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(54) **Title:** PALATABLE FORMULATIONS OF IBUPROFEN

(57) **Abstract:** The present invention relates to oral palatable pharmaceutical formulations of ibuprofen. Taste-masked oral formulation of ibuprofen is provided wherein the disagreeable taste and the associated unpleasant throat burning sensation of ibuprofen is masked by coating with at least one lipophilic agent. The present invention also relates to providing oral palatable pharmaceutical compositions of such taste-masked ibuprofen in the form of orally disintegrating tablets, bite-dispersion tablets, granules, dispersible tablets, or the like. Further process for preparation of such taste-masked palatable formulations is also disclosed.



PALATABLE FORMULATIONS OF IBUPROFEN

Field of the Invention

The present invention relates to oral palatable pharmaceutical formulations of ibuprofen. In particular the present invention relates to taste-masked oral formulations of ibuprofen wherein the disagreeable taste and the associated unpleasant throat burning sensation of ibuprofen is masked by coating with at least one lipophilic agent. Particularly, the lipophilic agent is applied in an aqueous emulsified form. The present invention also relates to providing oral palatable pharmaceutical compositions of such taste-masked ibuprofen in the form of orally disintegrating tablets, swallow tablets, bite-dispersion tablets, capsules, granules, dispersible tablets, dry suspensions or the like. The present invention further relates to process for preparation of such taste-masked palatable formulations.

Background of the Invention

Taste is one of the most important parameter influencing patient compliance in case of drugs to be administered orally. It refers to a perception arising from the stimulation of taste buds present on the surface of the tongue. Since majority of the pharmaceutical actives are unpalatable due to their bitter and undesirable taste with varying intensities, taste masking has become a prerequisite to develop orally administering systems of such drugs and improve the patient compliance especially in the pediatric and geriatric populations. Moreover, masking the bitter taste of drugs is a potential tool for the improvement of its acceptability and compliance eventually determining the product value and commercial success of the product. Developing oral formulations of bitter and undesirable tasting actives having unpleasant taste with acceptable degree of palatability has remained a key challenge to the formulators.

The methods commonly used for achieving taste masking include various chemical and physical methods that prevent the drug substance from interacting with taste buds. The simplest method involves use of flavor enhancers and sweeteners whereas other methodologies include coating, granulation, inclusion complex formation with cyclodextrin, complexation with ion exchange resins, use of taste suppressants and potentiators, solid dispersions, pH modifiers and adsorbates, viscosity modifiers etc. More complex techniques such as microencapsulation, multiple emulsions, vesicles and

liposomes, prodrug formation and salt formation have also been employed by the formulators to mask the disagreeable taste of the bitter actives.

Further various attempts to use hydrophilic agents to mask the bitter tasting actives have been made. However, use of hydrophilic agents, due to their nature is associated with handling or processing problems. Some researchers have investigated use of lipophilic agents such as waxes and lipids to mask the taste of bitter actives. Various techniques such as hot-melt technique wherein waxes and lipids are first melted and then utilized in various pharmaceutical processes involving the active have been investigated. Another technique employing lipophilic agents for taste-masking makes the use of organic solvent solutions of waxy materials to coat the active agents. But none of these processes have been completely satisfactory. These methods involve cumbersome procedures and require special equipments. In case of hot-melt technique, the drug is exposed to high temperature that may degrade or alter drug substance. Use of organic solvents is further associated with lot of regulatory restrictions due to cumbersome procedures and undesirable effects including explosion, toxic release and environmental pollution. Further use of lipophilic agents has also in certain cases shown to impact the desired release profile of the active agents. Need therefore exists to develop compositions wherein lipophilic agents have been employed to mask the taste of bitter actives in a manner that does not deleteriously impact the stability of the active agent nor does it involve the use of organic solvents while providing desired palatable formulations.

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) that has been widely prescribed as an analgesic, anti-inflammatory and anti-pyretic. It is propionic acid derivative and chemically it is (RS)-2-(4-Isobutylphenyl) propionic acid. There are two possible enantiomers of ibuprofen in which S form or (+)-ibuprofen is found to be pharmacologically active. However, ibuprofen is usually administered as racemic compound to treat mild to moderate pain related to dysmenorrhoea, migraine, postoperative, and dental pain and in the management of spondylitis, osteo-arthritis, rheumatoid arthritis, and soft tissue disorders. Ibuprofen has also antipyretic properties. Ibuprofen is regarded one of the safest NSAIDs available. It acts by inhibiting the enzyme cyclooxygenase (COX) responsible for prostaglandin synthesis. It is considered a nonselective COX inhibitor since it inhibits both COX-1 and COX-2. It is usually given as the free acid but various salts, esters and other complexes are also used. It has

molecular formula of $C_{13}H_{18}O_2$ and molecular weight is 206.28. It is a white to off-white crystalline powder and is practically insoluble in water in the pH range of 1 to 4, but shows increased solubility at pH 5 and readily soluble in organic solvents such as ethanol and acetone.

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However, ibuprofen has characteristic bitter taste that makes it highly unpalatable. In addition ibuprofen delivers a powerful and unacceptable burning sensation to the roof the mouth and the back of the throat that resemble the consumption of hot chilli peppers. Such undesirable organoleptic characteristics of ibuprofen have restricted the formats in which it can be consumed and necessitates masking of its said disagreeable taste and burning sensation. Therefore, in order to make wider use of ibuprofen and achieve improved patient compliance, various approaches have been attempted to eliminate its bitter taste, after taste and adverse mouth feel and make the ibuprofen compositions more palatable upon oral administration. Researchers have employed various techniques such as complexation, coating, use of flavoring and sweetening agents, etc to provide palatable ibuprofen formulations. Use of flavors and sweeteners alone have been found to be little effective to achieve complete taste masking of ibuprofen and overcome throat burning sensation associated therewith. Complexation technique requires use of higher ratios of complexing agents which increase the size of the dosage form and also make the process tedious and expensive. Many processes employ organic solvent based polymeric coatings which require special expensive equipments, these are not environmentally friendly and their use is associated with health and safety concerns. In case of coating a delicate balance between taste-masking and in-vitro drug release profile is essential since many polymeric coating systems may also affect desired release characteristics of the formulation and bioavailability of the active. Other approaches such as microencapsulation are complex, tedious and expensive. Thus despite numerous efforts, there still remains a need to develop an effective measure which provides palatable formulations of ibuprofen and ensures delivery of the active in its desired concentration while simultaneously avoiding extremely bitter taste, lingering after taste and adverse mouth feel associated with ibuprofen and thereby encouraging the patient compliance.

