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(54) **Title:** NOVEL BUCCOADHESIVE COMPOSITIONS AND PROCESS OF PREPARATION THEREOF

(57) **Abstract:** Novel buccoadhesive compositions comprising at least one bioactive agent(s), at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s), optionally with other excipients are provided, wherein the said composition has improved cohesiveness, enhanced intactness and improved adhesion at the desired site of the mucosa for substantially longer duration and releases the bioactive agent(s) in a sustained manner in the oral cavity for extended time period. The bioactive agent(s) is a pharmaceutically active agent(s) or a nutritional supplement(s) or a food product(s), or combinations thereof. Also provided is a process of preparation of such novel compositions and method of using them.

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NOVEL BUCCOADHESIVE COMPOSITIONS AND PROCESS OF PREPARATION THEREOF

FIELD OF THE INVENTION

The present invention describes novel buccoadhesive compositions comprising at least one bioactive agent(s), at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s), optionally with other excipients, wherein the said composition has improved cohesiveness, enhanced intactness and improved adhesion at the desired site of the mucosa for substantially longer duration and releases the bioactive agent(s) in a sustained manner in the oral cavity for extended time period. bioactive agent(s) selected from a group comprising pharmaceutically active agent(s) or its salts, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms, derivatives or mixtures thereof; nutritional supplement(s) and food product(s), or combinations thereof. Further, the present invention also provides process of preparation of such novel compositions and method of using them.

BACKGROUND OF THE INVENTION

Several approaches to deliver pharmaceutically active agents, nutritional supplements or food products in a sustained manner to the body have resulted in a variety of bioadhesive delivery systems. Various types of materials found to adhere to mucous membranes (bioadhesive) without exerting a harmful effect on the membranes. The compositions particularly comprise the drug or other agent incorporated into a bioadhesive dosage form that is intended to be placed in contact with a mucous membrane to which it adheres. The drug or other agent is dissolved from the dosage form and delivered into a body cavity or into the body through the mucous membrane. The advantages of sustained release products are well-known particularly in the pharmaceutical field and include the ability to release the medicament in a sustained manner over an extended period of time while increasing patient compliance by reducing the number of administrations necessary to achieve the desired drug level. Several sustained release compositions for delivering different pharmaceutically active agents or nutritional supplements or food products and involving different release mechanisms had been described in the prior art. The sustained release compositions disclosed previously comprise nutritional supplements such as vitamins, minerals, antioxidants, etc. that are used to supplement the nutritional deficiencies in individuals or food products such as

carbohydrates, proteins, etc. Pharmaceutical compositions intended for buccal or sub-lingual delivery preferably comprises of pharmaceutically active agent that has reduced bioavailability due to presystemic metabolism and/or intended to be delivered in a sustained manner into the body. Oral mucosal drug delivery such as buccal delivery is an alternative method of systemic drug delivery. It offers several advantages over both injectable and enteral delivery. Drugs absorbed via the oral mucosa avoid the low pH gastric fluid and proteases, as well as first-pass metabolism in the liver. Also the onset of action is faster than oral administration. Oral transmucosal delivery is non-invasive and not painful and can even be self-administered by a patient.

Ondansetron acts as a selective 5-HT_3 receptor antagonist with anti-emetic activity. It is used in the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy and is also indicated for the prevention and treatment of postoperative nausea and vomiting. The drug undergoes extensive first pass metabolism, thereby resulting in decreased absolute bioavailability (48-60%). Ondansetron (Zofran®) is generally administered as an intramuscular/intravenous injection (as 8 mg dose) immediately before treatment and/or followed by maintenance therapy (two 8 mg doses) in case of highly emetogenic chemotherapy with acute emesis. However, in less severe cases of emesis due to chemotherapy/radiotherapy, it may be administered parenterally, rectally or orally. In postoperative nausea and vomiting, it is administered thrice daily as 4 mg /8 mg dose in form of immediate release tablets or oral solution.

Domperidone is a medicine that increases the movements or contractions of the stomach and bowel. Domperidone is a dopamine antagonist with antiemetic and gastrokinetic properties; however, domperidone does not readily cross the blood-brain barrier and hence seldom causes extrapyramidal side effects. Domperidone is rapidly absorbed following intramuscular and oral administration with peak plasma concentrations (C_{max}) occurring at approximately 10 and 30 minutes (T_{max}) respectively. Systemic bioavailability of intramuscular domperidone is about 83% whereas that of oral domperidone is 13% to 17% (probably due to first pass metabolism in the liver and gut wall). Domperidone is available as Motilium® and is orally administered as 10 mg tablets 2-3 times a day.

