The present invention provides extended release pharmaceutical compositions structured for once a day administration comprising skeletal muscle relaxant such as cyclobenzaprine or its pharmaceutically acceptable salt thereof that extends the release of the drug under in-vitro conditions for at least 8 to 12 hours. The invention also provides process for the preparation of such structured compositions.
Extended Release Compositions of Cyclobenzaprine

FIELD OF THE INVENTION
This invention relates to extended release pharmaceutical compositions comprising skeletal muscle relaxant such as cyclobenzaprine or its pharmaceutically acceptable salt thereof and a process for preparation thereof.

BACKGROUND OF THE INVENTION
Cyclobenzaprine Hydrochloride, a skeletal muscle relaxant is currently available as immediate release tablets containing 5mg or 10mg of the active and also as extended release capsules containing 15mg or 30mg of the active. Immediate release tablets are recommended to be administered three times a day to achieve relief from muscle spasm. Administration of such tablets three times a day is a major compliance issue especially in elderly patients. To substantially enhance patient compliance, it is desirable to provide cyclobenzaprine hydrochloride in extended release dosage form for once a day administration.


• an active-containing core particle comprising a skeletal muscle relaxant selected from the group consisting of cyclobenzaprine, pharmaceutically acceptable salts or derivatives thereof and mixtures thereof; and
• an extended release coating comprising a water insoluble polymer membrane surrounding the said core, wherein the membrane comprises a water insoluble polymer and a plasticizer.

The dosage form exhibits the following in-vitro dissolution profile in USP apparatus 2 (paddles @ 50 rpm) in 900 ml of 0.1N HCl at 37°C:

• not more than 40% of the total active is released at 2 hour;
• from about 40-65% of the total active is released at 4 hour;
• from about 60-85% of the total active is released at 8 hour.
OBJECTS OF THE INVENTION

The object of the invention is to provide extended release pharmaceutical compositions structured for once a day administration comprising skeletal muscle relaxant such as cyclobenzaprine or its pharmaceutically acceptable salt thereof that exhibits in-vitro drug release profile for at least 8 to 12 hours.

It is another object of the invention to provide the said structured compositions comprising cyclobenzaprine or its pharmaceutically acceptable salt thereof, wherein the composition comprises of a core, a layer comprising of one or more extended release agents, and the said drug either in the extended release layer or in between the core and the extended release layer or in the core.

It is yet another object of the invention to provide the above compositions in the form of pellets capable of being filled in capsules.

It is yet another object of the invention to provide extended release compositions which would substantially minimize the incidence of dose dumping.

It is yet another object of the invention to provide process for the preparation of extended release pharmaceutical compositions comprising cyclobenzaprine or its pharmaceutically acceptable salts thereof that exhibits in-vitro drug release profile for at least 8 to 12 hours.

DESCRIPTION OF THE INVENTION

Description of figures:

Figures 1(a), 1(b), and 1(c) illustrate the manner in which the compositions of the present invention can be structured.

The present invention provides extended release pharmaceutical compositions structured for once a day administration comprising skeletal muscle relaxant such as cyclobenzaprine or it’s pharmaceutically acceptable salt thereof that extends the release of the drug under in-vitro conditions for at least 8 to 12 hours.

Such structured compositions comprising skeletal muscle relaxant such as cyclobenzaprine or its pharmaceutically acceptable salt thereof comprises of
a) a core;
b) a layer comprising of one or more extended release agents; and
c) the said cyclobenzaprine or its pharmaceutically acceptable salt thereof is either
   (i) in the extended release layer, or (ii) in between the core and the extended
   release layer, or (iii) in the core.

Structuring the Composition:
In a preferred embodiment of the invention, the extended release pharmaceutical
compositions comprise of:
   a) inert core;
   b) said inert core being coated with a matrix comprising cyclobenzaprine or its
      pharmaceutically acceptable salt thereof such as cyclobenzaprine HCl and one or
      more extended release agents.

