Abstract: Present invention relates to effervescent formulations comprising cefaclor and process for their preparation.
PRESENT INVENTION

Present invention relates to effervescent formulations comprising cefaclor and process for their preparation.

BACKGROUND OF THE INVENTION

Cefaclor is a semi-synthetic, wide spectrum, second generation cephalosporin antibiotic which is shown with Formula (I) and which is disclosed in US3925372 (A) for the first time by Eli Lilly.

![Formula I](image)

Cefaclor, which is physically in white or slightly yellow powder form, dissolve in water slightly but does not dissolve in methanol and methylene chloride. The product sold in the market under the tradename CECLOR® is present in 250 and 500 mg capsule and 125 and 250 mg suspension forms.

Cefaclor is used for treatment of infections caused by gram positive microorganisms; staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus saprophyticus, Staphylococcus pneumonia, Streptococcus pyogenes (group A streptococci), gram negative microorganisms; Haemophilus parainfluenzae, Haemophilus influenzae, Moraxella (Branhamella) catarrhalis, Escherichia coli, Klebsiella pneumonia, respiratory tract infections caused by Proteus mirabilis in such as (pneumonia, bronchitis, acute inflammations of chronic bronchitis, phangitis, tonsilitis), middle-ear infections, sinusitis, skin and soft tissue infections and urinary tract infections (cystitis and pyelonephritis).

Formulations comprising cefaclor are commonly present in the forms of tablet, oral suspension and capsul. The activity of cefaclor increases when cefaclor is used in the dosages of more than 500 mg. To benefit from the active agent with a maximum efficiency, the use of
cefaclor in 500 mg and more than 500 mg of dosages is preferred. In the preferred dosage forms comprising 500 mg and more, large amounts of antibiotic become bigger in size when formulated with the excipients and this makes the use of drug difficult for pediatric and geriatric patients. Alternatively, the use of reliable and user-friendly effervescent forms is suggested.

Generally, the most important matters for the patient in drug usage are the suitability of drug for use, its bioavailability and long shelf life. The use of the drugs formulated in effervescent form is reliable and easy. However, it is inevitable that the drug is exposed to the possible chemical, physical and microbial reactions and/or the active agents interact with the other excipients during the process of converting the effervescent formulations into the final product and their storage. Moreover, chemical degradation arising from possible chemical reactions between active agent and excipients such as oxidation and hydrolsis and/or physical degradation arising from some factors such as pH, temperature, light, carbondioxide and moisture lead to obtaining the drugs which are not suitable for use. During the use or storage of the active agent, these unstable drugs cause the loss or inactivation of the active agent; conversion of it into undesirable forms or failure in complete dispersion in water or failure in homogenous dispersion even though it does disperse; loss of content uniformity and therefore, a decrease in the bioavailability of the medicament.

As is seen, there is a need for development of new effervescent formulations in order to obtain stable drugs that do not degrade easily, have long shelf-life, have high bioavailability and are suitable for use.

Inventors have surprisingly seen that efferescent formulations comprising cefaclor prepared according to present invention solve the problems in the prior art.

**Description of the Invention**

The present invention is related to effervescent formulations comprising cefaclor active agent and process for the preparation of these formulations. Surprisingly, when pharmaceutically acceptable amounts of cefaclor in hydrate form, at least one acid anhydrous and carbonate anhydrous are used, effervescent formulations which, do not undergo chemical or physical degradation, do not have problems by means of content uniformity or active agent loss, can disperse in water homogeneously and have high bioavailability, thus are highly stable are obtained.
Another aspect of the present invention is that the effervescent formulations comprise cefaclor in an amount of more than 500mg, preferably in the range of 500 mg- 1500 mg or its pharmaceutically acceptable derivative in an equivalent amount of that per unit dose.

Accordingly, the first aspect of the present invention is that effervescent formulations comprise pharmaceutically acceptable amounts of cefaclor in hydrate form, at least one acid anhydrous and carbonate anhydrous.

Acid anhydrous which is used as effervescent acid in the effervescent formulation in accordance with the present invention can be selected from anhydrous organic acids such as citric acid anhydrous, tartaric acid anhydrous, malic acid anhydrous, fumaric acid anhydrous, ascorbic acid anhydrous, adipic acid anhydrous and succinic acid anhydrous. Preferably citric acid anhydrous is used.