Carvedilol is a nonselective β-adrenergic blocking agent with α_1-blocking activity. Carvedilol is rapidly and extensively absorbed following oral administration, with absolute bioavailability of approximately 25% to 35% due to a significant degree of first-pass metabolism. Carvedilol is available as Coreg® at starting low dose of 3.125 mg, twice daily tablets for 2 weeks followed by 6.25, 12.5, and 25 mg twice daily over successive intervals of at least 2 weeks. Carvedilol is indicated for the treatment of mild-to-severe heart failure of ischemic or cardiomyopathic origin.

Sumatriptan is an agonist for a vascular 5-hydroxytryptamine (5-HT_1) receptor subtype having only a weak affinity for 5-HT_{1A}, 5-HT_{5A}, and 5-HT_7 receptors. The bioavailability is approximately 15%, primarily due to presystemic metabolism and partly due to incomplete absorption. Sumatriptan is generally administered as Imitrex® 25, 50, or 100 mg of sumatriptan succinate film coated tablets. Sumatriptan succinate tablets are indicated for the acute treatment of migraine attacks with or without aura in adults.

Sustained release preparations are known to those skilled in the art to achieve a slow release of a drug over an extended period of time, thereby extending the duration of drug action over that achieved by conventional delivery. Preferably such a preparation maintains a drug concentration in the blood within the therapeutic range for 12 hours or more. Hence, buccoadhesive composition comprising particularly a pharmaceutically active agent provides advantages over conventional dosage forms including reduced fluctuations in plasma active agent levels, and reduced toxicity.

US Patent No. 5,288,498 discloses a composition for both lipophilic and non-lipophilic candidates for transmucosal delivery that enables therapeutic agents to be incorporated into non-dissolvable drug containment matrices to which an appliance or holder is preferably attached. US Publication No. 20030185886 relates to process for the preparation of a rapidly disintegrating tablet having an enhanced strength as well as a high disintegrating rate in the oral cavity, which comprises spray-drying of the active ingredient. US Publication No. 20030118653 pertains to a quick dissolving oral mucosal drug delivery device, comprising a mucosal surface-coat-forming inner layer disposed between two moisture barrier coating layers; wherein the mucosal surface-

coat-forming inner layer comprises a water-soluble hydrocolloid and an active agent; and wherein the two moisture barrier coating layers comprise a non-crosslinked polymer and a moisture barrier modifier.

US Patent No. 3,972,995 relates to dosage forms for buccal administration of a drug and is directly applicable to the interior surfaces of the mouth. The dosage form is comprised of a support member, which is water insoluble, waterproof and flexible, a moisture activated, adhesive precursor applied to one surface of the support member and an active ingredient applied to the central portion of the support member either directly or dispersed in a matrix. The active ingredient is exposed to a limited area of the oral mucosa while isolating the active ingredient from the remainder of the oral environment.

US Publication No. 20030211071 relates to a delivery system for pharmaceutical compositions relying in part on an ionic interaction to control and facilitate release of the treating agent. More specifically, the invention relates to an extended controlled-release system having an ionic treating agent and an ionic polymer, wherein the polymer is sufficiently ionized to release the treating agent in a controlled manner over an extended period of time and the composition does not require an emulsion system for administering the treating agent. US Publication No. 20040115258 describes a solid oral pharmaceutical preparation, adapted for oral administration by dispersion of pharmaceutically active ingredient from the solid preparation in the mouth, or by drinking an aqueous dispersion of the solid preparation; the preparation comprising a blend of said active ingredient with cyclodextrin as taste-masking agent for the active ingredient which is not complexed thereby. US Publication No. 20040228919 describes a non-compressed fast-dispersing solid dosage form suitable for oromucosal administration of a pharmaceutically active substance comprising a first matrix forming agent in the form of maltodextrin and a second matrix forming agent in the form of sorbitol, and the active substance.

