation is depicted below.

No.	Name of the ingredient	% wt/wt
1.	Furazidin	50
2.	Gelatinized corn starch	30.5
3.	Sucrose	16.9
4.	Anhydrous colloidal silica	0.5
5	Stearic acid 50	2.1
	SUM:	100

Description of technological process: in the apparatus for wet granulation e.g. in a mixer granulator the ingredients 1 and 2 were placed. A solution of binding agent being a water solution of the ingredient 3 was prepared. The ingredients 1 and 2 were mixed until smooth, however not shorter than 5 minutes. Granulation was performed with use of the water solution of the ingredient 3. The water solution of the ingredient 3 shall have the concentration from 50 to 200 % wt/wt, and it is possible to use maximal ratio of the solvent : ingredient 3 as 1:2. After granulation the granules obtained were calibrated and dried to achieve dryness from 0.5 to 15%. In case of need the dried granules were calibrated. The ingredient 4 was added. The whole was mixed until smooth, but not less than 3 min. The ingredient 5 was added. The whole was mixed until smooth, but not less than 3 min. The product obtained may be used as a filling for

hard capsules or may be used for obtaining pellets or minitablets, where may then constitute a filling for hard capsules.

Example 10

Quantitative-qualitative composition of the formulation is depicted below.

No.	Name of the ingredient	% wt/wt
1.	Furazidin	1,111
2.	Gelatinized corn starch	0,678
3.	Sucrose	0,376
4.	Anhydrous colloidal silica	0,011
5.	Stearic acid 50	0,047
6.	Orange flavor	2,502
7.	Acesulfame potassium	0,084
8.	Sodium saccharin	0,084
9.	Sucralose	0,133
10.	Riboflavin	0,018
11.	Sorbitol (powder)	94,956
	SUM:	100

Description of technological process: in the apparatus for wet granulation e.g. in a mixer granulator the ingredients 1 and 2 were placed. A solution of binding agent being a water solution of the ingredient 3 was prepared. The ingredients 1 and 2 were mixed until

smooth, however not shorter than 5 minutes. Granulation was performed with use of the water solution of the ingredient 3. The water solution of the ingredient 3 shall have the concentration from 50 to 200 % wt/wt, and it is possible to use maximal ratio of the solvent : ingredient 3 as 1:2. After granulation the granules obtained were calibrated and dried to achieve dryness from 0.5 to 15%. In case of need the dried granules were calibrated. The ingredient 4 was added. The whole was mixed until smooth, but not less than 3 min. The ingredients 7 to 11 were added and mixed until smooth, but but not less than 3 min. It is possible to mix each ingredient in a separate cycle of mixing or/and all ingredients together. The ingredient 5 was added. The whole was mixed until smooth, but not less than 3 min. The mass obtained was filled into sachets. The product obtained may be administered directly to a patient or/and used for preparation of a suspension directly before administration.

Example 11

Quantitative-qualitative composition of the formulation is depicted below.

No.	Name of the ingredient	% wt/wt
1.	Furazidin	2,77

2.	Lactose monohydrate	1,94
3.	Polyvinylpyrrolidone	1,11
4.	Talc	0,03
5.	Magnesium stearate	0,33
6.	Orange flavor	3,12
7.	Sucrose	55,38
8.	Sorbitol (powder)	35,33
	SUM:	100

Description of technological process: in the apparatus for wet granulation e.g. in a mixer granulator the ingredients 1 and 2 were placed. A solution of binding agent being a water solution of the ingredient 3 was prepared. The ingredients 1 and 2 were mixed until smooth, however not shorter than 5 minutes. Granulation was performed with use of the water solution of the ingredient 3. The water solution of the ingredient 3 shall have the concentration from 5 to 50 % wt/wt. After granulation the granules obtained were calibrated and dried to achieve dryness from 0.5 to 15%. In case of need the dried granules were calibrated. The ingredient 4 was added. The whole was mixed until smooth, but not less than 3 min. The ingredients 6 to 8 were added and mixed until smooth, but but not less than 3 min. It is possible to mix each ingredient in a separate cycle of mixing or/and all ingredients together. The ingredient 4 and 5 was added. The whole was mixed until smooth, but not less than 3 min.