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A yet another approach for masking undesirable taste of the pharmaceutical actives as discussed above employs lipophilic agents. However, use of lipophilic agents for taste-

masking has not seen wide applications and their use has remained restricted to hot-melt technique or organic solvent solutions, both having disadvantages as discussed earlier. US 2007/0292508 A1 describes an orally disintegrating dosage form comprising a plurality of lipid coated active and silicified microcrystalline cellulose wherein lipid used
5 is a wax or a fatty acid glycerol ester or combinations thereof. It involves microencapsulating the active like ibuprofen by using a solution of ethyl cellulose in lipid component such as hydrogenated soybean oil or hydrogenated castor oil prepared by hot-melt procedure. WO9718798A1 relates to prompt-release pharmaceutical composition comprising microcrystals and microgranules of the active such as ibuprofen
10 that is spray coated with lipidic materials such as mono-, di- or tri- glycerides of fatty acids and waxes and optionally contains hydrophilic additive. The process involves melting the lipids at a temperature of approximately 110°C and then spraying in the melted state on active, with the temperature maintained at approximately 80°C. WO9425006A1 discloses a method of producing an aqueous stable drug composition
15 which masks the undesired taste of drugs like ibuprofen and comprises the steps of (a) mixing a drug in particulate form into a molten surfactant (b) solidifying the mixture of step (a) and reducing the solidified mixture into a powder (c) admixing the powder of step (b) with a lipid in a molten or semi-solid state to form lipid coated particles and (d) blending an aqueous solution with the lipid coated particles. The aqueous dosage forms
20 can be stored in flavor masked form for about 4 days but not for longer duration. US5320848 describes a non-aqueous, chewable composition of unpalatable drugs such as ibuprofen in which the unpalatable taste of the drug is masked by dispersing the active in a lipid and the composition further comprises a matrix for said drug and lipid wherein the matrix is consisting of granulating agents, a rapid dispersal agent and other
25 additives. The preparation process also involves hot melting of wax to which the active is added.

None of the above mentioned research attempts describe use of lipophilic agents for taste-masking without subjecting the active to the deleterious hot-melt procedure, and
30 more particularly do not use the lipophilic agents from an aqueous base for taste-masking ibuprofen. There thus exists a long felt need in the pharmaceutical industry for the development of palatable formulations of ibuprofen using lipophilic agents that can not only be applied as an aqueous based composition in the form of an emulsion or dispersion but also do not require specialized equipments and processes to provide

desired stability and release characteristics to the compositions. Further such a formulation also needs to provide complete taste masking of ibuprofen, eliminate after taste and burning sensation without compromising desired release profile of ibuprofen and its bioavailability. It is also required that such taste-masked ibuprofen is formulated in various palatable dosage forms for immediate release or controlled release in the form of orally disintegrating tablets, swallow tablets, bite-dispersion tablets, capsules, granules, dispersible tablets, dry suspensions or the like.

The present inventors, after rigorous experimentation, have surprisingly found that coating ibuprofen using a lipophilic agent wherein the lipophilic agent is employed in an aqueous emulsified form provides taste-masked ibuprofen that is stable, provides desired in-vitro release profile and can be incorporated in various formulations orally disintegrating tablets, swallow tablets, bite-dispersion tablets, capsules, granules, dispersible tablets, dry suspensions or the like thereby improving patient compliance. Coating of ibuprofen with the aqueous lipophilic agent coating system provides effective taste-masking without the use of any expensive and specialized equipment or process.

Summary of the Invention

The present invention relates to palatable oral pharmaceutical formulations of ibuprofen comprising coated ibuprofen comprising ibuprofen and tastemasking coating comprising at least one lipophilic agent. In particular the present invention relates to taste-masked oral formulations of ibuprofen wherein the disagreeable taste and the associated unpleasant throat burning sensation of ibuprofen is masked by coating with at least one lipophilic agent applied in an aqueous emulsified form.

Detailed Description of the Invention

Palatability and mouth feel are extremely important factors for achieving total compliance of patients who are being administered the unpleasant or disagreeable or objectionable tasting active pharmaceutical agent. Several taste-masking technologies are known however, not all taste-masking technologies can work with every drug. Taste-masking technologies and processes employed to achieve the same can, in certain instances, interfere with disintegration, release, affect stability, provide inadequate taste-masking for a given active or interfere with the bioavailability or pharmacokinetic properties of the drug. Therefore, it becomes important to develop taste-masking technology for an active

agent that not only enhances the organoleptic properties of the dosage form containing the same, but also does not interfere with the release and bioavailability of the drug.

5 The present inventors, after thorough research, have developed palatable pharmaceutical formulations of ibuprofen wherein the bitter, unpleasant or otherwise undesirable taste of the active is masked and unacceptable after taste and burning sensation associated with ibuprofen is eliminated, without compromising on its in-vitro release profile, using ecofriendly and cost effective processes. The present invention provides a palatable oral pharmaceutical formulation comprising coated ibuprofen
10 comprising ibuprofen and tastemasking coating comprising at least one lipophilic agent.

Ibuprofen, a propionic acid derivative, is a non-steroidal anti-inflammatory drug (NSAID) commonly prescribed as an analgesic, anti-inflammatory and anti-pyretic. Ibuprofen may be used in the form of, but not limited to, free acid, racemate, pharmaceutically
15 acceptable salt, polymorph, solvate, hydrate, anhydrous form, ester, complex, amide, prodrug, active metabolite, analog, enantiomer, stereoisomer, diastereomer or any combination thereof. In one embodiment, ibuprofen is used as free acid which is a racemic compound or racemate. In further embodiment, ibuprofen may be present in the form of a pharmaceutically acceptable salt. In another embodiment, it may be present in
20 its lysine salt form sometimes termed as ibuprofen lysinate. All different polymorphs, solvates, hydrates, anhydrous forms are within the purview of this invention. Also included within the scope of the present invention are the salts, esters, other complexes, amides, prodrugs, active metabolites, analogs, enantiomers, stereoisomers, diastereomers, and the like or combinations thereof of ibuprofen.

25 In a further embodiment, the compositions of the present invention may provide ibuprofen in an amount of from about 100 mg to about 3200 mg. In one embodiment, the compositions of the present invention may provide ibuprofen in an amount of from about 200 mg to about 3200 mg. In another embodiment, ibuprofen may be employed in an
30 amount effective to provide analgesic, antipyretic and anti-inflammatory effect. In one embodiment, the amount of ibuprofen in the formulation can vary from about 1 weight % to about 95 weight % based upon the total weight of the composition. In another embodiment, the amount of ibuprofen in the formulation can vary from about 5 weight % to about 90 weight % based on the total weight of the composition.

In a further embodiment, ibuprofen may be in the form of, but not limited to, powder, granules, pellets, pearls, beads, minitables, tablets or the like. In one embodiment, ibuprofen granules may be prepared by wet granulation, dry granulation or roll compaction or the like. In a further embodiment, ibuprofen granules may be prepared of
5 ibuprofen alone or of mixture of ibuprofen with at least one pharmaceutically acceptable excipient. In an aspect of the present invention, pellets of ibuprofen may be prepared using extrusion spherization. In another aspect of the present invention, ibuprofen can be loaded on an inert carrier before taste-masking. The inert carrier as used herein
10 includes beads, pellets, pearls, spheres or similar particles that do not contain an active ingredient. Non-limiting examples of inert carriers include microcrystalline cellulose, sugar or silicon dioxide. In another aspect of the present invention ibuprofen can be blended with an anti-static agent before taste-masking. Non-limiting examples of anti-static agents include colloidal silica, silica gel, precipitated silica, or combinations thereof.

15 In accordance with the present invention, ibuprofen is taste-masked by coating with at least one lipophilic agent. Such coated ibuprofen is employed in palatable oral formulations of the present invention.

20 In one embodiment, the lipophilic agents used in the present invention are non polymeric agents. The lipophilic agents that may be employed for taste-masking include, but are not limited to, fats, waxes, fatty acids, fatty acid esters, long chain monohydric alcohols or esters thereof, hydrogenated vegetable oil or any combinations thereof.