US Patent No. 4,292,299 pertains to a slow-releasing medical preparation to be administered by adhering to a wet mucous surface comprising an adhesive layer composed of a polymer which has the adhesiveness to a wet mucous surface and a

property to swell upon moistening and a nonadhesive, either water soluble or disintegrable, layer which has no adhesiveness to a wet mucous surface and at least either one of said adhesive layer and nonadhesive layer is made to contain a medicament. US Patent No. 4,915,948 describes a tablet having improved bioadhesion to mucous membranes comprising a water-soluble natural biopolymer selected from the group consisting of a xanthan gum, pectin and mixtures thereof and a solid polyol preferably a sugar alcohol selected from the group consisting of sorbitol, xylitol, and mixtures thereof. US Patent Nos. 4,226,848 and 4,250,163 are directed to a methods for administering a medicament which comprises adhering to the mucosa of the oral or nasal cavity a pharmaceutical preparation comprising a water-swellable and mucosa-adhesive polymeric matrix, and a pharmaceutically effective amount of the medicament dispersed therein. The polymeric matrix comprises about 50-95% by weight of cellulose ether and about 50 to 5% by weight of a homo or copolymer of acrylic acid or a pharmaceutically acceptable salt thereof. US Patent No. 4,572,832 is directed to a soft buccal containing a pharmaceutically effective amount of a medicament to be absorbed through the oral mucosa, a water-soluble protein, a polyhydric alcohol, and a fatty acid ester and/or a carboxyvinyl polymer.

US Patent No. 4,597,959 discloses a breath freshener composition, in a wafer form which can be directly applied to the gums and palate or the wafer can be directly applied to the inner or outer surfaces of full or partial dentures having slow release. The composition comprises a multiplicity of microencapsulated liquid droplets of flavoring materials. The microencapsulated droplets are soluble in saliva to slowly release the flavoring materials. The microencapsulates are present in a wafer form which comprises a base of gelatin, gum arabic and/or carrageenan with an adhesive distributed throughout.

PCT Publication Nos. WO 9947124, WO 2003009831, WO 2004064810, WO 9315724, WO 2005105049, US Publication No. 20050100599 and US Patent No. 5,576,014 describe quick disintegrating tablets in buccal cavity comprising a drug and sugar or sugar alcohols and/or one or more binders and/or one or more other pharmaceutically acceptable excipients.

Thus, buccal tablets possessing the ability to adhere to the oral mucosa and release active agent(s) or nutritional supplements to the oral cavity are known in the art. The dosage forms are composed of different natural or synthetic polymers. In formulating such dosage form compositions, the primary intention is on providing dosage forms which are adherent to the mucosa during the period of use, i.e., stay in place, are capable of continued release of an active agent over a desired time period, and are comfortable to the user. However, the problems associated with such buccal delivery systems disclosed in the prior art is related to the tenacity with which the dosage form adheres to the mucous membrane. Sometimes the dosage forms become separated from the mucous membrane even before the desired dose of active agent or a nutritional supplement has been completely delivered.

Thus there still exists a need for novel buccal compositions that can provide improved adhesion, reside at the desired site of the mucosa for substantially longer duration and is capable of continual release of active agent in a sustained manner for extended time period with greater patient compliance. The novel compositions of the present invention overcomes the limitations of the prior art.

SUMMARY OF THE INVENTION

It is an objective of the present invention to provide novel buccoadhesive compositions comprising at least one bioactive agent(s), at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s), optionally with other excipients, wherein the said composition has improved cohesiveness, enhanced intactness and improved adhesion at the desired site of the mucosa for substantially longer duration and releases the bioactive agent(s) in a sustained manner in the oral cavity for extended time period.

It is an objective of the present invention to provide novel buccoadhesive compositions which releases the bioactive agent(s) in the oral cavity of the subject such that the bioactive agent is absorbed through the mucosal tissues of the oral cavity thereby bypassing the hepatic metabolism and resulting in increased bioavailability.

It is an objective of the present invention to provide novel buccoadhesive compositions comprising at least one bioactive agent(s) selected from a group comprising

pharmaceutically active agent(s) or its salts, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms, derivatives or mixtures thereof; nutritional supplement(s) and food product(s), or combinations thereof.

It is also an objective of the present invention to provide novel buccoadhesive compositions comprising at least one bioactive agent(s), at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s), optionally with other excipients, wherein the said composition has improved cohesiveness, enhanced intactness and improved adhesion at the desired site of the mucosa for substantially longer duration and releases the bioactive agent(s) in a sustained manner in the oral cavity for extended time period, and wherein the said composition additionally comprises of at least one taste masking agent(s).