The mass obtained was filled into sachets. The product obtained may be administered directly to a patient or/and used for preparation of a suspension directly before administration.

Example 12

No.	Name of the ingredient	% wt/wt
1.	Furazidin	2,5
2.	Lactose monohydrate	1,75
3.	Polyvinylpyrrolidone	1
4.	Talc	0,025
5.	Magnesium stearate	0,3
6.	Orange flavor	5,6
7.	Sucrose	61,1
8.	Mannitol	25
9.	Citric acid	1
10.	Sodium citrate	1,35
11.	Mixture of polyoxyethylene derivatives of sorbitan and oleic acid	0,375
	SUM:	100

Description of technological process: A water solution of the ingredients 3 and 11 was prepared. In the apparatus for wet granulation the ingredients 1, 2 and 7 were placed. The whole was mixed until smooth, however not shorter than 3 minutes. It is possible to mix all ingredients together or separately. The mixture was granulated with use of the water solution of the ingredient 3 and 11. In case of need the obtained granules were calibrated. The granules were

dried to achieve dryness from 0.5 to 25%. In case of need granules were calibrated. The ingredients 6, 8, 9 and 10 were added to the obtained granules. The whole was mixed until smooth, but not less than 3 min. It is possible to mix each ingredient in a separate cycle of mixing or/and all ingredients together. The ingredient 4 and 5 was added. The whole was mixed until smooth, but not less than 3 min. The mass obtained was filled into sachets. The product obtained may be administered directly to a patient or/and used for preparation of a suspension directly before administration.

Example 13

No.	Name of the ingredient	% wt/wt
1.	Furazidin	13,692
2.	Lactose monohydrate	0,479
3.	Mixture of copolymers of methacrylic or/and acrylic acid	0,685
4.	Talc	0,021
5.	Magnesium stearate	0,014
6.	Orange flavor	1,534
7.	Sucrose	41,076
8.	Sorbitol	41,076
9.	Citric acid	0,548
10.	Sodium citrate	0,739
11.	Mixture of polyoxyethylene derivatives of sorbitan and oleic acid	0,137
	SUM:	100

Description of technological process: A dispersion of the ingredients 3 and 11 was prepared. In the apparatus for wet granulation the ingredients 1, 2 and part of portion of the ingredient 7 were placed. It is possible to use the ingredient 7 in proportion from 0 to 100%. Granulation was performed with use of the solution of the ingredients 3 and 11. Obtained granules were calibrated in case of need, and then dried to achieve dryness from 0.5 to 25%. After drying the granules obtained were calibrated in case of need. The rest of the portion of the ingredient 7 was added to the obtained granules. (if 100% of the portion of the ingredient 7 is used for granulation, this step shall be omitted). Next ingredients 6, 9 and 10 were added to the mixture. The whole was mixed until smooth, but not less than 3 min. It is possible to mix each ingredient in a separate cycle of mixing or/and all ingredients together. The ingredient 4 and 5 was added. The whole was mixed until smooth, but not less than 3 min. It is possible to mix each ingredient in a separate cycle of mixing or/and all ingredients together. The product obtained may be administered directly to a patient or/and used for preparation of a suspension directly before administration.