In the effervescent formulation in accordance with the present invention, a second acidic agent can be used in addition to citric acid anhydrous used as effervescent acid.

Second acidic agent is selected from a group comprising sodium citrate, sodium acetate, dibasic sodium phosphate, tribasic sodium phosphate, monobasic sodium phosphate, sodium acid pyrophosphate and sodium acid sulphite.

In the effervescent formulation in accordance with the present invention, carbonate anhydrous used as effervescent base can be selected from anhydrous basic agents such as sodium carbonate anhydrous, sodium bicarbonate anhydrous, potassium carbonate anhydrous, lysine carbonate anhydrous, arginine carbonate anhydrous and calcium carbonate anhydrous. Preferably sodium bicarbonate anhydrous is used.

Cefaclor that is used in the present invention can be present in one of the forms of monohydrate, dihydrate, trihydrate and/or anhydrous. Preferably, it is used in monohydrate form.

In another aspect, the present invention is related to effervescent formulations comprising cefaclor monohydrate as active agent, citric acid anhydrous and sodium carbonate anhydrous as effervescent couple.

Generally, non-homogeneous solutions are obtained when effervescent formulations can not disperse completely upon releasing into water and/or the active agent in the formulation does
not dissolve completely. This case results in a decrease in the cell absorption of active agent of the formulation and thus decrease in its bioavailability.

As a result of the studies relative to the present invention, the formulations comprising cefaclor: acid anhydrous ratio in the range of 1:10 to 8:10, preferably 2:10 to 7:10 and cefaclor: carbonate anhydrous ratio in the range of 1:10 to 9:10, preferably 1:10 to 8:10 can disperse in water easily and a homogeneous and smooth solution is obtained via the complete dissolution of the active agent present in this formulation.

In this aspect, the present invention is related to effervescent formulations comprising cefaclor: acid anhydrous ratio in the range of 1:10 to 8:10, preferably 2:10 to 7:10 and cefaclor: carbonate anhydrous ratio in the range of 1:10 to 9:10, preferably 1:10 to 8:10.

Another aspect of the present invention is that the effervescent formulation comprises cefaclor in an amount in the range of 1-60%, preferably 5-50% and more preferably 10-45% compared to the total dosage weight.

Another aspect of the present invention is pharmaceutical composition comprising cefaclor as active agent, at least one effervescent acid, at least one effervescent base and also pharmaceutically acceptable excipients.

Pharmaceutical composition formulated in the effervescent form in accordance with the present invention comprises cefaclor as active agent, at least one effervescent acid, at least one effervescent base and additionally one or more of pharmaceutically acceptable agents such as binder, lubricant, sweetener and/or taste regulator, flavoring agent, glidant, diluents, disintegrant, coloring agent, surfactant, anti-foaming agent, humectants, acidic agent and basic agent.

Binder used in the effervescent formulation in accordance with the present invention can be selected from, but not limited with, a group comprising; alginic acid, chitosan, carborner, carboxymethyl cellulose sodium, dextrin, hydroxyethyl cellulose, hydroxymethyl cellulose, hydroxypropyl cellulose ethyl cellulose, gelatine, hypomellose, magnesium aluminium silicate, maltodextrin, polyethylene oxide and povidone or a combination thereof. Preferably povidone is used.
Lubricant used in the effervescent formulation in accordance with the present invention can be selected from, but not limited with, a group comprising PEG 6000 or sodium benzoate. Preferably, PEG 6000 is used.

Sweetener and/or taste regulator that can be used in effervescent formulations of the present invention can be selected from, but not limited with, a group of acesulfame, aspartame, dextrose, fructose, saccharine, sucralose, sucrose, , saccharin sodium, lactitol, maltitol, maltose, sorbitol, sodium cyclamate, sucrose and xylitol or a combination thereof.

Flavoring agent that can be used in effervescent formulations of the present invention can be selected from, but not limited with, natural aroma oils (peppermint oil, oil of wintergreen, oil of cloves, parsley oil, eucalyptus oil, lemon oil, orange oil), menthol, menthane, anethole, methyl salicylate, eucalyptol, cinnamon, 1-methyl acetate, sage, eugenol, oxanon, alpha-isirison, marjoram, lemon, orange, blackberry, propenyl guaethol acetyl, cinnamon, vanilla, thymol, linalol, cinnamaldehyde glycerol acethal, N-quadric p-menthan-3-carboxamide, 3,1-methoxy propane 1,2-diol or a combination thereof.

