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The present invention relates to novel coating compositions for application to solid dosage forms such as tablets or caplets, solid dosage forms coated with the composition, and methods of preparing said coating compositions.

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(54) Title: FILM COATING FOR TABLETS AND CAPLETS

(57) Abstract: The present invention relates to novel coating compositions for application to solid dosage forms such as tablets or caplets, solid dosage forms coated with the composition, and methods of preparing said coating compositions.

Film coating for tablets and caplets

The present invention relates to novel coating compositions for application to solid dosage forms such as tablets or caplets, solid dosage forms coated with the composition, and methods of preparing said coating compositions.

EP-A-0 891 180 describes a process for encapsulation of caplets in a capsule wherein caplets are encapsulated in capsule shells. To obtain tamper-proof solid dosage forms, the caplets which are to be included into capsule shells, are coated with an acceptable coating for caplet processing. As described in EP-A-0 891 180 said coating is selected from a material selected from the group consisting of cellacephate, polyvinyl acetate phthalate, methacrylic acid polymers, hypromellose phthalate, hydroxyalkyl methyl cellulose phthalate or mixtures thereof.

After being coated with such a coating the caplet is usually feeded on a vibratory feed, filled into capsule shell parts and the encapsulated dosage form is dried so as to obtain capsules.

In several studies carried out by the present invention on finished capsules prepared as mentioned above, it has, however, been found that after obtaining said capsules the shell parts can be removed so as to lay free intact shell parts and caplets.

This should be prohibited so as to avoid any exchange of the caplets contained in said capsules by non-authorized persons after putting said capsules on the market.

An object of an aspect of the present invention therefore is to provide coating compositions which give raise to capsules in a tamper-proof form which cannot be easily freed from the shell parts without deteriorating the shell parts and/or the caplets.

It is another object of an aspect of the present invention to provide a coating composition which improves a feeding of solid dosage forms such as caplets or tablets, coated with said coating composition, on a vibratory feed used for example in a capsule manufacturing process.

It is yet another object of an aspect of the present invention to provide a method for coating solid dosage form such as caplets or tablets with said coating composition.

It is yet another object of an aspect of the present invention to provide a method for encapsulating caplets in a capsule in a tamper-proof form.

According to a first aspect, the present invention provides a coating composition comprising a film forming agent in an amount of from 0 to about 85% by weight, an adhesion enhancing agent in an amount of from about 10 to about 90% by weight, and a glidant in an amount of from about 5 to about 50% by weight, based on the weight of the coating composition.

According to a second aspect the present invention provides a solid dosage form coated with a coating composition comprising a film forming agent in an amount of from 0 to about 85% by weight, an adhesion enhancing agent in an amount of from about 10 to about 90% by weight, and a glidant in an amount of from about 5 to about 50% by weight, based on the weight of the coating composition.

According to a third aspect, the present invention provides a method of preparing a coating composition comprising bringing into association a film forming agent in an amount of from 0 to about 85% by weight, an adhesion enhancing agent in an amount of from about 10 to about 90% by weight, and a glidant in an amount of from about 5 to about 50% by weight, based on the weight of the coating composition.

According to a forth aspect, the present invention provides a method of preparing a solid dosage form which comprises coating a solid dosage form core with a

coating composition comprising a film forming agent in an amount of from 0 to about 85% by weight, an adhesion enhancing agent in an amount of from about 10 to about 90% by weight, and a glidant in an amount of from about 5 to about 50% by weight, based on the weight of the coating composition.

In accordance with a fifth aspect, the present invention provides a tamper-proof capsule comprising at least one capsule shell part and enclosing a solid dosage form core, said core being coated with a coating composition comprising a film forming agent in an amount of from 0 to 85% by weight, an adhesion enhancing agent in an amount of from 10 to 90% by weight, and a glidant in an amount of from 5 to 50% by weight, based on the weight of the coating composition.

In accordance with a sixth aspect, the present invention provides a method of preparing a tamper proofed capsule which comprises coating a solid dosage form core with a coating composition comprising a film forming agent in an amount of from 0 to 85% by weight, an adhesion enhancing agent in an amount of from 10 to 90% by weight, and a glidant in an amount of from 5 to 50% by weight, based on the weight of the coating composition and which further comprises the steps of filling the solid dosage form coated with the coating composition into capsule shell parts and treating the combined capsule shell parts so as to obtain capsules.