25 Waxes are esters of fatty acids with long chain monohydric alcohols. Natural waxes are often mixtures of such esters, and may also contain hydrocarbons. Waxes that may be employed in the present invention include, but are not limited to, natural waxes, such as animal waxes, vegetable waxes, and petroleum waxes (*i.e.*, paraffin waxes, microcrystalline waxes, petrolatum waxes, mineral waxes), and synthetic waxes. Specific
30 examples include but are not limited to spermaceti wax, carnauba wax, Japan wax, bayberry wax, flax wax, beeswax, yellow wax, Chinese wax, shellac wax, lanolin wax, sugarcane wax, candelilla wax, castor wax paraffin wax, microcrystalline wax, petrolatum wax, carbowax, and the like, and mixtures thereof. Waxes are also monoglycerol esters, diglycerol esters, or triglycerol esters (glycerides) and derivatives thereof formed from a

fatty acid having from about 10 to about 22 carbon atoms and glycerol, wherein one or more of the hydroxyl groups of glycerol are substituted by a fatty acid. Glycerides employed in the present invention include, but are not limited to, glyceryl monostearate, glyceryl distearate, glyceryl tristearate, glyceryl dipalmitate, glyceryl tripalmitate, glyceryl monopalmitate, glyceryl palmitostearate, glyceryl dilaurate, glyceryl trilaurate, glyceryl monolaurate, glyceryl didocosanoate, glyceryl tridocosanoate, glyceryl monodocosanoate, glyceryl monocaproate, glyceryl dicaproate, glyceryl tricaproate, glyceryl monomyristate, glyceryl dimyristate, glyceryl trimyristate, glyceryl monodecenoate, glyceryl didecenoate, glyceryl tridecenoate, glyceryl behenate (COMPRITOL®), polyglyceryl diisostearate, lauroyl macrogolglycerides, oleoyl macrogolglycerides, stearyl macrogolglycerides, and the like or combinations thereof. Hydrogenated vegetable oils that may be employed include, but are not limited to, hydrogenated palm kernel oil, hydrogenated peanut oil, hydrogenated palm oil, hydrogenated rapeseed oil, hydrogenated rice bran oil, hydrogenated soybean oil, hydrogenated sunflower oil, hydrogenated castor oil, hydrogenated cottonseed oil, and the like or mixtures thereof. Other fatty acids include, but are not limited to, decenoic acid, docosanoic acid, stearic acid, palmitic acid, lauric acid, myristic acid, and the like, or mixtures thereof, and mixtures thereof. Long chain monohydric alcohols having not less than 6 carbon atoms and their esters include, but are not limited to, cetyl alcohol, and stearyl alcohol, and mixtures thereof. In one embodiment, the lipophilic agents that may be incorporated include, but are not limited to, hydrogenated vegetable oils such as hydrogenated cottonseed oil (LUBRITAB®), hydrogenated soyabean oil (STEROTEX® HMNF), hydrogenated castor oil, hydrogenated palm oil, hydrogenated rapeseed oil, or the like, carnauba wax, candelilla wax, spermaceti, beeswax, montan wax, microcrystalline wax, lecithin, hydrogenated tallow, paraffin wax, shellac wax, petrolatum, glyceryl behenate, cetyl alcohol, cetostearyl alcohol, precinol, stearic acid and synthetic waxes e.g. polyethylene and the like, or any combinations thereof. In another embodiment, the lipophilic agents employed include, but not limited to, Cutina (hydrogenated castor oil), Hydrobase (hydrogenated soybean oil), Castorwax (hydrogenated castor oil), Croduret (hydrogenated castor oil), Carbowax, Compritol (glyceryl behenate), Sterotex (hydrogenated cottonseed oil), Lubritab (hydrogenated cottonseed oil), Apifil (wax yellow), Akofine (hydrogenated cottonseed oil), Softisan (hydrogenated palm oil), Hydrocote (hydrogenated soybean oil), Corona (lanolin), Gelucire (macrogolglycerides lauriques), Precinol (glyceryl palmitostearate), Emulcire

(cetyl alcohol), Plurol diisostearique (polyglyceryl diisostearate), and Geleol (glyceryl stearate), and the like or mixtures thereof.

5 In one embodiment, the lipophilic agent/s is applied to ibuprofen in an aqueous emulsified form.

U.S. Patent Publication 20080096979 (the '979 publication) which is incorporated herein in its entirety by reference, describes the process of preparing such an aqueous emulsified form of these lipophilic agents. Such a lipophilic coating system comprising a wax or any of the non-limiting examples of lipophilic agents described above, an emulsifying agent and a plasticizer is employed in an embodiment of the present invention as taste-masking coating composition. The aqueous emulsified coating system disclosed in the '979 publication comprises a) emulsified wax or lipophilic substance wherein its content is up to about 9% by weight and an emulsifying agent at about 0.1 to about 10% by weight, and b) a plasticizer at about 5 to about 40% by weight of the wax. Emulsifying agent herein is selected from, but not limited to, one or more of non ionic emulsifiers, or ionic emulsifiers and the like or combinations thereof. Non-ionic emulsifiers include, but not limited to, mono and diglycerides such as, but not limited to, glyceryl monooleate (Peceol); medium chain glycerides (capmul), glyceryl ricinoleate, glyceryl laurate, glyceryl caprylate; PEG sorbitan fatty acid esters such as PEG-20 sorbitan monolaurate (Tween 20), PEG 20 sorbitan monostearate (Tween 60), PEG sorbitan monooleate (Tween 80); sorbitan fatty acid esters like sorbitan monolaurate (span 20); sugar ester surfactants like sucrose distearate (sucro ester 7); glyceryl monostearate; polyethylene glycol esters; cellulose derivatives like hydroxypropyl methylcellulose, hydroxypropyl cellulose and the like or combinations thereof. Ionic emulsifiers that may be employed include, but are not limited to, sodium caprylate, sodium lauryl sulphate, phospholipids, alginate salts. Plasticizer herein is a polymeric selected from, but not limited to, one or more of polyvinyl alcohol, mixture of polyvinyl acetate with povidone (Kollidon® SR) methylcellulose, ethyl cellulose, sodium carboxy methylcellulose, hydroxypropylcellulose, hydroxypropylmethyl cellulose, polyethylene glycol, cellulose acetate, cellulose propionate (lower, medium or higher molecular weight), cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose triacetate, poly (methyl methacrylate) poly (ethyl methacrylate), poly (butyl methacrylate), poly (isobutyl methacrylate), and poly (hexyl methacrylate), poly

(isodecyl methacrylate), poly (lauryl methacrylate), poly (phenyl methacrylate), poly (methyl acrylate), poly (isopropyl acrylate), poly (isobutyl acrylate), poly (octadecyl acrylate), poly (ethylene), poly (ethylene) low density, poly (ethylene) high density, poly (ethylene oxide), poly (ethylene terphthalate), poly (vinyl isobutyl ether), poly (vinyl acetate) poly (vinyl chloride), polyurethane and the like or combinations thereof.