Example 14

No.	Name of the ingredient	% wt/wt
1.	Furazidin	13,692
2.	Lactose monohydrate	0,479
3.	Mixture of copolymers of methacrylic or/and acrylic acid	0,685
4.	Talc	0,021
5.	Magnesium stearate	0,014
6.	Orange flavor	1,534
7.	Sucrose	41,076
8.	Sorbitol	41,076
9.	Citric acid	0,548
10.	Sodium citrate	0,739
11.	Mixture of polyoxyethylene derivatives of sorbitan and oleic acid	0,137
	SUM:	100

Description of technological process : A water dispersion of the ingredient 7 was prepared. The water solution of the ingredient 7 shall have the concentration from 50 to 200 % wt/wt, and it is possible to use maximal ratio of the solvent : ingredient 3 as 1:2. Non-used part of the portion of the ingredient 7 will be used in the next step of the process. In the apparatus for wet granulation the ingredients 1 and 2 were placed. It is possible to use the ingredient 8 in proportion from 0 to 100%. Granulation was performed with use of the solution of the ingredient 7. Obtained granules were calibrated in case of need. They

were dried to achieve dryness from 0.5 to 25%. A water solution of the ingredient 3 was prepared. Dried granules were fluid coated with the solution of the ingredient 3. To the obtained granules the remaining portions of the ingredients 7 and 8 were added, and then 8 and 9. The whole was mixed until smooth, but not less than 3 min. It is possible to mix each ingredient in a separate cycle of mixing or/and all ingredients together. The ingredients 4 and 5 were added. It is possible to mix each ingredient in a separate cycle of mixing or/and all ingredients together. The product obtained may be administered directly to a patient or/and used for preparation of a suspension directly before administration.

Example 15

No.	Name of the ingredient	% wt/wt
1.	Furazidin	64,412
2.	Sucrose	32,206
3.	Mixture of copolymers of methacrylic or/and acrylic acid	3,221
4.	Talc	0,097
5.	Magnesium stearate	0,064
	SUM:	100

Description of technological process: A water solution of the ingredient 3 was prepared. In the apparatus for wet granulation the

ingredients 1 and 2 were placed. The ingredients 1 and 2 were mixed. Granulation was performed in a fluid bed with use of the solution of the ingredient 3. In case of need the obtained granules were calibrated. The ingredients 4 and 5 were added to the obtained granules. The whole was mixed until smooth, but not less than 3 min. It is possible to mix each ingredient in a separate cycle of mixing or/and all ingredients together. The ingredient 4 and 5 was added. The whole was mixed until smooth, but not less than 3 min. The product obtained is intended for obtaining pellets or minitablets, that may be coated and constitute a filling for hard capsules or/and may be suspended in a dispersion phase what enables filling of soft capsule or/and hard capsule.

PATENT CLAIMS

1. An oral pharmaceutical composition comprising furazidin, characterized in that it is in the form of suspension.

2. The composition according to claim 1, characterized in that it comprises from 0,5% by weight to 20% by weight of furazidin.

3. The composition according to claim 1 or 2, characterized in that it comprises at least one polyhydric alcohol or/and at least one sugar or their mixture in an amount from 5 to 80% by weight and water in an amount to 80% by weight.

4. The composition according to claim 3, characterized in that it comprises at least one substance chosen from the group consisting of sorbitol, glycerol, mannitol, sucrose, glucose or/and fructose.

5. The composition according to any of the preceding claims, characterized in that it comprises at least one suspending agent.

6. The composition according to claim 5, characterized in that it comprises at least one suspending agent chosen from the group consisting of arabic gum, carbomer, xanthan gum, modified

or/and unmodified starch, mixture of microcrystalline cellulose and croscarmellose sodium and/or their mixtures.

7. The composition according to claim 5 or 6, characterized in that it comprises a suspending agent in an amount from 0,1% by weight to 10% by weight.

8. The composition according to any of the preceding claims, characterized in that it comprises at least one flavoring agent or/and preservative.

9. The composition according to any of the preceding claims, characterized in that it comprises at least one buffering mixture.

10. The composition according to any of the preceding claims, characterized in that its pH is between 2 and 9.

11. A method of using the composition as defined in any of the preceding claims, characterized in that the composition is administered to a mammal, including a human, in an amount providing a daily intake of furazidin from 25 to 600 mg.