Glidant that can be used in effervescent formulations of the present invention can be selected from, but not limited with, sodium lauryl sulfate, sodium benzoate, sodium chloride, sodium acetate, sodium acetate, sodium fumarate, carbowax 4000, L-leucine(17), PEG or a combination thereof.

Diluent that can be used in effervescent formulations of the present invention can be selected from, but not limited with, a group comprising calcium carbonate, calcium sulfate, dibasic calcium phosphate, tribasic calcium phosphate, calcium sulfate, microcrystalline cellulose, lactose, magnesium carbonate, magnesium oxide, maltodextrin, maltose, mannitol, sodium chloride, sorbitol, starch and xylitol or combinations thereof.

Disintegrate that can be used in effervescent formulations of the present invention can be selected from, but not limited with, a group comprising carboxymethyl cellulose calcium, carboxymethyl cellulose sodium, microcrystalline cellulose, silicone dioxide, croscarmellose sodium, crospovidone, hydroxypropyl cellulose, methyl cellulose, povidone, magnesium aluminium silicate and starch or a combination thereof.

Coloring agent that can be used in effervescent formulations of the present invention can be selected from, but not limited with, caratenoids and chlorophyl and a combination thereof.
Surfactant that can be used in effervescent formulations of the present invention can be selected from, but not limited with, sodium lauryl sulfate, magnesium lauryl sulfate, sodium sulfate anhydrous or a combination thereof. Preferably, sodium sulfate anhydrous is used.

Anti-foaming agent that can be used in effervescent formulations of the present invention can be selected from, but not limited with, simethicone and dimethyl siloxane, silicone oil or a combination thereof.

Humectant that can be used in effervescent formulations of the present invention can be selected from, but not limited with, anhydrous sodium sulphate, silica gel and potassium carbonate or combinations thereof.

Acidic agent that can be used in effervescent formulations of the present invention can be selected from, but not limited with, a group comprising acetic acid, citric acid, lactic acid, malic acid, phosphoric acid, propionic acid, tartaric acid or combinations thereof.

Basic agent that can be used in effervescent formulations of the present invention can be selected from, but not limited with, a group comprising potassium carbonate, potassium bicarbonate, potassium citrate, potassium hydroxide, sodium carbonate, sodium bicarbonate, or combinations thereof.

"Effervescent couple" term means the use of acidic agent and basic agent together.

"Effervescent formulations" term comprises effervescent tablets, effervescent granules and effervescent powder. Effervescent formulations comprising cefaclor in accordance with the present invention is preferably compressed into tablets.

"Final product" term means that the final state of effervescent tablet, effervescent granule or effervescent powder which is obtained by producing effervescent formulations in a dosage form and ready for use.

In the effervescent pharmaceutical composition according to the present invention, 1-60% of cefaclor, 5-70 % of acid anhydrous, 5-40 % of carbonate anhydrous, 1-20 % of 0 %, surfactant, 0.3-6 % of binder, 2-10 % of %, lubricant, 0.5-7% of sweetener and/or taste regulator, 1-4 % of %, flavoring agent % and 0-3% of coloring agent with respect to the total weight of the unit dosage can be used.
In the effervescent cefaclor formulation in accordance with the present invention, optionally a second active agent can be used. The second active agent can be selected from beta lactamase and cephalosporins, preferably clavulanic acid or combinations thereof.

Clavulanic acid used in the effervescent cefaclor formulation in accordance with the present invention, can be present in the form of its solvates, hydrates, enantiomers, racemates, organic salts, inorganic salts, polymorphs, crystal and amorphous forms or in free form and/or as a combination of these. Preferably, potassium clavulanate is used.

Clavulanic acid and/or derivatives thereof (for example potassium clavulanate) is very sensitive to moisture. Therefore, in the pharmaceutical composition according to the present invention, potassium clavulanate is preferably used together with a humidity absorbing agent in a ratio of 1:1.

One or more than one of the following substances can be used as a humidity absorbing agent; silica; colloid silica, for instance colloidal silica anhydrous, magnesium trisilicate, powdered cellulose, magnesium oxide, calcium silicate, Syloid®, starch, microcrystalline cellulose and talc.

In the effervescent cefaclor formulation in accordance with the present invention, potassium clavulanate is preferably used with syloid or microcrystalline cellulose in an amount in the ratio of 1:1.