In another embodiment, ibuprofen may be partially, substantially completely or completely coated with the tastemasking coating comprising at least one lipophilic agent. In one embodiment, the level of taste-masking coating of at least one lipophilic agent that is applied for the formulations of the present invention is in the range from about 1% to about 90% by weight of the active ibuprofen. In another embodiment, the lipophilic agent/s is present in an amount of about 1% to about 95% by weight of the composition. In a further embodiment, the tastemasking coating comprising at least one lipophilic agent is applied to ibuprofen at a temperature that does not result in the melting of the active agent. In another embodiment, the tastemasking coating comprising at least one lipophilic agent is applied to ibuprofen at a temperature that does not result in the degradation of the active. In a further embodiment, the tastemasking coating is applied or sprayed on the active in emulsified form.

In a further embodiment, the taste-masking coating composition of at least one lipophilic agent further comprises polymeric agent, emulsifier, anti-tacking agent, sweetener and the like or combinations thereof. In another embodiment, the taste-masking coating composition comprises at least one lipophilic agent and at least one polymeric agent in an emulsified form. In a further embodiment, the taste-masking coating composition comprises at least one lipophilic agent, at least one polymeric agent and at least one emulsifier. In one embodiment, the polymeric agent is present in the taste-masking coating composition comprising lipophilic agent as a plasticizer discussed above. Suitable emulsifiers as discussed above may be employed in the taste-masking coating composition of the present invention comprising at least one lipophilic agent. In a further embodiment, the tastemasking coating composition comprises anti-tacking agent and sweetener along with the lipophilic agent, polymeric agent and emulsifier. Suitable anti-tacking agents include, but are not limited to, talc, glyceryl monostearate, silicon dioxide and metallic stearates such as magnesium stearate, or the like or combinations thereof. Suitable sweeteners that may be employed include sucralose, aspartame, stevia extract,

- glycyrrhiza, saccharine, saccharine sodium, acesulfame, dipotassium glycyrrhizinate, mannitol, xylitol, erythritol, isomalt, isomaltitol, lactitol, and the like or any combination thereof. In one embodiment, optionally, the taste-masking coating composition comprising at least one lipophilic agent further comprises additional pharmaceutically acceptable excipients such as disintegrants and the like. Suitable disintegrants include, but are not limited to, natural, modified or pregelatinized starch, crospovidone, croscarmellose sodium, sodium starch glycolate, low-substituted hydroxypropyl cellulose, calcium silicate, or the like or any combinations thereof.
- 10 In one embodiment, the emulsifying agent may be employed in an amount of about 0.01% to about 70% by weight of the composition. In another embodiment, the emulsifying agent is present in an amount of about 0.05% to about 60% by weight of the composition. In a further embodiment, the polymeric agent of the tastemasking coating may be employed in an amount of about 0.5% to about 90% by weight of the composition. In another embodiment, the polymeric agent of the tastemasking coating may be employed in an amount of about 1% to about 85% by weight of the composition. In one embodiment, the polymeric agent of the tastemasking coating may be employed in an amount of about 0.5% to about 90% by weight of the composition.
- 20 In a still further embodiment of the present invention, ibuprofen is optionally first coated or seal coated with a layer of at least one polymeric agent and then coated with a tastemasking layer of at least one lipophilic agent. Such a first coating in one embodiment is intended to dimensionally stabilize ibuprofen, give desired round shape to the needle shaped crystals of the ibuprofen if employed and thereby aid the uniform, intact and effective application of taste-masking coating composition comprising at least one lipophilic agent. In another embodiment, the palatable oral pharmaceutical formulation of the present invention comprises coated ibuprofen comprising ibuprofen, seal coating of at least one polymeric agent and tastemasking coating of at least one lipophilic agent thereon. In one embodiment, polymeric agent as seal coat may be employed in an amount of about 0.01% to about 90% by weight of the composition. In another embodiment, polymeric agent as seal coat may be employed in an amount of about 0.01% to about 80% by weight of the composition. In a further embodiment, polymeric agent as seal coat may be employed in an amount of about 0.01% to about 70% by weight of the composition.

Suitable polymeric agents that may be employed in the taste-masking compositions of the present invention include, but are not limited to, cellulose derivatives, saccharides or polysaccharides, polyhydric alcohols, poly (oxyethylene)-poly(oxypropylene) block copolymers (poloxamers), vinyl derivatives or polymers or copolymers thereof, acrylic acid derivatives or the like or any combinations thereof.

Cellulose derivatives, include but are not limited to, ethyl cellulose, methylcellulose, hydroxypropylmethylcellulose (HPMC), hydroxypropyl cellulose (HPC), hydroxyethyl cellulose, hydroxymethyl cellulose, hydroxypropyl ethylcellulose, carboxymethylethyl cellulose, carboxy ethylcellulose, carboxymethyl hydroxyethylcellulose, hydroxyethylmethyl carboxymethyl cellulose, hydroxyethyl methyl cellulose, carboxymethyl cellulose, methylhydroxyethyl cellulose, methylhydroxypropyl cellulose, carboxymethyl sulfoethyl cellulose, sodium carboxymethyl cellulose, cellulose acetate, cellulose acetate phthalate, cellulose acetate butyrate, hydroxypropylmethylcellulose acetate succinate, hydroxypropylmethylcellulose phthalate, hydroxymethyl ethylcellulose phthalate, cellulose acetate phthalate, cellulose acetate succinate, cellulose acetate maleate, cellulose acetate trimellitate, cellulose benzoate phthalate, cellulose propionate phthalate, methylcellulose phthalate, ethylhydroxy ethylcellulose phthalate, or combinations thereof. Saccharides or polysaccharides include but are not limited to, guar gum, xanthan gum, gum arabic, tragacanth or combinations thereof. Polyhydric alcohols include but are not limited to, polyethylene glycol (PEG) or polypropylene glycol. Vinyl derivatives, polymers and copolymers thereof include but are not limited to polyvinyl alcohol, polyvinyl acetate, polyvinylacetate aqueous dispersion (Kollicoat SR 30D), copolymers of vinyl pyrrolidone, copolymers of vinyl alcohol (Kollicoat IR), polyvinyl alcohol phthalate, polyvinylacetal phthalate, polyvinyl butylate phthalate, polyvinylacetoacetal phthalate, polyvinylpyrrolidone (PVP) or combinations thereof. Acrylic acid derivatives include but are not limited to, methacrylic acids, polymethacrylic acids, polyacrylates, especially polymethacrylates like a) copolymer formed from monomers selected from methacrylic acid, methacrylic acid esters, acrylic acid and acrylic acid esters b) copolymer formed from monomers selected from butyl methacrylate, (2-dimethylaminoethyl)methacrylate and methyl methacrylate c) copolymer formed from monomers selected from ethyl acrylate, methyl methacrylate and trimethylammonioethyl methacrylate chloride or d) copolymers of acrylate and methacrylates* with/without quarternary ammonium group in combination with sodium

carboxymethylcellulose, e.g. those available from Röhm GmbH under the trademark Eudragit[®] like Eudragit EPO (dimethylaminoethyl methacrylate copolymer; basic butylated methacrylate copolymer), Eudragit RL and RS (trimethylammonioethyl methacrylate copolymer), Eudragit NE30D and Eudragit NE40D (ethylacrylate methymethacrylate copolymer), Eudragit RD 100 (ammoniomethacrylate copolymer with sodium carboxymethylcellulose), or the like or any combinations thereof.