12. A method of manufacturing the composition as defined in any of the preceding claims, characterized in that a phase I is obtained in such a way, that the suspending agent is dispersed in a part of purified water, then polyhydric alcohol or/and sugar, furazidin and possibly flavoring agents are added, the whole is homogenized, then a phase II is obtained in such a way that preservatives or/and the buffering mixture is dissolved in the remaining part of the purified water, then the phase II is added to the phase one, the whole is homogenized and de-aerated.

13. A method of manufacturing the composition as defined in any of the preceding claims, characterized in that the suspending agent is dispersed in purified water, then polyhydric alcohol or/and sugar, and possibly flavoring agents, preservatives and buffering mixtures are dissolved, the whole is homogenized, and then furazidin is added, the whole is mixed and homogenized until a homogeneous suspension is obtained, and then it is de-aerated.

14. A pharmaceutical composition comprising furazidin, characterized in that it is in the form of powder or/and granules or/and coated granules.

15. The composition according to claim 14, characterized in that it has non-modified release characteristics.

16. The composition according to claim 14, characterized in that it has modified release characteristics.

17. The composition according to any of the claims 14-16, characterized in that it comprises from 0.5% by weight to 95% by weight of furazidin.

18. The composition according to any of the claims 14-17, characterized in that it comprises at least one compound having binding or/and coating properties in an amount from 0.1% by weight to 30 % by weight.

19. The composition according to claim 18, characterized in that the compound having binding or/and coating properties is chosen from the group consisting of saccharides, polyhydric alcohols, polymers of acrylic acid derivatives, polymers of methacrylic acid derivatives, polymers of vinyl alcohol derivatives, chemically modified cellulose derivatives, polyvinylpyrrolidones and/or polyethylene oxides.

20. The composition according to any of the claims 14-19, characterized in that it comprises at least one compound having emulsifying properties in an amount from 0.1% by weight to 45% by weight chosen from the group consisting of phospholipids, polyoxyethylene sorbitan derivatives, fatty acids and/or fatty alcohols.

21. The composition according to any of the claims 14-20, characterized in that it comprises at least one compound chosen from the group of surfactants in an amount from 0.1% by weight to 15% by weight.

22. The composition according to any of the claims 14-21, characterized in that it comprises at least one bulking agent in an amount from 5% by weight to 99% by weight.

23. The composition according to any of the claims 14-22, characterized in that it comprises at least one lubricant in an amount from 0.1% by weight to 10% by weight.

24. The composition according to any of the claims 14-23, characterized in that it comprises at least one substance chosen

from the group consisting of sweetening agents, flavoring agents and buffering agents in an amount from 0.01% by weight to 25% by weight.

25. A method of manufacturing the composition as defined in claims from 14 to 24, characterized in that a water or/and organic solution of the substance having binding properties is prepared, then furazidin is mixed with the substance having emulsifying properties and/or with the bulking agent, then the mixture of furazidin with the substance having emulsifying properties and/or with the bulking agent is granulated with addition of the binding substance solution, after granulation the obtained granules are calibrated and dried, and then they are mixed with a bulking agent and/or a lubricant and/or surfactant and/or a sweetening agent and/or a flavoring agent and/or a buffering agent.

26. The method according to claim 25, characterized in that the water or/and organic solution of the substance having binding and/or coating properties has concentration from 5% by weight to 90% by weight.

27. The method according to claim 25 or 26, characterized in that granules directly after drying or after drying and calibration, and before mixing with other substances is coated with coating agents.

28. A method of manufacturing the composition as defined in claims from 14 to 24, characterized in that furazidin is mixed with a bulking agent or/and a binding agent or/and an emulsifying agent or/and a surfactant or/and a lubricant or/and a sweetening agent or/and a flavoring agent or/and a buffering agent.