In the effervescent formulation comprising cefaclor in accordance with the present invention, with respect to the total weight of the unit dosage; 5-80%, preferably 10-70% of clavulanic acid or pharmaceutically acceptable salts, hydrates, solvates or a combination thereof in an amount equivalent to that can be used.

A process for the preparation of effervescent formulations comprising cefaclor in accordance with the present invention comprises the steps of:

1. Obtaining a granulation solution by mixing at least one binder, at least one lubricant and deionized water

2. Sieving effervescent acid, effervescent base and surfactant and granulating them with the granulation solution
3. Adding cefaclor, sweetener and flavoring agent after drying and sieving the granules obtained in the second step. The obtained effervescent formulation is optionally compressed into tablets in the tablet pressing machine.

In cases where effervescent formulations comprising cefaclor comprise a second active agent, for example potassium clavulanate, the process used for the preparation of said formulation comprises the steps of:

1. Blending effervescent acid, effervescent base, sweetener and binder and granulating the mixture with water and then drying and sieving the obtained granules,

2. Adding lubricant, potassium clavulanate:humidity absorbing agent (1:1) mixture, cefaclor, coloring agent and flavoring agent into the obtained granules and blending them. The obtained effervescent formulation is optionally compressed into tablets in the tablet pressing machine.

Another aspect of the present invention is that the pharmaceutical composition prepared according to the invention is used for the treatment of the diseases relatd to the upper respiratory tract infections such as pharangitis, tonsillitis, otitis media; lower respiratory tract infections such as acute pneumonia, acute and chronic broncihia and urinary tract infections such as acute cystitis and cystourethritis.

Though not limited with these examples, effervescent formulations according to present invention can be prepared according to the examples given below.

**Example 1: Formulation and process for preparation of effervescent tablet formulation**

A granulation solution comprising binder, lubricant and deionized water is prepared. Effervescent acid, base and surfactant are granulated with the granulation solution by adding them into fluidized bed dryer. Cefaclor, sweetener and flavoring agent are added into the obtained mixture and this mixture is dried. Finally, the dried mixture is compressed into tablets.
<table>
<thead>
<tr>
<th>Component name</th>
<th>% amount in unit dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefaclor</td>
<td>15 %</td>
</tr>
<tr>
<td>Effervescent acid</td>
<td>35 %</td>
</tr>
<tr>
<td>Effervescent base</td>
<td>25.5 %</td>
</tr>
<tr>
<td>Surfactant</td>
<td>18 %</td>
</tr>
<tr>
<td>Binder</td>
<td>0.5 %</td>
</tr>
<tr>
<td>Sweetener</td>
<td>0.75 %</td>
</tr>
<tr>
<td>Lubricant</td>
<td>2.5 %</td>
</tr>
<tr>
<td>Flavoring Agent</td>
<td>2.75 %</td>
</tr>
</tbody>
</table>

**Example 2: Formulation and process for preparation of effervescent tablet**

The mixture comprising effervescent acid, effervescent base, sweetener and binder is granulated with water in the fluidized bed dryer. The obtained granules are dried and sieved. Lubricant, potassium clavulanate: humidity absorbing agent (1:1) mixture, cefaclor, coloring agent and flavoring agent are added into the obtained granules and blended. The obtained final mixture is compressed into tablets.
<table>
<thead>
<tr>
<th>Component name</th>
<th>% amount in unit dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefaclor</td>
<td>13 %</td>
</tr>
<tr>
<td>potassium clavulanate:humidity</td>
<td>8 %</td>
</tr>
<tr>
<td>absorbing agent (1:1) mixture</td>
<td></td>
</tr>
<tr>
<td>Effervescent acid</td>
<td>36 %</td>
</tr>
<tr>
<td>Effervescent base</td>
<td>34 %</td>
</tr>
<tr>
<td>Coloring agent</td>
<td>2.5 %</td>
</tr>
<tr>
<td>Binder</td>
<td>2 %</td>
</tr>
<tr>
<td>Sweetener</td>
<td>2 %</td>
</tr>
<tr>
<td>Lubricant</td>
<td>1 %</td>
</tr>
<tr>
<td>Flavoring Agent</td>
<td>1.5 %</td>
</tr>
</tbody>
</table>
CLAIMS

1. A pharmaceutical composition formulated in effervescent form characterized in that said composition comprises pharmaceutically acceptable amounts of cefaclor in hydrate form, at least one acid anhydrous and carbonate anhydrous.