It is also an objective of the present invention to provide novel buccoadhesive compositions comprising at least one bioactive agent(s), at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s), optionally with other excipients, wherein the said composition has improved cohesiveness, enhanced intactness and improved adhesion at the desired site of the mucosa for substantially longer duration and releases the bioactive agent(s) in a sustained manner in the oral cavity for extended time period, and wherein the said composition additionally comprises one or more hydrophobic polymers and/or taste masking agents and/or permeation enhancers and/or sweeteners.

It is another objective of the present invention to provide process for preparation of such composition which comprises of the following steps:

i) mixing the bioactive agent(s) with at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s),

ii) optionally adding one or more other excipients, and

iii) formulating of the mixture into a suitable dosage form.

It is yet another objective of the present invention to provide method of using such compositions which comprises administration of an effective amount of the composition.

The novel compositions of the present invention may be in the form of uncoated or coated tablets, layered tablets, patches or other dosage forms suitable for oral administration preferably for topical and/or systemic use. The novel buccoadhesive compositions are intended for use as a pharmaceutical or as a nutritional supplement or as a food product.

DETAILED DESCRIPTION OF THE INVENTION

The present invention describes novel buccoadhesive compositions comprising at least one bioactive agent(s), at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s), optionally with other excipients. The compositions have improved cohesiveness which lends integrity and enhanced intactness to the formulation. Further the compositions of the present invention exhibit improved adhesion at the desired site of the mucosa in the oral cavity for substantially longer duration and release the bioactive agent(s) in a sustained manner for extended time period. The novel buccoadhesive compositions releases the bioactive agent(s) in the oral cavity of the subject such that the bioactive agent is absorbed through the mucosal tissues of the oral cavity thereby bypassing the hepatic metabolism and resulting in increased bioavailability.

In an embodiment of the present invention, the bioactive agent(s) is selected from a group comprising pharmaceutically active agent(s) or its salts, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms, derivatives or mixtures thereof; nutritional supplement(s) and food product(s), or combinations thereof. The bioactive agent(s) is released from the compositions in a sustained manner in the oral cavity for extended time period preferably for topical and/or systemic use. The 'topical' use herein refers to the mucosal surface of the oral cavity. It must be appreciated that some active agents used in the present invention may act topically or systemically or have both effects. The novel buccoadhesive compositions are intended for use as a pharmaceutical or as a nutritional supplement or as a food product.

In another embodiment of the present invention, the novel buccoadhesive compositions comprise at least one bioactive agent(s), at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s), optionally with other

excipients, wherein the said composition has improved cohesiveness, enhanced intactness and improved adhesion at the desired site of the mucosa for substantially longer duration and releases the bioactive agent(s) in a sustained manner in the oral cavity for extended time period, and wherein the said composition additionally comprises of at least one taste masking agent(s).

In another embodiment of the present invention, the novel buccoadhesive compositions comprise at least one bioactive agent(s), at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s), optionally with other excipients, wherein the said composition has improved cohesiveness, enhanced intactness and improved adhesion at the desired site of the mucosa for substantially longer duration and releases the bioactive agent(s) in a sustained manner in the oral cavity for extended time period, and wherein the said composition additionally comprises one or more hydrophobic polymers and/or taste masking agents and/or permeation enhancers and/or sweeteners.

In one embodiment, the pharmaceutically active agent(s) or nutritional supplement(s) or food product(s) is formulated as spray dried or lyophilized complex with a cyclodextrin, preferably with a beta-cyclodextrin, more preferably with Hydroxypropyl beta cyclodextrin (HPβ-CD) which primarily aims at masking the bitter taste of the pharmaceutically active agent or nutritional supplement or food product. In an embodiment, the pharmaceutically active agent or nutritional supplement or food product is preferably formulated as an aqueous or non-aqueous solution or dispersion with HPβ-CD and then spray dried or lyophilized using techniques known to the art to obtain dry powder which is then further processed with other excipients to form the desired buccoadhesive composition. In another embodiment of the present invention, the pharmaceutically active agent(s) or nutritional supplement(s) or food product(s) and cyclodextrin may simply exist in the form of a physical mixture rather than in the form of a complex.