In another preferred embodiment of the invention, the extended release pharmaceutical
compositions comprise of:
   a) inert core;
   b) said inert core being coated with a matrix comprising cyclobenzaprine or its
      pharmaceutically acceptable salt thereof such as cyclobenzaprine HCl and one or
      more extended release agents and one or more plasticizer.

As shown in figure 1(a), the composition is structured to form a matrix that comprises of
an inert core (i), the inert core being coated with a layer (ii) comprising of
cyclobenzaprine or its pharmaceutically acceptable salt thereof such as cyclobenzaprine
hydrochloride and one or more extended release agents.

The process for the preparation of composition to obtain the structure as shown in figure
1(a) comprises steps of:
i. providing an inert core;
ii. applying a layer comprising of cyclobenzaprine or its pharmaceutically acceptable salt
   thereof such as cyclobenzaprine hydrochloride, one or more extended release agents
   and optionally at least one additive selected from binder, anti-tack agent, plasticizer,
   diluent, or mixtures thereof on the inert core to obtain extended release pellets.
Creation of the said layer on the inert core comprises steps of

i) dispersing and/or dissolving cyclobenzaprine or its pharmaceutically acceptable salt thereof such as cyclobenzaprine hydrochloride in a solvent selected from water, alcohol, organic solvent, or mixtures thereof to obtain drug dispersion or solution

ii) dispersing and/or dissolving one or more extended release agents in a solvent selected from water, alcohol, organic solvent, or mixtures thereof to obtain dispersion or solution,

iii) mixing dispersion or solution of step (ii) with drug dispersion or solution of step (i)

iv) optionally adding at least one additive selected from binder anti-tack agent, plasticizer, diluent, or mixtures thereof to dispersion or solution of step (ii)

v) spraying the resulting dispersion or solution on inert cores to obtain extended release pellets,

vi) drying and sizing the extended release pellets

In one of the embodiments of the invention, the extended release pharmaceutical compositions comprises of

a) inert core,

b) first layer comprising of cyclobenzaprine or its pharmaceutically acceptable salt thereof such as cyclobenzaprine HCl on the inert core, and

c) second layer comprising of one or more extended release agents on the first layer, wherein the said second layer does not contain plasticizer

As shown in figure 1(b), the compositions are structured to provide an inert core (i), first layer (ii) comprising of cyclobenzaprine or its pharmaceutically acceptable salt thereof such as cyclobenzaprine hydrochloride on the inert core and second layer (iii) comprising one or more extended release agents on the first layer, wherein the said second layer does not contain plasticizer

The process for the preparation of composition to obtain the structure as shown in figure 1(b) comprises steps of

a) providing an inert core,

b) creating a first layer comprising of cyclobenzaprine or its pharmaceutically acceptable salt thereof such as cyclobenzaprine hydrochloride on the inert core to obtain drug core, and
c) creating a second layer comprising of one or more extended release agents on the first layer to obtain extended release pellets, wherein the second layer does not contain plasticizer.

Creation of the said first layer on the inert core comprises steps of
i) dispersing and or dissolving cyclobenzaprine or its pharmaceutically acceptable salt thereof such as cyclobenzaprine hydrochloride in a solvent selected from water, alcohol, organic solvent, or mixtures thereof to obtain drug dispersion or solution,
H) optionally dispersing and or dissolving at least one additive selected from binder diluent, plasticizer, anti-tack agent, or mixtures thereof in a solvent selected from water, alcohol, organic solvent, or mixtures thereof,
in) mixing dispersion or solution of step (i) with drug dispersion or solution of step (v),
iv) spraying the resulting dispersion or solution of step (in) on inert cores to obtain drug cores,
v) drying and sizing the drug cores.

Creation of the second layer (extended release layer) on the drug core comprises steps of
i) dispersing and or dissolving one or more extended release agents in a solvent selected from water, alcohol, organic solvent, or mixtures thereof to obtain dispersion or solution,
ii) optionally adding at least one additive selected from anti-tack agent diluents or mixtures thereof,
in) spraying the resulting dispersion or solution on drug pellets to obtain extended release pellets,
iv) drying and sizing the extended release pellets.