2. A pharmaceutical composition according to claim 1, wherein cefaclor in an amount of more than 500 mg or its pharmaceutically acceptable derivative in an amount equivalent to that is present in unit dose.

3. A pharmaceutical composition according to claim 2, wherein cefaclor is in the range of 500 mg to 1500 mg or a pharmaceutically acceptable derivative thereof in an amount equivalent to that is present in unit dose.

4. A pharmaceutical composition according to claim 1, wherein acid anhydrous which is used as effervescent acid is selected from anhydrous organic acids such as citric acid anhydrous, tartaric acid anhydrous, malic acid anhydrous, fumaric acid anhydrous, ascorbic acid anhydrous, adipic acid anhydrous and succinic acid anhydrous.

5. A pharmaceutical composition according to claim 4, wherein citric acid anhydrous is used as acid anhydrous.

6. A pharmaceutical composition according to claim 1, wherein carbonate anhydrous used as effervescent base is selected from anhydrous basic agents such as sodium carbonate anhydrous, sodium bicarbonate anhydrous, potassium carbonate anhydrous, lysine carbonate anhydrous, arginine carbonate anhydrous and calcium carbonate anhydrous.

7. A pharmaceutical composition according to claim 6, wherein sodium bicarbonate anhydrous is used as carbonate anhydrous.

8. A pharmaceutical composition according to claim 1, wherein cefaclor that is used as active agent is present in one of the forms of monohydrate, dihydrate, trihydrate and/or anhydrous.

9. A pharmaceutical composition according to claim 8, wherein cefaclor that is used as active agent is in monohydrate form.
10. A pharmaceutical composition according to claim 1, wherein said composition comprises pharmaceutically acceptable amounts of cefaclor monohydrate and additionally citric acid anhydrous and sodium carbonate anhydrous.

11. A pharmaceutical composition according to claim 1, wherein said composition is in the form of effervescent powder, granule or tablet.

12. A pharmaceutical composition according to claim 11, wherein said composition is in the form of effervescent tablet.

13. A pharmaceutical composition according to claim 1, wherein said composition comprises 1-60%, preferably 5-50%, more preferably 10-45% of cefaclor with respect to the total weight of the unit dosage.

14. A pharmaceutical composition according to claim 1, wherein said composition further comprises at least one pharmaceutically acceptable excipient in addition to cefaclor in hydrate form, at least one effervescent acid and effervescent base.

15. A pharmaceutical composition according to claim 14, wherein said composition comprises cefaclor as active agent, at least one effervescent acid, at least one effervescent base and additionally binder, lubricant, sweetener and/or taste regulator, flavoring agent, glidant, diluents, disintegrant, coloring agent, surfactant, anti-foaming agent, humectants, acidic agent and basic agent.

16. A pharmaceutical composition according to claim 15, wherein binder is selected from a group comprising: alginic acid, chitosan, carboromer, carboxymethyl cellulose sodium, dextrin, hydroxyethyl cellulose, hydroxymethyl cellulose, hydroxypropyl cellulose ethyl cellulose, gelatine, hypromellose, magnesium aluminium silicate, maltodextrin, polyethylene oxide and povidone or a combination thereof.

17. A pharmaceutical composition according to claim 16, wherein povidone is used as binder.

18. A pharmaceutical composition according to claim 15, wherein lubricant is selected from a group comprising PEG 6000 and sodium benzoate.

19. A pharmaceutical composition according to claim 18, wherein PEG 6000 is used as lubricant.
20. A pharmaceutical composition according to claim 15, wherein surfactant is selected from sodium lauryl sulfate, magnesium lauryl sulfate and sodium sulfate anhydrous or a combination thereof.

21. A pharmaceutical composition according to claim 15, wherein diluent is selected from a group comprising calcium carbonate, calcium sulfate, dibasic calcium phosphate, tribasic calcium phosphate, calcium sulfate, microcrystalline cellulose, lactose, magnesium carbonate, magnesium oxide, maltodextrin, maltose, mannitol, sodium chloride, sorbitol, starch and xylitol or combinations thereof.