In a preferred embodiment, the pharmaceutically active agent of the present invention is selected from a group comprising agents that show poor bioavailability primarily due to presystemic metabolism and/or have a bitter taste and/or required to exhibit a sustained release profile. In an embodiment, the pharmaceutically active agent(s) or nutritional

supplement(s) is selected from but not limited to a group comprising abortifacients; ACE inhibitors; alpha-adrenergic agonists; beta-adrenergic agonists; alpha-adrenergic blockers; beta-adrenergic blockers; adrenocortical steroids; adrenocorticotrophic hormones; alcohol deterrents e.g. disulfiram, etc.; aldose reductase inhibitors; aldosterone antagonists; anabolics e.g. androstenediol, nandrolone, etc.; analgesics; androgens; angiotensin II receptor antagonists; anorexics e.g. aminorex, anphetamine, norpseudoephedrine, etc.; anthelmintics; antiallergics; antiamoebics; antiarrhythmics; antiarthritics/antirheumatics; antiasthmatics e.g. azelastine, ketotifen, montelukast, seratrodast, zafirlukast, zileuton, beclomethasone, budesonide, dexamethasone, flunisolide, triamcinolon acetonide, etc.; antibacterials e.g. cefazolin, cefipime, amoxicillin, ampicillin, erythromycin, vancomycin, tetracycline, trimethoprim, sulfadiazine, isoniazid, streptomycin, etc.; anticholinergics; anticoagulants; anticonvulsants e.g. carbamazepine, clonazepam, nitrazepam, etc.; antidepressant e.g. citalopram, amytriptiline, clomipramide, desipramide, bupropion, etc.; antidiabetic; antidiarreal e.g. loperamide, mebiquine, etc.; antidiuretic e.g. desmopressin, vasopressin, etc.; antidyskinetic e.g. amantidine, clonidine, haloperidol, etc.; antiemetic e.g. alizapride, azasentron, chlorpromazine, cyclizine, domperidone, granisetron, meclizine, metoclopramide, ondansetron, prochlorperazine, scopolamine, sulpiride, tropistron, etc.; antifungal e.g. miconazole, tolindate, fluconazole, triacetin, etc.; antihistaminic e.g. acrivastine, chlorpheniramine, clemastine, diphenhydramine, cetirizine, chlorcyclizine, cinnarizine, promethazine, loratadine, astemizole, azelastine, fexofenadine, terfenadine, etc.; antihyperlipoproteinemic e.g. cholestiramine, clofibrate, gemfibrozil, atorvastatin, lovastatin, etc.; antihypertensive e.g. atenolol, metoprolol, chlorthiazide, benazepril, lisinopril, amlodipine, hydralazine, phentolamine, reserpine, furosemide, etc.; antihypotensive e.g. norepinephrine, etc.; anti-inflammatory/analgesic e.g. acetaminophen, aspirin, mefenamic acid, indomethacin, diclofenac, ibuprofen, piroxicam, phenylbutazone, pentazocine, hydrocortisone, prednisolone, dexamethasone, triamcinolone acetonide, betamethasone, ketorolac, ketoprofen, naproxen, bendazac, nimesulide, etc.; anticancer drugs e.g. vinblastine, cisplatin, 5-fluorouracil, methotrexate, etc.; antifungal e.g. amphotericin, clotrimazole, fluconazole, griseofulvin, itraconazole, ketoconazole, miconazole, nystatin, terbinafine, etc.; anti-malarial; antiarrhythmics; antimigraine e.g. dolasetron, sumatriptan, etc.; antiparkinsonian; antipsychotic e.g. risperidone, haloperidol, chlorpromazine, etc.; antipyretic; antispasmodic e.g. aminopromazine, fentonium, rociverine, tiropramide, etc.; antitussive e.g. dextromethorphan, etc.; antiulcerative e.g.