In accordance with a seventh aspect, the present invention provides use of a coating composition comprising a film forming agent in an amount of from 0 to 85% by weight, an adhesion enhancing agent in an amount of from 10 to 90% by weight, and a glidant in an amount of from 5 to 50% by weight, based on the weight of the coating composition, for applying to a solid dosage form core so as to improve adhesion of said solid dosage form core to at least one capsule shall part filled in with said coated solid dosage form core.

According to another aspect of the present invention, there is provided a tamper-proof capsule comprising at least one capsule shell part and enclosing a solid dosage form core, said solid dosage form core being a caplet, and said core being coated with a coating composition comprising a film forming agent in an

amount of from 0 to 85% by weight, an adhesion enhancing agent in an amount of from 10 to 90% by weight, and a glidant in an amount of from 5 to 50% by weight, based on the weight of the coating composition.

In a preferred embodiment of the first aspect said coating composition comprises a film forming agent in an amount of from about 0 to about 40% by weight, an adhesion enhancing agent in an amount of from about 35 to about 80% by weight, and a glidant in an amount of from about 5 to about 25% by weight, based on the weight of the coating composition.

In an especially preferred embodiment of the first aspect said coating composition comprises a film forming agent in an amount of about 20% by weight, an adhesion enhancing agent in an amount of about 60% by weight, and a glidant in an amount of about 20% by weight, based on the weight of the coating composition.

In another especially preferred embodiment of the first aspect said coating composition comprises a film forming agent in an amount of about 30% by weight, an adhesion enhancing agent in an amount of about 50% by weight, and a glidant in an amount of about 20% by weight, based on the weight of the coating composition.

In another especially preferred embodiment of the first aspect said coating composition comprises an adhesion enhancing agent in an amount of about 80% by weight, and a glidant in an amount of about 20% by weight, based on the weight of the coating composition.

Examples of said film forming agent suitable for incorporation into the coating composition of the first aspect of the present invention include cellulosephthalateacetate, microcrystalline cellulose, methylcellulose,

hydroxypropyl methylcellulose, alginates, gum arabic, carboxymethylcellulose, hydroxyethylcellulose and methylcellulose.

Preferred film forming agents to be used according to the first aspect of the present invention are methylcellulose, hydroxypropyl methylcellulose, gum arabic, carboxymethylcellulose, hydroxyethylcellulose and methylcellulose, more preferable hydroxypropyl methylcellulose.

Examples of said adhesion enhancing agent suitable for incorporation into the coating composition of the first aspect of the present invention include dextrose, sorbitol, mannitol, sucrose, polyvinylpyrrolidone, lactose, starch, sodium starch glycolate, hydroxypropylcellulose, ethylcellulose and maltodextrines.

Preferred adhesion enhancing agents suitable for incorporation into the coating composition of the first aspect of the present invention are sucrose, polyvinylpyrrolidone, hydroxypropylcellulose, ethylcellulose and maltodextrines, more preferable hydroxypropylcellulose.

Examples of said glidant suitable for incorporation into the coating composition of the first aspect of the present invention include polyethylene glycol, polypropylene glycol, triethyl citrate, mono-, di- or triacetates of glycerol and 1,2-propyleneglycol.

A preferred glidant suitable for incorporation into the coating composition of the first aspect of the present invention is polyethylene glycol.

Usually, the coating composition according to the first aspect has a gel point of about 40°C or more, i.e. close to the transition point.

The solid dosage form coated with a coating composition, of the second aspect of the present invention usually is a caplet or a tablet to be coated with the coating composition of the present invention.

According to a further aspect of the present invention, there is provided a method of preparing a coating composition comprising bringing into association a film forming agent in an amount of from 0 to about 85 % by weight, an adhesion enhancing agent in an amount of from ab out 10 to about 90 % by weight, and a glidant in an amount of from about 5 to about 50 % by weight, based on the weight of the coating composition.

According to a further aspect of the present invention, there is provided a method of preparing solid dosage form which comprises coating a solid dosage form core with a coating composition comprising a film forming agent in an amount of from 0 to about 85 % by weight, an adhesion enhancing agent in an amount of from about 10 to about 90 % by weight and a glidant in an amount of from about 5 to about 50 % by weight, based on the weight of the coating composition.

Usually, said solid dosage form is a caplet or a tablet, preferably a caplet.