In another embodiment of the invention, the extended release pharmaceutical compositions comprises of
a) a core comprising of cyclobenzaprine or its pharmaceutically acceptable salt thereof such as cyclobenzaprine HCl,
b) a layer comprising of or more extended release agents coated on the core wherein the said layer does not contain plasticizer.
As shown in figure 1(c), the compositions are structured to form a core (ι) comprising of cyclobenzaprine or its pharmaceutically acceptable salt thereof such as cyclobenzaprine hydrochloride, the core being coated with a layer (i,) comprising of one or more extended release agents, wherein the said coating layer does not contain plasticizer.

The process for the preparation of the compositions as shown in figure 1 (c) comprises steps of

1. providing a matrix core comprising of cyclobenzaprine or its pharmaceutically acceptable salt thereof such as cyclobenzaprine hydrochloride and at least one additive selected from binder, anti-tack agent, plasticizers, diluents or mixtures thereof,
2. creating a layer comprising of one or more extended release agents on the matrix core to obtain extended release pellets, the layer optionally comprises of at least one additive selected from anti-tack agent, diluents, or mixtures thereof, wherein the said layer does not contain plasticizer.

Preparation of the said matrix core comprises steps of

1. mixing cyclobenzaprine or its pharmaceutically acceptable salt thereof such as cyclobenzaprine hydrochloride with at least one additive selected from binder anti-tack agent, plasticizers, diluents, or mixtures thereof in a mixer to obtain drug mixture
2. granulating drug mixture with a granulating solvent selected from water, alcohol, organic solvent, or mixtures thereof to obtain the granules,
3. extruding the granules in an extruder to obtain the extrudates,
4. spheronizing the extrudates in the spheronizer to obtain the matrix core,
5. drying and sizing the matrix core

Creation of the said extended release layer on the said matrix core comprises steps of

1. dispersing and or dissolving one or more extended release agents in a solvent selected from water, alcohol, organic solvent, or mixtures thereof to obtain dispersion or solution,
2. optionally adding at least one additive selected from anti-tack agent diluents or mixtures thereof,
3. spraying the resulting dispersion or solution on the matrix cores to obtain extended release pellets,
4. drying and sizing the extended release pellets.
Cyclobenzaprine salt is the addition salt of cyclobenzaprine with an inorganic acid such as hydrochloric, hydrobromic, phosphoric, nitric or sulphuric or of organic acid such as tartaric, acetic, propionic, hydroxyacetic, oxaloacetic, oxalic, pyruvic succinic malic malonic, fumaric, lactic, glutaric, maleic, sulphonic, benzenesulphonic, and the like. The preferred cyclobenzaprine salt is cyclobenzaprine HCl and is usually administered in the dose of 15mg and 30mg strength.

There is no limitation on the particle sizes of cyclobenzaprine HCl used in the invention. However, the particle size of cyclobenzaprine HCl ranges from 0.1 microns to 1000 microns, preferably from 0.5 micron to 500 microns, more preferably from 1 micron to 200 microns and most preferably from 2 microns to 100 microns.

Cyclobenzaprine HCl in the composition is from 0.01% to 50% by weight, preferably from 0.05% to 40%, more preferably from 0.1% to 25%, and most preferably from 2.5% to 15% by weight of the composition.

Extended release agent is selected from the group of cellulose ethers, cellulose esters, polymethacrylates, wax, fatty acid, fatty alcohol, polyalkylene glycol, or mixtures thereof. However, any other suitable agent(s) that extends the release of cyclobenzaprine HCl from the dosage form may also be used.