The above listed polymeric agents can also be employed as seal coating prior to application of tastemasking coating. The polymeric coating agents can be used in the seal coating layer along with additional excipients such as, but not limited to, plasticizers, stabilizers, surfactants, anti-tacking agents and the like or combinations thereof. Polymeric coating agents can also be employed in the form of an aqueous dispersion stabilized by surfactants and suitable stabilizers. In one embodiment of the present invention, ibuprofen is seal coated with Eudragit NE 40D prior to coating with a coating composition comprising at least one lipophilic agent.

In a further embodiment, the lipophilic agent/s is applied to ibuprofen in an aqueous emulsified or dispersion form by a standard coating process. In another embodiment, the taste-masking coating composition of the present invention comprising at least one lipophilic agent in the form of an emulsion is applied to the active, ibuprofen by a standard coating process. In one embodiment the taste-masking lipophilic agent in an aqueous emulsified form is applied to ibuprofen using standard or conventional coating processes such as, but not limited to, fluidized bed coating, wet granulation or spray drying. The taste-masking coating layer comprising at least one lipophilic agent is applied to ibuprofen in any suitable equipment where coating can be achieved. Non-limiting examples of such equipments include, coating pan, granulator, fluidized bed processor or the like. The coating can be partial or complete, yet sufficient to mask the bitter and disagreeable taste of ibuprofen effectively without compromising on the desired release characteristics of the active.

Without being bound by any theory, the lipophilic agents employed in an aqueous emulsified form for taste-masking the active in the present invention forms excellent barrier coating on the bitter tasting active thereby preventing the active from interacting with taste buds and reduces the burning sensation associated with ibuprofen. The

coating with a lipophilic agent further protects the active from surrounding atmosphere thus providing good stability to the actives and compositions thereof. The use of lipophilic agents in aqueous emulsified form eliminates the use of organic solvents and specialized manufacturing instruments and does not deleteriously affect the stability of ibuprofen.

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The palatable taste masked ibuprofen compositions of present invention comprising coated ibuprofen, further comprises at least one pharmaceutically acceptable excipient. Depending on the final dosage form of the palatable ibuprofen formulation suitable pharmaceutically acceptable excipients may be employed. The coated taste-masked
10 ibuprofen of the present invention in the form of, but not limited to, powder, granules, pellets, pearls, beads, minitablets, tablets or the like is suitable for incorporation into various oral dosage forms including, but not limited to, suspensions, syrups, dry suspensions or syrups for reconstitution, fast melt granules, orally disintegrating, dispersible, chewable or effervescent tablets, granules, sprinkle granules, fast melt
15 granules, lozenge, chewing gum or the like. These oral formulations may contain from about 5% to about 95% of coated taste-masked ibuprofen.

In one embodiment, coated taste-masked ibuprofen is incorporated in an orally disintegrating tablet. Orally disintegrating tablets (ODTs) disintegrate/dissolve in the
20 mouth rapidly without administering extra water, providing the convenience of a tablet formulation while allowing the ease of swallowing provided by a liquid formulation.

The orally disintegrating tablets comprising coated taste-masked ibuprofen can further comprise directly compressible coprocessed excipient. PCT Application WO2007052289
25 describes directly compressible coprocessed excipient comprising of at least one water soluble excipient and water insoluble inorganic excipient such as calcium silicate. The water soluble carbohydrate can be a monosaccharide, disaccharide, oligosaccharide or polysaccharide. Examples of carbohydrates include, but are not limited to, monosaccharides such as sorbitol, glucose, dextrose, fructose, maltose or xylitol,
30 disaccharides such as sucrose, trehalose, lactose, glucose, galactose or mannitol, and oligosaccharides and polysaccharides such as dextrans and maltodextrins. The water soluble and water insoluble excipients in the directly compressible coprocessed excipient can be in a ratio of water-soluble excipient to water insoluble excipient of from about 50:1 to about 1:50. In one embodiment of the present invention, this ratio is about 30:1 to

about 1:30. In a further embodiment of the present invention, this ratio is from about 20:1 to about 1:20. The amount of directly compressible coprocessed excipient employed in the orally disintegrating tablet compositions comprising taste-masked ibuprofen is about 5% to about 95 % by weight of the said dosage form.

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The orally disintegrating tablet compositions based on coated taste-masked ibuprofen dissolve or disintegrate in the oral cavity, preferably within about 60 seconds. The orally disintegrating tablet compositions comprising coated taste-masked ibuprofen can be prepared by any of the known non limiting techniques such as freeze-drying, molding and sublimation, compression, cotton candy process, mass extrusion, etc or with use of specialized excipients such as effervescent couple, highly micronized agents, coprocessed excipients or the like.

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The compositions of the present invention may include in addition to the coated taste-masked ibuprofen and directly compressible coprocessed excipient, additional pharmaceutically excipients such as, but not limited to, one or more binders, disintegrants, superdisintegrants, diluents, salivating agents, surfactants, flavors, sweeteners, colorants, souring agents, glidants or lubricants, solubilizers, stabilizers, viscolizers, pH modifiers and the like or combinations thereof.

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Examples of suitable binders that may be employed include, but are not limited to, starch, pregelatinized starch, polyvinyl pyrrolidone (PVP), copovidone, cellulose derivatives, such as hydroxypropylmethyl cellulose (HPMC), hydroxypropyl cellulose (HPC) and carboxymethyl cellulose (CMC) and their salts, and the like or mixtures thereof. Examples of suitable diluents that may be employed include, but are not limited to, starch, microcrystalline cellulose, lactose, xylitol, mannitol, maltose, polyols, fructose, guar gum, sorbitol, magnesium hydroxide, dicalcium phosphate, and the like or any combinations thereof. Examples of lubricant that may be employed include, but are not limited to, magnesium stearate, calcium stearate, stearic acid, talc, and sodium stearyl fumarate, and the like or any mixtures thereof. Suitable glidants that may be employed include, but are not limited to, colloidal silica, silica gel, precipitated silica, and the like or combinations thereof. Suitable salivating agents that may be employed include, but are not limited to, micronised polyethylene glycol, sodium chloride or precipitated micronised silica, and the like or combinations thereof to improve the disintegration properties of the