famotidine, omeprazole, ranitidine, sucralfate, etc.; anxiolytic e.g buspirone, alprazolam, lorazepam, etc.; bronchodilator e.g. salmeterol, terbutaline, theophilline, etc.; calcium channel blocker e.g. diltiazem, verapamil, amlodipine, nifedipine, etc.; cardiotonics; cholinergics; CNS stimulants; diuretic e.g. acetazolamide, furosemide, isosorbide, etc.; dopamine receptor antagonist e.g. amisulpride, etc.; enzymes; gastroprokinetic e.g. cinitapride, cisapride, fedotozine, loxiglumide, etc.; glucocorticoid; leukotriene antagonist e.g ibudilast, montelukast, zafirlukast etc.; mineralcorticoids; monoamine oxidase inhibitors; muscle relaxants; narcotic antagonist e.g. amiphenazole, naltaxone etc; progestogen; prolactin inhibitor e.g. bromocriptine, etc.; prostaglandin/prostaglandin analogs; peptide or protein drugs or polysaccharides e.g. goserelin, leuprorelin, calcitonin, cyclosporin, somatostatin, vasopressin, interferon, human growth hormone, immunogenic proteins/polysaccharides, etc.; antivirals e.g. lamivudine, stavudine, zidovudine, etc.; sedative/hypnotic e.g. zolpidem, flurazepam, methaqualone, glutethimide, etc; serotonin noradrenaline reuptake inhibitor e.g. duloxetine, velanfaxine, etc.; serotonin reuptake agonist e.g buspirone, ergotamine, sumatriptan etc.; serotonin receptor antagonist e.g. dolasetron, granisetron, ondansetron, ritanserin, tropisetron, etc.; serotonin uptake inhibitor e.g. fluoxetine, paroxetine, etc.; vasodilators e.g cinnarizine, nitroglycerin, etc.; vasoconstrictors e.g. oxymetazoline, etc.; vitamins e.g. calcitriol, ergosterol, vitamin D, ascorbic acid, beta-carotene, vitamin B, etc.; breath fresheners; tooth-whitening agents e.g. carbamide peroxide, etc.; tooth-desensitizing agents e.g. potassium nitrate and strontium chloride; and the like, or their pharmaceutically acceptable salts, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms, derivatives or mixtures thereof used either alone or in combinations thereof. Some agents, as will be appreciated by those of ordinary skill in the art, are encompassed by two or more of the aforementioned groups. Preferably the pharmaceutically active agent is selected from a group comprising ondansetron, domperidone, carvedilol, and sumatriptan or their pharmaceutically acceptable salts, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms, derivatives or mixtures thereof.

In an embodiment, the pharmaceutically active agent(s) of the present invention is selected from a group comprising peptides, polypeptides or proteins including but not limited to a group comprising enzymes, heparin, antigens, calcitonin, cyclosporin, insulin, oxytocin, tyrosine, enkephalin, tyrotropin releasing hormone (TRH), follicle

stimulating hormone (FSH), luteinizing hormone (LH), growth hormone, clotting factor VIII & IX, glucocerebrosidase, vasopressin and vasopressin analogs, catalase, superoxide dismutase, interleukin-II (IL2), interferon, colony stimulating factor (CSF), tumor necrosis factor (TNF) or melanocyte-stimulating hormone, erythropoietin, thrombopoietin, etanercept, and the like, or mixtures thereof. Other peptide or protein drugs known to the art may also be contained in the buccoadhesive delivery system of the present invention.

In an embodiment, the nutritional supplement(s) is selected from but not limited to a group comprising vitamins, peptide, polypeptides, proteins, carbohydrates, lipids and minerals. Food products are selected from a group comprising caffeine, chocolates, breath fresheners, flavors, agents that provide cooling effect in the oral cavity such as peppermint oil, sugars or sugar alcohols such as mannitol, herbal products, and the like or mixtures thereof.

In an embodiment, the present invention provides novel buccoadhesive compositions comprising at least one pharmaceutically active agent(s) selected from a group comprising ondansetron, domperidone, carvedilol, and sumatriptan or their pharmaceutically acceptable salts, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms, derivatives or mixtures thereof, at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s), optionally with other excipients.

In an embodiment, the pharmaceutically active agent(s) or nutritional supplement(s) may be administered to provide a local or topical effect within the oral cavity (e.g., as a topical anti-infective or anaesthetic), or to achieve a systemic effect by passing through the mucosal membranes within the oral cavity and into an individual's blood stream. The dosage forms of the invention are well-suited to administer pharmaceutically active agent(s) or nutritional supplement(s) whose efficacy increases as a result of an extended residence time in the oral cavity, which results in greater oral mucosal absorption of any particular agent e.g. agents that are degraded in or otherwise rendered unstable in the gastrointestinal tract, agents which the stomach may not tolerate and allergy medications for rapid relief of allergic symptoms.