Representative examples of such agent includes ethylcellulose powder aqueous dispersion of ethylcellulose (such as SURELEASE RTM, AQUACOAT RTM ECD 30), hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose, carboxymethylcellulose, sodium carboxymethylcellulose, calcium carboxymethylcellulose, methylcellulose, cellulose acetate phthalate, hydroxypropylmethylcellulose phthalate, hydroxypropylmethylcellulose acetate succinate, cellulose acetate butyrate, cellulose acetate trimellitate, cellulose acetate polyvinyl alcohol, polyvinyl acetate (such as KOLLICOAT SR 30D), povidone, polyethylene glycol, cetyl alcohol, stearyl alcohol, beeswax, carnauba wax, stearic acid, vinyl pyrrohydrovinyl acetate copolymer (such as KOLLIDON VA 64 KOLLIDON SR), dimethylaminoethyl methacrylate and other neutral methacrylic acid esters (such as Eudragit E), methacrylic acid copolymers type A (such as Eudragit L), methacrylic acid copolymers type B (such as Eudragit S), methacrylic acid copolymers type C (such as Eudragit L 30D 55), ammoniomethacrylate copolymers (such as Eudragit RL, Eudragit...
RS), neutral copolymer of polymethacrylic acid ester (Such as Eudragit NE 30D), or mixtures thereof.

Mixtures of extended release agents are generally used in the ratio of 1 0 0 5 to 0 0 5 1 preferably in the ratio of 1 0 1 5 to 0 1 5 1 more preferably in the ratio of 1 0 3 to 0 3 1 and most preferably in the ratio of 1 0 5 to 0 5 1

These extended release agents, in general, are available in various viscosity grades. For example hydroxypropylmethylcellulose is available in viscosity grade of 5cps, 6cps, 15cps, 100cps, 4000cps, 15000cps and 100000 cps. Similarly, ethyl cellulose powder is available in viscosity grade of 3cps, 5cps, 7cps, 10cps, 20cps, 45cps, 50cps and 100cps. Such agents may be used alone or in mixture i.e. mixture of two or more different viscosity grade. For example, extended release layer may comprise of mixture of ethyl cellulose (10cps) and ethyl cellulose (45cps). Such mixtures are generally used in the ratio of 1 0 0 5 to 0 0 5 1, preferably in the ratio of 1 0 1 5 to 0 1 5 1, more preferably in the ratio of 1 0 3 to 0 3 1, and most preferably in the ratio of 1 0 5 to 0 5 1

The extended release agent in the composition is from 0 5% to 90% by weight preferably from 1% to 75%, more preferably from 2 5% to 60%, most preferably from 5% to 50% by weight of the composition.

Plasticizer is selected from the group of triacetin, triethyl citrate, tributyl citrate, polyethylene glycol, acetylttributylictrate, miglyol, hydrogenated oils, propylene glycol acetyltributylictrate, polysorbate, castor oil, oleic acid, dibutylsebacate, diethylphthalate, acetylated mono- and di-glycerides, or mixtures thereof.

Plasticizer in the composition is from 0 1% to 30% by weight, preferably from 0 5% to 20%, more preferably from 1% to 10%, and most preferably from 1 5% to 5% by weight of the composition.

The inert core used in the composition is non-pareil seeds or sugar sphere or any other suitable inert material. Examples of such material include sugar, starch, cellulose microcrystalline cellulose, resin, glass beads, or mixtures thereof. The average particle size of inert core in the present invention is from about 150 microns to about 2000 microns, preferably from about 250 microns to about 1000 microns, more preferably from
about 350 microns to about 850 microns, and most preferably from about 500 microns to about 600 microns.

Inert core in the composition is from 15% to 80% by weight, preferably from 25% to 75%, more preferably from 30% to 60%, and most preferably from 40% to 50% by weight of the composition.

Diluent is selected from microcrystalline cellulose, starch, pregeiatinized starch, starch 1500, cellulose, sucrose, lactose, glucose, dextrose, mannitol, sugar, cross linked povidone, sodium starch glycolate, croscarmellose sodium, croscarmellose potassium croscarmellose calcium, monobasic sodium phosphate, dibasic sodium phosphate, tribasic sodium phosphate, calcium phosphate, dibasic calcium phosphate, tribasic calcium phosphate, calcium sulfate, calcium carbonate, or mixtures thereof.