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said compositions. Examples of solubilizers include, but are not limited to cetostearyl alcohol, cholesterol, diethanolamine, ethyl oleate, ethylene glycol palmitostearate, glycerin, glyceryl monostearate, isopropyl myristate, lecithin, medium-chain glyceride, monoethanolamine, oleic acid, propylene glycol, polyoxyethylene alkyl ether, polyoxyethylene castor oil glycoside, polyethylene sorbitan fatty acid ester, polyoxyethylene stearate, propylene glycol alginate, sorbitan fatty acid ester, stearic acid, sunflower oil, triethanolmine, and the like or mixtures thereof. Suitable stabilizers that may be employed include, but not limited to, benzoic acid, sodium benzoate, citric acid, and the like or combinations thereof. Examples of surfactants include, but are not limited to, sodium docusate, glyceryl monooleate, polyethylene alkyl ether, polyoxyethylene sorbitan fatty acid ester, sodium lauryl sulfate, sorbic acid, sorbitan fatty acid ester, and the like or mixtures thereof. Suitable souring agents that may be employed include, but are not limited to, monosodium fumarate and/or citric acid and the like, or mixtures thereof. The compositions of the present invention may optionally include viscolizers such as polyalkylene oxides; polyols; starch and starch-based polymers; chitosan; polysaccharide gums; polyethylene oxide, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, hydroxyethyl cellulose, sodium carboxy methylcellulose, calcium carboxymethyl cellulose, methyl cellulose, polyacrylic acid, gum acacia, gum tragacanth, xanthan gum, guar gum and polyvinyl alcohol and copolymers and the like or mixtures thereof. Suitable sweetening agents include, but are not limited to, aspartame, stevia extract, glycyrrhiza, saccharine, saccharine sodium, acesulfame, sucralose and dipotassium glycyrrhizinate, mannitol, xylitol, erythritol, isomalt, isomaltitol, lactitol, and the like or mixtures thereof. Suitable flavors that may be employed include, but are not limited to, mint flavour, orange flavour, lemon flavor, bubble gum flavor, strawberry aroma, vanilla flavour, raspberry aroma, cherry flavor, tutti frutty flavor, magnasweet 135, key lime flavor, grape flavor, trusil art 511815, and fruit extracts and the like or combination thereof. Suitable pH modifiers that may be incorporated include, but are not limited to, citric acid, fumaric acid, tartaric acid or a combination thereof. Suitable superdisintegrant that may be employed includes, but is not limited to, natural, modified or pregelatinized starch, croscovidone, croscarmellose sodium, sodium starch glycolate, low-substituted hydroxypropyl cellulose as well as effervescent disintegrating systems, and the like or combinations thereof. Suitable disintegrants that may be employed include, but are not limited to, croscovidone, calcium silicate and starch, and the like or combinations thereof.

In one embodiment of the present invention, the coated taste-masked ibuprofen is incorporated in fast melt granules or quick dissolve granules. Fast melt granules or quick dissolve granules are meant to be taken without water and disperse easily, and quickly, when taken orally. These granules comprise various pharmaceutically acceptable
5 excipients as have been discussed under orally disintegrating tablets in addition to excipients which may be specifically employed for fast melt granules or quick dissolve granules. Such granules may further be formulated into tablets.

In another embodiment of the present invention, the coated taste-masked ibuprofen can
10 be incorporated in chewable tablets. Chewable tablets are taken slowly by chewing or sucking in the mouth, and enable coated taste-masked ibuprofen contained therein to be orally administered without water. These chewable tablets comprise various pharmaceutically acceptable excipients as have been discussed under orally disintegrating tablets in addition to excipients which may be specifically employed for
15 chewable tablets.

In yet another embodiment, coated taste-masked ibuprofen is incorporated in dispersible tablets. Dispersible tablet refers to a tablet which disperses in aqueous phase, e.g. in water before administration. A water-dispersible tablet, according to the British
20 Pharmacopoeia and European Pharmacopoeia, should meet the requirements of the test for dispersible tablets as regards dispersion time (<3 minutes) and dispersion quality (i.e. to pass through a 710 μ m sieve).

The dispersible tablet compositions comprising coated taste-masked ibuprofen can
25 further comprise in addition to pharmaceutically acceptable excipients as disclosed under orally disintegrating tablets, one or more viscolizers.

Suitable viscolizers which can be used include, but are not limited to, polyalkylene oxides such as polyethylene oxide; cellulose ethers such as hydroxyethyl cellulose,
30 hydroxypropylcellulose, hydroxypropyl methyl cellulose, methyl cellulose, ethyl cellulose, sodium carboxy methylcellulose, calcium carboxymethyl cellulose, microcrystalline cellulose; gums such as gum arabic alginates, agar, guar gum, locust bean, carrageenan, tara, gum arabic, tragacanth, pectin, xanthan, gellan, maltodextrin, galactomannan, pusstulan, laminarin, scleroglucan, gum arabic, inulin, karaya, whelan;

polyols such as dipropylene glycol, polypropylene glycol, propylene glycol, polyethylene glycol (PEG), sorbitol and glycerol; carbopol, starch and starch-based polymers such as pregelatinized starch, acrylic acid and methacrylic acid polymers, and esters thereof, maleic anhydride polymers; polymaleic acid; poly(acrylamides); poly(olefinic alcohol)s; 5 poly(N-vinyl lactams); polyoxyethylated saccharides; polyoxazolines; polyvinylamines; polyvinylacetates; polyimines; povidone vinylpyrrolidone/vinyl acetate copolymer and polyvinyl acetate, mixture of polyvinyl acetate and polyvinylpyrrolidone, chitin, cyclodextrin, gelatin, chitosan, and combinations thereof. In one embodiment, the viscolizers that may be employed include, but are not limited to, hydroxypropyl cellulose, 10 hydroxypropyl methylcellulose, hydroxyethyl cellulose, polyethylene oxide; sodium carboxy methylcellulose, microcrystalline cellulose, guar gum, xanthan gum, alginates and combinations thereof. The weight percent of the viscolizer in the dosage form is about 2 to 75 weight percent, preferably about 10 to 70 weight percent, and most preferably about 5 to 50 weight percent. The viscolizers act to control sedimentation rate 15 of dispersed ibuprofen thereby producing homogeneous dispersions when the dispersible tablets are dispersed in water before administration thus ensuring substantially uniform dosing. They rapidly generate viscosity when the dispersible tablets come in contact with water, and a homogenous suspension is formed, which can be easily swallowed by children and the elderly, with minimal effect of the release properties 20 of the biologically active ingredient.

Effervescent tablets are intended to be dissolved or dispersed in water before administration and generally contain acid substances and carbonates or bicarbonates, which react rapidly in the presence of water releasing carbon dioxide. These tablets 25 comprise various pharmaceutically acceptable excipients as have been discussed under dispersible tablets and orally disintegrating tablets. The effervescent tablets can comprise effervescent couples selected from, but not limited to, thermolabile gas generating agents such as sodium bicarbonate, sodium glycine carbonate, potassium bicarbonate, ammonium bicarbonate, sodium bisulfite, sodium metabisulfite, and the like 30 or combinations thereof and an acid source such as citric acid, maleic acid or tartaric acid, and the like or combinations thereof.

The terms "tablet" and "tablet composition" are used synonymously within the context of the present invention. These terms should be construed to include a compacted or

compressed powder composition obtained by compressing or otherwise forming the composition to form a solid having a defined shape. Tablets in accordance with the invention may be manufactured using conventional techniques of common tableting methods known in the art such as direct compression, wet granulation, dry granulation and extrusion/ granulation. In one embodiment, the process is direct compression which involves compression of taste-masked drug-exciipient blend after mixing them for a definite time period. The tablet may vary in shape such as oval, triangle, almond, peanut, parallelogram, round, pentagonal, hexagonal, and trapezoidal. The preferred shapes are round, oval and parallelogram forms. In an embodiment of the present invention, the formulation is presented in the form of a tablet in tablet dosage form or inlay tablet. In one embodiment, the formulation is presented in the form of tablet in tablet or inlay tablet, wherein the inner tablet composition comprises excipients such as but not limited to sweeteners, flavourants, or the like and the outer tablet comprises coated taste-enhanced ibuprofen.

In a still another embodiment of the present invention, the coated taste-masked ibuprofen can be incorporated in suspensions, syrups or dry suspensions or syrups for administration.