22. A pharmaceutical composition according to claim 15, wherein disintegrant is selected from a group comprising carboxymethyl cellulose calcium, carboxymethyl cellulose sodium, microcrystalline cellulose, silicone dioxide, croscarmellose sodium, crospovidone, hydroxypropyl cellulose, methyl cellulose, povidone, magnesium aluminium silicate and starch or a combination thereof.

23. A pharmaceutical composition according to claim 15, wherein flavoring agent is selected from natural aroma oils (peppermint oil, oil of wintergreen, oil of cloves, parsley oil, eucalyptus oil, lemon oil, orange oil), menthol, menthane, anethole, methyl salicylate, eucalyptole, cinnamon, 1-methyl acetate, sage, eugenol, oxanon, alpha-irison, marjoram, lemon, orange, blackberry, propenyl guaethol acetyl, cinnamon, vanilla, thymol, linalol, cinnamaldehyde glycerol acetal, N-quadric p-menthan-3-carboxamide, 3,1-methoxy propane 1,2-diol or a combination thereof.

24. A pharmaceutical composition according to claim 15, wherein sweetener and/or taste regulator is selected from a group of acesulfame, aspartame, dextrose, fructose, sucralose, saccharin, saccharin sodium, lactitol, maltitol, maltose, sorbitol, sodium cyclamate, sucrose and xylitol or a combination thereof.

25. A pharmaceutical composition described in any of the preceding claims, wherein 1-60% of cefaclor, 5-70% of effervescent acid, 5-40% of effervescent base, 1-20% of surfactant, 0.3-6% of binder, 2-10% of lubricant, 0.5-7% of sweetener and/or taste regulator, 1-4% of flavoring agent and 0-3% of coloring agent are used in said composition.

26. A pharmaceutical composition according to claim 1, wherein a second acidic agent as effervescent acid is used in addition to acid anhydrous.
27. A pharmaceutical composition according to claim 26, wherein second acidic agent is selected from a group comprising sodium citrate, sodium acetate, dibasic sodium phosphate, tribasic sodium phosphate, monobasic sodium phosphate, sodium acid pyrophosphate and sodium acid sulphite.

28. A pharmaceutical composition according to claim 1, wherein in said composition cefaclor: acid anhydrous ratio is in the range of 1:10 to 8:10 and cefaclor: carbonate anhydrous ratio is in the range of 1:10 to 9:10.

29. A pharmaceutical composition according to claim 28, wherein in said composition cefaclor: acid anhydrous ratio is in the range of 2:10 to 7:10 and cefaclor: carbonate anhydrous ratio is in the range of 4:10 to 8:10.

30. A pharmaceutical composition described in any of the previous claims, wherein said composition may further comprise a second active agent, which is selected from beta lactamase and cephalasporins.

31. A pharmaceutical composition according to claim 30, wherein clavulanic acid or a pharmaceutically acceptable derivative thereof is used as a second active agent.

32. A pharmaceutical composition according to claim 31, wherein potassium clavulanate is used as second active agent.

33. A pharmaceutical composition according to claim 32, wherein potassium clavulanate is used with a humidity absorbing agent in a ratio of 1:1.

34. A pharmaceutical formulation according to claim 33, wherein humidity absorbing agent is selected from silica, colloid silica, magnesium trisilicate, powdered cellulose, magnesium oxide, calcium silicate, starch, microcrystalline cellulose and/or talc.

35. A process for the preparation of the pharmaceutical composition according to claims 1-29, wherein said process comprises the steps of obtaining the granulation solution by mixing at least one binder, at least one lubricant and deionized water; sieving effervescent acid, effervescent base and surfactant and granulating them with the granulation solution; adding cefaclor, sweetener and flavoring agent after drying and sieving the granules obtained in the second step.
36. A process for the preparation of the pharmaceutical composition according to claim 30, wherein said process comprises the steps of blending effervescent acid, effervescent base, sweetener and binder, granulating the mixture with water, drying and sieving the obtained granules, adding lubricant, potassium clavulanate:humidity absorbing agent (1:1) mixture, cefaclor, coloring agent and flavoring agent into the obtained granules and blending them.

37. A process for the preparation of the pharmaceutical composition according to claim 1, wherein said formulation is used for the treatment of the diseases relative to the upper respiratory tract infections such as pharyngitis, tonsillitis, otitis media; lower respiratory tract infections such as acute pneumonia, acute and chronic bronchiha and urinary tract infections such as acute cystitis and cystourethritis.