Diluent in the composition is from 5% to 95% by weight, preferably from 20% to 90%, more preferably from 35% to 80%, most preferably from 50% to 70% by weight of the composition.

Binder is selected from xanthan gum, guar gum, acacia, tragacanth, gelatin, carrageenan, polyvinylpyrrolidone, carbomer, locust bean gum, karaya gum, copovidone, agar, hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxyethylcellulose, polyethylene oxide, sodium carboxymethylcellulose, chitosan, sodium alginate, or mixtures thereof.

Binder in the composition is from 0.1% to 30% by weight, preferably from 0.5% to 20%, more preferably from 1% to 10%, and most preferably from 1.5% to 5% by weight of the composition.

Anti-tack agent is selected from talc, colloidal silicon dioxide, glyceryl monostearate, sodium benzoate, sodium lauryl sulfate, waxes, glyceryl behenate, stearic acid, magnesium stearate, calcium stearate, sodium stearyl fumarate, or mixtures thereof.

Anti-tack agent in the composition is from 0.1% to 30% by weight, preferably from 0.5% to 20%, more preferably from 1% to 10%, and most preferably from 1.5% to 5% by weight of the composition.
The solvent is selected from water, alcohol, organic solvent, or mixtures thereof. Examples of such solvent include methanol, ethanol isopropanol, dichloromethane acetone, halogenated hydrocarbon, ethylmethylketone, or mixtures thereof.

The pharmaceutical composition of the present invention comprises of Cyclobenzaprine or its pharmaceutically acceptable salt thereof such as Cyclobenzaprine HCl and one or more agents for extended release that exhibits in-vitro drug release for at least 8 to 12 hours.

Extended release compositions comprising Cyclobenzaprine hydrochloride when analyzed in-vitro in USP apparatus 2, in 0.1N HCl exhibits in-vitro dissolution profile of:

- at least 5% of cyclobenzaprine HCl at 1st hour,
- at least 30% of cyclobenzaprine HCl at 4th hour,
- at least 50% of cyclobenzaprine HCl at 8th hour,
- at least 60% of cyclobenzaprine HCl at 16th hour.

Preferably, extended release compositions comprising Cyclobenzaprine hydrochloride when analyzed in-vitro in USP apparatus 2, in 0.1N HCl exhibits in-vitro dissolution profile of:

- from 5% to 50% of cyclobenzaprine HCl at 1st hour,
- from 30% to 80% of cyclobenzaprine HCl at 4th hour,
- from 50% to 100% of cyclobenzaprine HCl at 8th hour,
- at least 75% of cyclobenzaprine HCl at 16th hour.

Extended release pellets comprising cyclobenzaprine HCl complying with the desired dissolution profile are filled in empty hard gelatin capsule to delivery therapeutic effective amount of cyclobenzaprine HCl.

The invention further provides non-limiting examples.

**Example 1: Preparation of Extended Release Pellets**

a) Cyclobenzaprine HCl (30 g) was dissolved in purified water (100 g) to obtain drug solution,
b) Eudragit L 100 (75 g) was dissolved in the mixture of acetone (300 g) and water (30 g),
c) Eudragit RSPO (75 g) was dissolved in acetone (160 g),
d) The solutions obtained in step a, step (b), and step (c) were mixed and the resulting solution was sprayed on inert core (20 - 25 mesh ASTM) (150 g) in fluid bed bottom spray processor with inlet air temperature of about 20°C to about 80°C, outlet air temperature of about 20°C to about 60°C, atomization air pressure of about 0.5 - 3.5 bars, fluidization flap open from about 10% to about 90% w/w to obtain extended release pellets;
e) Extended release pellets were dried in fluid bed bottom spray processor to arrive at the moisture content of less than 5%w/w, preferably less than 3%w/w, and more preferably less than 2%w/w;
f) The dried pellets were sized, optionally lubricated with purified talc and were filled in empty hard gelatin capsule.