The formulation of the present invention masks the bitter taste of ibuprofen and also enhances the overall taste of the formulation, whereby upon administration the formulation comprising such a coated active, imparts excellent taste and mouthfeel over the entire period of intake of the formulation greatly influencing patient acceptability. The formulations of the present invention comprising ibuprofen taste masked by coating with at least one lipophilic agent provide a pleasant tasting formulation without compromising on the in-vitro release profile.

In an embodiment of the present invention, a palatable pharmaceutical formulation comprising ibuprofen coated with at least one lipophilic agent releases at least about 85 weight % of ibuprofen within 30 minutes in 0.1N HCl. In another embodiment a palatable pharmaceutical formulation comprising ibuprofen coated with at least one lipophilic agent releases at least about 90 weight % of ibuprofen within 30 minutes in 0.1N HCl.

In a further aspect of this invention a process for preparation of a palatable pharmaceutical formulation of ibuprofen comprises the steps of:

- 5 (a) coating ibuprofen provided with a taste-masking coating composition comprising at least one lipophilic agent in the form of an aqueous emulsion to obtain coated taste-masked ibuprofen;
- (b) optionally blending coated ibuprofen of step (a) with at least one pharmaceutically acceptable excipient;
- (c) compressing the blend of step (b) into tablets and packaging into unit or multiple dose packages or packaging the blend of step (b) or coated ibuprofen
10 of step (a) into unit or multiple dose packages.

In yet another aspect of this invention is process for preparation of a palatable pharmaceutical formulation of ibuprofen comprising the steps of:

- 15 (a) providing ibuprofen for coating in the form of powder, granules, pellets, beads, pearls, minitables, tablets;
- (b) coating ibuprofen provided in step (a) with a taste-masking coating composition comprising at least one lipophilic agent and at least one polymeric agent in the form of an aqueous emulsion to obtain coated taste-masked ibuprofen;
- (c) optionally blending coated ibuprofen of step (b) with at least one
20 pharmaceutically acceptable excipient;
- (d) compressing the blend of step (c) into tablets and packaging into unit or multiple dose packages or packaging the blend of step (c) or coated ibuprofen of step (b) into unit or multiple dose packages.

- 25 The various dosage forms as described in the present invention comprising taste-masked ibuprofen are immediate release dosage forms that release the coated taste-enhanced ibuprofen instantly upon reaching either stomach or intestine. In one embodiment of the present invention, the dosage forms of the present invention comprise a composition wherein coated taste-masked ibuprofen is released in a
30 controlled manner over a period of time, for example, from about 2 to about 24 hours. In such a formulation, ibuprofen is coated with at least one lipophilic agent described above or any combinations thereof along with other pharmaceutical excipients such as release retardants. The lipophilic taste-masking coating employed can not only ensure the taste-masking but also control the release of ibuprofen.

In another embodiment of the present invention, pellets or granules or the like of ibuprofen are prepared comprising at least one release retardant in combination with one or more pharmaceutically acceptable excipients. Suitable release retardants, as discussed above can be polymeric or non-polymeric in nature and include, but are not limited to, cellulose ethers, such as hydroxypropylmethylcellulose (HPMC), hydroxypropylcellulose (HPC), hydroxyethylcellulose, ethyl cellulose and carboxymethylcellulose sodium; polysaccharides, such as carageenan, guar gum, xanthan gum, tragacanth and ceratonia; polymethacrylates, such as copolymers of acrylic and methacrylic acid esters containing quarternary ammonium groups; cellulose esters, such as cellulose acetate; acrylic acid polymers, such as carbomers; waxes, such as hydrogenated castor oil, hydrogenated vegetable oil, carnauba wax and microcrystalline wax; alginates, such as alginic acid and sodium alginate; and fatty acid derivatives, such as glyceryl monostearate and glyceryl palmitostearate. These pellets or granules or the like are further coated using lipophilic agents described above in order to achieve taste-masking and controlled release of ibuprofen. In one embodiment, the amount of release retardant in the formulation is from about 1 to 90% by weight of the dosage form. In another embodiment, the amount of release retardant in the formulation is about 5 to 80% by weight of the dosage form.

One embodiment of the present invention relates to the use of compositions of the present invention for treatment of conditions where ibuprofen is prescribed. Further embodiment of the present invention relates to method of treatment of conditions where ibuprofen is prescribed comprising administering to the patient in need thereof palatable oral formulations of the present invention. In a still further embodiment of the present invention the coated taste-masked ibuprofen compositions of the present invention may be adapted to deliver one or more active agents in addition to ibuprofen. The active agent may be selected from, but not limited to, pseudoephedrine hydrochloride, paracetamol, dextromethorphan hydrobromide, chlorpheniramine maleate, tramadol hydrochloride, dextromethorphan hydrochloride, omeprazole, phenylephrine, ibuprofen, naproxen, flurbiprofen, fenopropfen, ketoprofen, fenbufen, metoclopramide, cetirizine, trimethoprim, sulfamethoxazole, hydrocodone, oxycodone, diphenhydramine, celecoxib, sumatriptan, glutathione, nimodipine, aspirin, codeine phosphate, codeine sulfate, butalbital, caffeine, dihydrocodeine bitartrate, propoxyphene napsylate, diclofenac, aceclofenac, levocetirizine, methocarbamol, serratiopeptidase, chlorzoxazone, baclofen,

buprenorphine, etorocoxib, mefenamic acid, dextropropoxyphene, dexibuprofen, domperidone, ketorolac, lornoxicam, meloxicam, metoclopramide, nabumetone, nimesulide, racemethionine, ondansetron, pentazocine, parecoxib, piroxicam, betacyclodextrin, rizatriptan, loratadine, fexofendine, phenylpronolamine, pantoprazole, rabeprazole, esomeprazole, bromhexine HCl, activated dimethicone, dichloralphenazone, dicyclomine, dl-methionine, ergotamine tartrate, guaiphenesin maleate, isometheptene mucate, orphenadrine citrate, prochlorperazine maleate, promethazine, propyphenazone, serratiopeptidase or triprolidine HCl.

While the present invention has been described in terms of its specific embodiments, certain modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the present invention. Details of the present invention, including its objects and advantages, are provided in the non-limiting exemplary illustrations below.

EXAMPLES

Example 1: Palatable dispersible tablets of ibuprofen

1. Coating of ibuprofen with aqueous coating dispersion

Table 1: Composition of aqueous coating dispersion of lipophilic agent

Ingredient	%w/w
Hydrogenated vegetable oil Type 1, USP/NF	7.50
Glycerol monostearate 40-45 Type II, USP/NF (Cutina V PH)	2.00
Glyceryl ester of saturated fatty acids (Gelucire 39/01)	1.5
Demineralised Water	q.s.

Procedure: Hydrogenated vegetable oil, Gelucire 39/01 and Cutina V PH were heated in a water bath at 80°C-85°C. A part of the water was heated to 90°C and added to the molten waxy mass with constant stirring using a suitable laboratory stirrer to obtain a smooth emulsion. The emulsion was cooled to room temperature. The remaining quantity of water was added to the above emulsion under stirring. A stable homogenous emulsion was obtained which was further used for taste masking coating of ibuprofen.

Ibuprofen was then coated with this aqueous wax emulsion to 30 % weight gain using bottom spray assembly.