In an embodiment, the composition of the present invention comprises one or more anti-inflammatory, analgesic, antibiotic, antiviral or antiallergic agents that can be used for treating one or more diseases/disorders of the oral cavity, either for local and/or systemic action, such as gum disease, oral mucositis, cold sores, periodontal disease, aphthous ulcer, and pain following surgeries of the oral cavity or gums, bad breath, tooth-cavities, toothache, and the like, which requires the dosage form to be retained for longer duration in oral mucosa and release the active agent in a controlled manner for a prolonged duration.

In an embodiment of the present invention, the bioadhesive polymer is selected from but not limited to a group comprising cellulosic polymers such as sodium carboxymethylcellulose (e.g. Blanose® 7MXF, Blanose® 7HOF; Blanose® 7H4XF, Blanose® 7H3SXF, Blanose® 9MXF, Blanose® 12MXF, Cekol® 500T), methylcellulose, low molecular weight hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose (Klucel®EXF); enteric and non-enteric cellulose esters; low molecular weight polyvinyl alcohol; medium viscosity polyvinyl alcohol; polyoxyethylene glycols; alginates such as sodium alginate; polyethylene oxide; vinyl polymers or copolymers such as polyvinyl pyrrolidone; polyacrylic acid (PAA) such as carbomers and polycarbophil, and the like used either alone or in combination thereof.

In another embodiment of the present invention, the water soluble sugar component used to formulate the buccal compositions are preferably selected such that when the sugar(s) gets dissolved slowly in the environment of the oral mucosa, they do not produce any gritty or unpleasant feel in the mouth. The said component is selected from but not limited to a group comprising Sugar® DC (directly compressible sucrose), Nutab® (mixture of sucrose, invert sugar and magnesium stearate), maltodextrin, starch, sucrose, sucrose-based diluents, confectioner's sugar, dextrin, dextrose, dextran, dextrates, inositol, amylose, cellulose, maltose, dried invert sugar, lactose, mannose, xylose, ribose, glucose, fructose, levulose, galactose, corn syrup, high fructose corn syrup, partially hydrolyzed starch, saccharin, sorbitol, mannitol, xylitol, maltitol, isomalt, hydrogenated starch hydrolysate and the like, or combinations thereof.

In an embodiment of the present invention, the binder is used preferably to increase cohesiveness and promotes more gradual erosion of the dosage form in the oral cavity. The

said binder is preferably water soluble or at least hydrophilic or water miscible and is selected from but not limited to a group comprising vinyl polymers or copolymers such as polyvinyl pyrrolidone, vinyl acetate (Plasdone ® S630), starch, cellulosic polymers, polycarbophil, polyethylene oxide, arabic gum and the like, or mixtures thereof.

In an embodiment, the compositions of the present invention comprise at least one additional pharmaceutically active agent(s) or nutritional supplement(s) or food product(s). Any of the aforementioned pharmaceutically active agent(s) or nutritional supplement(s) or food product(s) may also be administered in combination using the present compositions. Active agents administered in combination may be from the same therapeutic class e.g. two antihistamines or from different therapeutic classes e.g. an antiemetic and an antimigraine drug or mineral(s) and vitamin(s).

In an embodiment of the present invention, the novel buccoadhesive compositions additionally comprise a water insoluble additive/polymer such as a hydrophobic polymer. In a further embodiment, the hydrophobic polymer is selected from but not limited to a group comprising acrylic polymers, including but not limited to acrylic acid and methacrylic acid copolymers such as Eudragit® RLPO and Eudragit® RSPO, methyl methacrylate copolymers, ethoxyethyl methacrylates, cyanoethyl methacrylate, aminoalkyl methacrylate copolymer, poly(acrylic acid), poly(methacrylic acid), methacrylic acid alkylamide copolymer, poly(methyl methacrylate), poly(methacrylic acid) (anhydride), methyl methacrylate, polymethacrylate, poly(methyl methacrylate), poly(methyl methacrylate) copolymer, polyacrylamide, aminoalkyl methacrylate copolymer, poly(methacrylic acid anhydride), glycidyl methacrylate copolymers, and the like, or mixtures thereof. In a preferred embodiment, the hydrophobic polymer which may be used is a hydrophobic cellulosic material such as ethylcellulose or alkyl cellulosic polymer(s). Those skilled in the art will appreciate that other hydrophobic polymers can also be used in the present invention.