**Example 2: Preparation of Extended Release Pellets**

a) Cyclobenzaprine HCl (30 g) was dissolved in purified water to obtain drug solution,
b) Polyethylene glycol 6000 (8 g) was added to the drug solution of step a) and stirred to obtain clear solution;
c) Ethyl cellulose (45 cps) (67.5 g) was dispersed in water to obtain dispersion,
d) Isopropanol was added to dispersion of step (c) and stirred to obtain clear solution

e) Kollidon SR (15 g) was added to the solution of step (d) and stirred to obtain clear solution;
f) The solution obtained in step (b) was mixed with the solution obtained in step (e) and the resulting solution was sprayed on sugar sphere (30 - 35 mesh ASTM) (80 g) in fluid bed bottom spray processor with inlet air temperature of about 20°C to about 80°C, outlet air temperature of about 20°C to about 60°C, atomization air pressure of about 0.5 - 3.5 bars, fluidization flap open from about 10% to about 90% w/w to obtain extended release pellets;
g) Extended release pellets were dried in fluid bed bottom spray processor to arrive at the moisture content of less than 5%w/w, preferably less than 3%w/w, and more preferably less than 2%w/w;
h) The dried pellets were sized, lubricated with purified talc (1.5 g) and were filled in empty hard gelatin capsule.
Example 3: Preparation of Extended Release Pellets

a) Cyclobenzaprine HCl (30 g) was dissolved in purified water to obtain drug solution;
b) Ethyl cellulose (10 cps) (67.5 g) and ethyl cellulose (45 cps) (15 g) were added to the
drug solution of step (a) to obtain dispersion;
c) Isopropanol was added to the dispersion of step (b) and stirred to obtain clear
solution;
d) Diethyl phthalate (4 g) was added to the solution of step (c) and the resulting solution
was sprayed on inert core (40 - 60 mesh ASTM) (123.5 g) in fluid bed bottom spray
processor with inlet air temperature of about 20°C to about 80°C, outlet air
temperature of about 20°C to about 60°C, atomization air pressure of about 0.5 - 3.5
bars, fluidization flap open from about 10% to about 90% w/w to obtain extended
release pellets;
e) Extended release pellets were dried in fluid bed bottom spray processor to arrive at
the moisture content of less than 5%w/w, preferably less than 3%w/w, and more
preferably less than 2%w/w;
f) The dried pellets were sized, lubricated with purified talc and were filled in empty hard
gelatin capsule.

Example 4: Preparation of Matrix Cores

a) Cyclobenzaprine HCl (30mg/unit), microcrystalline cellulose pH 101(100mg/unit) 
glyceryl monostearate (50mg/unit) and Kollidon SR (50mg) were mixed to obtain
drug mixture;
b) Drug mixture was granulated with the solution of sodium carboxymethylcellulose
7MF (2 mg) in water to obtain granules.
c) The granules were extruded and spheronized to obtain matrix core.
d) The matrix cores were dried and sized.

Example 5: Preparation of Drug Cores

a) Cyclobenzaprine hydrochloride (30mg/unit) was dissolved in the mixture of water
and isopropanol.
b) Colloidal silicon dioxide (6.02mg/unit) and iron oxide yellow (0.19 mg/unit) were
added to the above solution to obtain dispersion;
c) The dispersion was sprayed on inert cores (116.27 mg/unit) (18 - 20 mesh ASTM)
in fluid bed bottom spray processor with inlet air temperature of about 20°C to
The dispersion was sprayed on inert cores (16.27 mg/unit) (18 - 20 mesh ASTM) in fluid bed bottom spray processor with inlet air temperature of about 20°C to about 80°C, outlet air temperature of about 20°C to about 60°C, atomization air pressure of about 0.5 - 3.5 bars, fluidization flap open from about 10% to about 90% w/w to obtain drug cores.

d) The resulting drug cores were dried and sized.

Example 6: Preparation of Extended Release Pellets
The matrix cores of example 4 or the drug cores of example 5 were coated with extended release layer comprising ethyl cellulose 10cps (4.7% by weight of the composition) to obtain extended release pellets. These extended release pellets were dried sized lubricated and filled in capsule.