2. Preparation of ibuprofen dispersible tablets

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Table 2: Composition of ibuprofen dispersible tablets

Ingredients	mg/unit
Coated taste-masked ibuprofen equivalent to 200 mg ibuprofen	260
Mannitol, USP/NF	180
Microcrystalline cellulose, USP/NF	70
Croscarmellose sodium, USP/NF	35
Crospovidone, USP/NF	30
Talc, USP/NF	10
Colloidal silicon dioxide, USP/NF	8
Aspartame, USP/NF	50
Strawberry flavor	2
Magnesium stearate, USP/NF	5
Total	650

Procedure: Coated taste masked ibuprofen as prepared in the first step was mixed with the remaining excipients, except the lubricant, then lubricated and compressed into palatable dispersible tablets.

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Example 2: Palatable fast melt granules of ibuprofen

Table 3: Preparation of ibuprofen fast melt granules 100 mg

Ingredients	mg/unit
Ibuprofen	100
<i>Polymeric coating (12.50 % coating) 25% solid content</i>	
Ethyl acrylate and methyl methacrylate copolymer dispersion 40 per cent, USP/NF	6
Talc, USP/NF	4
Copovidone, Ph.Eur.	2.5

Total	112.5
<i>Aqueous coating dispersion of lipophilic agent (40% coating) 13.25% solid content</i>	
Hydrogenated Vegetable oil Type 1, USP/NF	25
Medium chain glycerides, USP/NF	9
Hydroxy propylmethyl cellulose, USP/NF	9
Talc, USP/NF	2
Total	157.5
<i>Extragranular Ingredients</i>	
Dextrose monohydrate, USP/NF	320.5
Directly compressible composite excipient comprising mannitol and calcium silicate	255
Xylitol, USP/NF	220
Sucralose, USP/NF	20
Strawberry flavor	12
Sodium stearyl fumarate, USP/NF	15
Total	1000

Procedure:

Copovidone was first dissolved in weighed quantity of water under continuous stirring. Then ethyl acrylate and methyl methacrylate copolymer and talc were added to the
5 above dispersion. Ibuprofen was later coated with the dispersion using Glatt powder coater granulator. Hydrogenated Vegetable oil Type 1 and medium chain glycerides were heated in a water bath at 80°C-85°C. A part of the water was heated to 90°C and added to the molten waxy mass with constant stirring using a suitable laboratory stirrer to obtain a smooth emulsion. The emulsion was cooled to room temperature. Hydroxy
10 propylmethyl cellulose was dissolved in the remaining water, and added to the above emulsion under stirring. A stable and uniform emulsion of lipophilic agent was obtained which was used for taste masking of ibuprofen. The aqueous coating dispersion of lipophilic agent prepared as described above was employed to coat polymer coated
15 ibuprofen to 40 % weight gain using bottom spray assembly. Coated ibuprofen was blended with all extragranular excipients except lubricant in a blender. The blend was then lubricated, blended and packed in sachets.

CLAIMS

We claim:

1. A palatable oral pharmaceutical formulation comprising coated ibuprofen
5 comprising:
ibuprofen; and
tastemasking coating comprising at least one lipophilic agent.
2. The formulation of claim 1 wherein ibuprofen is in the form of free acid, racemate,
10 pharmaceutically acceptable salt, polymorph, solvate, hydrate, anhydrous form,
ester, complex, amide, prodrug, active metabolite, analog, enantiomer,
stereoisomer, diastereomer or any combination thereof.
3. The formulation of claim 1 wherein ibuprofen is in the form of powder, granules,
15 pellets, pearls, beads, minitables, tablets or any combinations thereof.
4. The formulation of claim 1 wherein the lipophilic agent is fat, wax, fatty acid, fatty
acid ester, long chain monohydric alcohol or ester thereof, hydrogenated
vegetable oil or any combination thereof.
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5. The formulation of claim 4 wherein the lipophilic agent is hydrogenated
cottonseed oil, hydrogenated soyabean oil, hydrogenated castor oil, carbowax,
wax yellow, hydrogenated palm oil, carnauba wax, candelilla wax, spermaceti,
beeswax, montan wax, microcrystalline wax, hydrogenated tallow, paraffin wax,
25 shellac wax, petrolatum, glyceryl behenate, cetyl alcohol, cetostearyl alcohol,
precinol, stearic acid, synthetic waxes, lanolin, macrogolglycerides lauriques,
glyceryl palmitostearate, cetyl alcohol, polyglyceryl diisostearate, glyceryl
stearate, or mixtures thereof.
6. The formulation of claim 1 wherein the lipophilic agent is applied from an
30 aqueous emulsion.
7. The formulation of claim 1 wherein the tastemasking coating further comprises
polymeric agent, emulsifier, or any combination thereof.

- 5 8. The formulation of claim 7 wherein the polymeric agent is cellulose derivative, saccharide or polysaccharide, polyhydric alcohol, poly (oxyethylene)-poly(oxypropylene) block copolymer, vinyl derivative or polymer or copolymer thereof, acrylic acid derivative or any combination thereof.
9. The formulation of claim 7 wherein the emulsifier is non-ionic emulsifier, ionic emulsifier or any combination thereof.
- 10 10. The formulation of claim 1 wherein the tastemasking coating further comprises anti-tacking agent, sweetener, or any combination thereof.
11. The formulation of claim 10 wherein the anti-tacking agent is talc, glyceryl monostearate, silicon dioxide, metallic stearates or any combination thereof.
- 15 12. The formulation of claim 10 wherein the sweetener is sucralose, aspartame, stevia extract, glycyrrhiza, saccharine, saccharine sodium, acesulfame, dipotassium glycyrrhizinate, mannitol, xylitol, erythritol, isomalt, isomaltitol, lactitol, or any combination thereof.
- 20 13. The formulation of claim 1 wherein ibuprofen is seal coated with at least one polymeric agent prior to coating with the tastemasking coating.
- 25 14. The formulation of claim 13 wherein the polymeric agent is a cellulose derivative, saccharide or polysaccharide, polyhydric alcohol, poly (oxyethylene)-poly(oxypropylene) block copolymer, vinyl derivative or polymer or copolymer thereof, acrylic acid derivative or any combination thereof.
- 30 15. The formulation of claim 1 wherein the formulation further comprises at least one pharmaceutically acceptable excipient; said excipient being directly compressible coprocessed excipient, binder, disintegrant, superdisintegrant, diluent, salivating agent, surfactant, flavor, sweetener, colorant, souring agent, glidant, lubricants, solubilizer, stabilizer, viscolizer, pH modifier or any combination thereof.

16. The formulation of claim 1 wherein the formulation is in the form of suspension, dry suspension, fast melt granules, orally disintegrating tablet, dispersible tablet, chewable tablet, effervescent tablet, granules, sprinkle granules, lozenge, or chewing gum.

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17. The formulation of claim 1 wherein the formulation is an immediate release or controlled formulation.

18. The formulation of claim 1 wherein the formulation comprises an additional active agent.

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19. A process for preparation of tastemasked pharmaceutical formulation comprising

- a. coating ibuprofen with taste-masking coating composition comprising at least one lipophilic agent in aqueous emulsified form to obtain coated ibuprofen;
- b. optionally blending coated ibuprofen of step (a) with at least one pharmaceutically acceptable excipient;
- c. compressing the blend of step (b) into tablets and packaging into unit or multiple dose packages or packaging the blend of step (b) or coated ibuprofen of step (a) into unit or multiple dose packages.

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