In one embodiment of the forth aspect of the present invention thereafter one or more caplets coated with said coating composition, can be filled into at least one capsule part so as to obtain capsules.

The capsule shell in which the caplet is to be enclosed preferably comprises two shell halves, a body portion and a cap portion. Other capsule shells comprising more than two parts are also possible. In a preferred embodiment the capsule shells to be used may be those as described in EP-A-0 891 180.

Surprisingly, it has been found that caplets coated with the coating composition according to the present invention, show a superior adhesion to the capsule shell parts they have been filled in.

Especially, experimental results show that capsules filled with caplets coated with the coating composition according to the present invention, are tamper-proof in a way that the caplets show a superior adhesion to capsule shell parts and a better

adhesive strength than capsules of the prior art such as described in EP-A-0 891 180. This is also demonstrated below in the experimental part of the present specification.

If it was tried to remove capsule shell parts from capsules prepared by using caplets coated according to the present invention, it was found that a very high percentage of shell parts will break and pulling apart capsule shells without deteriorating the capsule shells is not possible.

Thus, in a further aspect the present invention provides a use of a coating composition comprising a film forming agent in an amount of from 0 to about 85 % by weight, an adhesion enhancing agent in an amount of from about 10 to about 90 % by weight, and a glidant in an amount of from about 5 to about 50 % by weight, based on the weight of the coating composition, for applying to a solid dosage form so as to improve adhesion of said solid dosage forms to capsule shells.

Furthermore, it has been found that feeding of caplets on a vibratory feed to be used in a capsule manufacturing process (typically the caplet feeding speed on a vibratory plate is in a range of from 1 to 7 cm/sec) is highly improved by using caplets coated with the coating composition claimed according to the present invention.

In a preferred embodiment of the process of preparing capsules by using caplets, in a further step caplets coated with the coating composition claimed according to the present invention are filled into capsule shell parts and then the combined capsule shell parts are treated by cold shrinking so as to obtain capsules.

As a preferred procedure the capsule manufacturing process described in EP-A-0 891 190 could be used.

To further illustrate the present invention, the following illustrative examples are presented, without limitation:

EXAMPLE 1

In a first example different coating compositions having a composition as shown in Table 1 below, were coated on Capsugel™ 707 Placebo caplet cores so as to obtain coated caplets. These coated caplets were subjected to a feeding on a vibratory feed (caplet feeding speed on vibratory plate: 1 to 7 cm/sec). The behaviour of these coated caplets was visually tested, and the results obtained were the following:

Table 1

Mixture (ratio, parts by weight)	vibratory feed
HPMC/PVP 50/50	good
HPMC/HPC 40/60	good
HPC/PEG 80/20	medium
HPMC/HPC/PEG 20/60/20	medium
HPMC/HPC/PEG 30/50/20	medium
HPMC/HPC/PEG 40/40/20	very good

Abbreviations used:

HPMC = hydroxypropyl methylcellulose

PVP = polyvinyl pyrrolidone

HPC = hydroxypropylcellulose

PEG = polyethylene glycol 6000

EXAMPLE 2

Adhesion results after stability storage

- In this example samples of Press-fit gelcaps made with a standard HPMC coating (sample 1) and made with a coating composition according to the present invention (sample 2) were manufactured according to a standard process.

Sample 1				
Cores	Capsugel 707 Placebo *			
Shells Body	White opaque			
Shells Cap	Green opaque			
3 months	Defects	Gap	Appearance	Quantity
40°C/ 75% RH	0	0	OK	150

* coated with HPMC

Sample 2				
Cores Shells Body	Capsugel 708 Placebo ** White opaque			
Shells Cap	Green opaque			
3 months	Defects	Gap	Appearance	Quantity
40°C/ 75% RH	0	0	OK	150

** coated with a mix of HPMC/HPC/PEG (40/40/20)

Thereafter these samples were stored for 3 months under room conditions and at 40°C 75%RH, and adhesion and disintegration were measured.

Conclusions:

- adhesion is stable at room conditions for both samples

- at 40°C/75%RH the adhesion drops for the samples made with HPMC whilst it remains stable for the sample made with the new coating mixture.

- Disintegration is equivalent for all samples and conforms to specifications.