Extended release compositions comprising cyclobenzaprine hydrochloride (examples 1 to 6) when analyzed in-vitro in USP apparatus 2, in 0.1 N HCl (900ml) exhibits in-vitro dissolution profile of:

- from 10% to 38% of cyclobenzaprine HCl at 1st hour;
- from 33% to 68% of cyclobenzaprine HCl at 4th hour;
- from 68% to 81% of cyclobenzaprine HCl at 8th hour;
- from 79 to 88% of cyclobenzaprine HCl at 16th hour.
We claim:

1. A extended release pharmaceutical compositions comprising cyclobenzaprine or its pharmaceutically acceptable salts thereof, wherein the composition comprises of:
   a) a core;
   b) a layer comprising of one or more extended release agents; and
   c) the said cyclobenzaprine or its pharmaceutically acceptable salts thereof is either
      (i) in the extended release layer, or (ii) in between the core and the extended release layer, or (iii) in the core.

2. A extended release pharmaceutical compositions comprising cyclobenzaprine HCl, wherein the composition comprises of:
   a) inert core;
   b) said inert core being coated with a matrix comprising cyclobenzaprine HCl and
      one or more extended release agents.

3. A extended release pharmaceutical compositions comprising cyclobenzaprine HCl, wherein the composition comprises of:
   a) inert core;
   b) first layer comprising of cyclobenzaprine HCl on the inert core, and
   c) second layer comprising of one or more extended release agents on the first layer;
   wherein, the said second layer does not contain plasticizer.

4. A extended release pharmaceutical compositions comprising cyclobenzaprine HCl wherein the composition comprises of:
   a) core comprising cyclobenzaprine HCl;
   b) said core being coated with a layer comprising of one or more extended release agents;
   wherein, the said coating layer does not contain plasticizer.

5. The compositions as claimed in claim 2, wherein the matrix further comprises one or more plasticizer.

6. The composition as claimed in any one of the claims 1 to 4, wherein the composition comprises of cyclobenzaprine hydrochloride from 0.01% to 50% by weight of the composition.
7. The composition as claimed in any one of the claims 1 to 4, wherein the extended release agent is selected from the group of cellulose ethers, cellulose esters polymethacrylates, wax, fatty acid, fatty alcohol, polyalkylene glycol, or mixtures thereof.

8. The composition as claimed in any one of the claims 1 to 4, wherein the extended release agent is selected from ethyl cellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose acetate succinate, cellulose acetate, polyvinyl alcohol, polyvinyl acetate, povidone, polyethylene glycol, cetyl alcohol, stearyl alcohol, bees wax, camauba wax, stearic acid, vinyl pyrrolidone-vinyl acetate copolymer, dimethylaminoethyl methacrylate and other neutral methacrylic acid esters, methacrylic acid copolymers type A, methacrylic acid copolymers type B, methacrylic acid copolymers type C, ammoniomethacrylate copolymers, neutral copolymer of polymethacrylic acid ester, or mixtures thereof.

9. The composition as claimed in any one of the claims 7 to 8, wherein the mixture of extended release agents are used in the ratio of 1:0.05 to 0.05:1.

10. The composition as claimed in any one of the claims 1 to 4 and 7 to 8, wherein the extended release agent is from 0.5% to 90% by weight of the composition.

11. The composition as claimed in any one of the claims 1 to 4, wherein the composition optionally comprises at least one additive selected from binder, diluent, anti-tack agent, or mixtures thereof.

12. The composition as claimed in claim 5, wherein the plasticizer is selected from triacetin, triethylcitrate, tributyl citrate, polyethylene glycol, acetylxybutylcitrate, miglyol, hydrogenated oils, propylene glycol, acetyltriethylcitrate, polysorbate, castor oil, oleic acid, dibutylsebacate, diethylphthalate, acetylated mono- and di-glycerides, or mixtures thereof.
13. A process for the preparation of extended release pharmaceutical composition,
wherein the process comprises steps of:
   a) dispersing and/or dissolving cyclobenzaprine hydrochloride in a solvent
      selected from water, alcohol, organic solvent, or mixture thereof;
   b) dispersing and/or dissolving one or more extended release agents in a solvent
      selected from water, alcohol, organic solvent, or mixture thereof;
   c) mixing the dispersion or solution of step b) with the dispersion or solution of step
      a);
   d) optionally adding at least one additive selected from binder, diluent, surfactant,
      plasticizer, anti-tack agent, lubricants, or mixtures thereof to dispersion of step
      c);
   e) spraying the resulting dispersion or solution on inert cores to obtain extended
      release pellets;
   f) drying and sizing the extended release pellets.

14. A process for the preparation of extended release pharmaceutical composition
wherein the process comprises steps of:
   a) mixing cyclobenzaprine hydrochloride with at least one additive selected from
      binder, diluent, surfactant, plasticizer, anti-tack agent, lubricants, or mixtures
      thereof in a mixer to obtain drug mixture;
   b) granulating drug mixture with a granulating solvent selected from water, alcohol,
      organic solvent, or mixture thereof to obtain granules;
   c) extruding the granules in an extruder to obtain extrudates,
   d) spheronizing the extrudates in the spheronizer to obtain matrix core,
   e) drying and sizing the matrix core;
   f) dispersing and/or dissolving one or more extended release agents in a solvent
      selected from water, alcohol, organic solvent, or mixture thereof;
   g) optionally adding at least one additive selected from binder, diluent, surfactant,
      anti-tack agent, lubricants, or mixtures thereof to dispersion of step f),
   h) spraying the resulting dispersion or solution on matrix cores of step e) to obtain
      extended release pellets;
   i) drying and sizing the extended release pellets.
15. A process for the preparation of extended release pharmaceutical composition, wherein the process comprises steps of:

a) dispersing and/or dissolving cyclobenzaprine hydrochloride in a solvent selected from water, alcohol, organic solvent, or mixture thereof;

b) optionally dispersing and/or dissolving at least one additive selected from binder, diluent, surfactant, plasticizer, anti-tack agent, lubricants, or mixtures thereof in a solvent selected from water, alcohol, organic solvent, or mixture thereof;

c) mixing the dispersion or solution of step b) with the dispersion or solution of step a);

d) spraying the resulting dispersion or solution on inert cores to obtain drug cores;

e) drying and sizing the drug cores;

f) dispersing and/or dissolving one or more extended release agents in a solvent selected from water, alcohol, organic solvent, or mixture thereof;

g) optionally adding at least one additive selected from binder, diluent, surfactant, anti-tack agent, lubricants, or mixtures thereof to dispersion of step f);

h) spraying the resulting dispersion or solution on drug core of step e) to obtain extended release pellets;

i) drying and sizing the extended release pellets.
### INTERNATIONAL SEARCH REPORT

**A CLASSIFICATION OF SUBJECT MATTER**

IPC®: **A61K 9/54** (2006.01); **A61K 31/135** (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

**B FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC®: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPODOC, WPI

**C DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
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<tr>
<td>X</td>
<td>US 2005/0106247 A1 (VENKATESH et al.) 19 May 2005 (19.05.2005) <strong>Claims 1, 2, 6-9, 11-15, 17, 18, 20; Description Paragraphs [0013], [0030], [0031], [0043]</strong></td>
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<td>X</td>
<td>US 2003/0180352 A1 (PATEL et al.) 25 September 2003 (25.09.2003) <strong>Description Paragraphs [0095], [0313], [0314]</strong></td>
<td>1, 3-12, 14, 15</td>
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**Further documents are listed in the continuation of Box C**

**See patent family annex**

**Date of the actual completion of the international search**

03 September 2010 (03.09.2010)

**Date of mailing of the international search report**

14 September 2010 (14.09.2010)

**Name and mailing address of the ISA/ AT**

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