1. Adhesion results:

Sample 1		Pullapart (N)	Std	Nb of broken
T= 24h	RC	22.5	2.5	0 %
T=6days	RC	22.7	4.1	0 %
T=6 weeks	RC	21.1	2.9	0 %
t=2months	RC	21.4	3.3	0 %
t=3 months	RC	22.6	4.2	0 %
t=3 months	40°C/75% RH	8.4	3.0	0 %

Sample 2		Pullapart (N)	Std	Nb of broken
T= 24h	RC	29.13	5.0	80 %
T=6days	RC	30.1	4.2	100 %
T=6 weeks	RC	33.2	4.8	90 %
t=2months	RC	32.0	5.2	74 %
t=3 months	RC	28.5	3.1	100 %
t=3 months	40°C/75% RH	27.2	3.7	100 %

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2. Disintegration results:

Sample 1		Disintegration time	STD
T=0	RC	4 min 38s	37s
T=3 months	40°C/75% RH	5 min 06s	19s

Sample 2		Disintegration time	STD
T=0	RC	3 min 41s	29s
T=3 months	40°C/75% RH	3 min 49s	40s

WHAT IS CLAIMED IS:

1. A tamper-proof capsule comprising at least one capsule shell part and enclosing a solid dosage form core, said solid dosage form core being a caplet, and said core being coated with a coating composition comprising a film forming agent in an amount of from 0 to 85% by weight, an adhesion enhancing agent in an amount of from 10 to 90% by weight, and a glidant in an amount of from 5 to 50% by weight, based on the weight of the coating composition.

2. The capsule according to claim 1, wherein the coating composition comprises a film forming agent in an amount of from 0 to 40% by weight, an adhesion enhancing agent in an amount of from 35 to 80% by weight, and a glidant in an amount of from 5 to 25% by weight based on the weight of the coating composition.

3. The capsule according to any one of claims 1 or 2, wherein the coating composition comprises a film forming agent in an amount of from 20 to 40% by weight, an adhesion enhancing agent in an amount of from 35 to 60% by weight, and a glidant in an amount of from 20 to 25% by weight based on the weight of the coating composition.

4. The capsule according to any one of claims 1 to 3, wherein said film forming agent is selected from methylcellulose, hydroxypropyl methylcellulose, gum arabic, carboxymethylcellulose, hydroxyethylcellulose and methylcellulose.

5. The capsule according to any one of claims 1 to 4, wherein said film forming agent is hydroxypropyl methylcellulose.

6. The capsule according to any one of claims 1 to 5, wherein said adhesion enhancing agent is selected from dextrose, sorbitol, mannitol, sucrose, polyvinylpyrrolidone, lactose, starch, sodium starch glycolate, hydroxypropylcellulose, ethylcellulose and maltodextrines.

7. The capsule according to any one of claims 1 to 6, wherein said adhesion enhancing agent is hydroxypropylcellulose.

8. The capsule according to any one of claims 1 to 7, wherein said glidant is selected from polyethylene glycol, polypropylene glycol, triethyl citrate, mono-, di- or triacetates of glycerol and 1,2-polyeneglycol.

9. The capsule according to any one of claims 1 to 8, wherein said glidant is polyethylene glycol.

10. The capsule according to any one of claims 1 to 9, wherein said film forming agent is hydroxypropyl methylcellulose, said adhesion enhancing agent is hydroxypropylcellulose and said glidant is polyethylene glycol.

11. The capsule according to any one of claims 1 to 10, wherein the film forming agent is hydroxypropyl methylcellulose in an amount of 40% by weight, the adhesion enhancing agent is hydroxypropylcellulose in an amount of 40% by weight, and the glidant is polyethylene glycol in an amount of 20% by weight, based on the weight of the coating composition.

12. A method of preparing a tamper proofed capsule which comprises coating a solid dosage form core with a coating composition comprising a film forming agent in an amount of from 0 to 85% by weight, an adhesion enhancing agent in an amount of from 10 to 90% by weight, and a glidant in an amount of from 5 to 50% by weight, based on the weight of the coating composition and which further comprises the steps of filling the solid dosage form coated with the coating composition into capsule shell parts and treating the combined capsule shell parts so as to obtain capsules.

13. Use of a coating composition comprising a film forming agent in an amount of from 0 to 85% by weight, an adhesion enhancing agent in an amount of from 10 to 90% by weight, and a glidant in an amount of from 5 to 50% by weight, based on the weight of the coating composition, for applying to a solid dosage form core so as to improve adhesion of said solid dosage form core to at least one capsule shall part filled in with said coated solid dosage form core.