In the present invention, the water insoluble additive/polymer such as a hydrophobic polymer is preferably used alongwith the bioadhesive polymer to aid in achieving a firm hydrogel which gradually erodes without creating a diffusional barrier and thus provides a better control over the erosion rate of the dosage form. Hydrogel forming materials such as sodium carboxymethylcellulose alongwith Eudragit® RLPO are selected in a manner such that they

are able to swell in the buccal cavity and at the same time erode, since, if they only swell, they will create a diffusional barrier (as in case of a conventional sustained release formulation) that will risk the synchronized release of the bioactive agent. In case of water insoluble hydrogels like Polyacrylic acid (PAA), the hydrophilic matrices are made such that they are capable of swelling when placed in aqueous medium. Normally, hydrogels are cross-linked so that they would not dissolve in the medium and would only absorb water initially. When drugs are loaded into these hydrogels, as water is absorbed into the matrix, chain relaxation occurs and drug molecules are released through the spaces or channels within the hydrogel network.

In yet another embodiment, the compositions of the present invention additionally comprises a permeation enhancer, preferably to increase permeation of bioactive agent(s) into the tissues of the oral cavity, and is selected from but not limited to a group comprising sodium cholate, sodium glycocholate, sodium glycodeoxycholate, taurodeoxycholate, sodium deoxycholate, sodium lithocholate chenocholate, chenodeoxycholate, ursocholate, ursodeoxy-cholate, hydrodeoxycholate, dehydrocholate, glycochenocholate, taurochenocholate, taurochenodeoxycholate, sodium dodecyl sulfate, dimethyl sulfoxide, sodium lauryl sulfate, salts and other derivatives of saturated and unsaturated fatty acids, surfactants, bile salt analogs, derivatives of bile salts. In a further embodiment, the permeation enhancer is a medium chain monoglyceride like glyceryl monocaprylate (Imwitor®), glyceryl caprylate/caprate (such as Capmul®) and polyoxyethylene glyceryl caproate (such as Labrasol®), di-fatty acid esters of polyethylene glycols such as Gelucire® 44/14 (primarily a fatty acid ester of polyethylene glycol (PEG-1500), available from Gattefossé, Saint-Priest, France) and Gelucire® 50/13, medium chain fatty acid esters such as medium chain triglycerides, or a mixture of glyceryl tricaprate and glyceryl tricaprilate (Miglyol® 612) and the like, used either alone or in combination thereof. Permeation enhancers useful in the present invention can also be small polar solvents, e.g. ethanol, propylene glycol, dimethylsulfoxide and amphiphilic compounds containing a polar head and a hydrophobic chain, e.g. fatty acids and alcohols, 1-dodecylazepan-2-one (Azone), 2-nonyl-1,3-dioxolane (SEPA 009), and dodecyl-2-dimethylaminopropanoate (DDAIP). Other permeation enhancers that are useful in the present invention include glycerol monooleate, azone, glycol, pyrrolidone, fatty alcohol, fatty acid and ester thereof, propylene glycol monolaurate (PGML), propylene glycol (PG), oleic acid, lauric acid, oleyl alcohol, lauryl

alcohol, vitamin E-TPGS (d-alpha-tocopheryl polyethylene glycol 1000 succinate), methyl sulfonyl methane, and the like or any other agent which enhances the permeation of the active agent. In another embodiment, two or more permeation enhancers can be used in a suitable mixture to act synergically. The permeation enhancer is used in making compositions according to the present invention for the administration of anti-inflammatory and/or antibiotic agents to treat oral mucositis, cold sores, periodontal disease, and pain following surgeries of the oral cavity or gums and/or for faster absorption of the active agent through the oral mucosa and into the bloodstream to achieve enhanced systemic levels of the agent that has low oral bioavailability and does not readily penetrate through mucosal tissue.

The excipients according to the present invention are selected from excipients generally used by persons skilled in the art e.g. diluents or fillers, binders, stabilizers, lubricants, anti-adherents or glidants, antioxidants, vehicles, buffers, preservatives, complexing agents, colorants, flavorants, pH modifiers, channel formers, viscosifiers, gelling agents, tonicity modifiers, lipid components, plasticizers, organic solvents, stabilizers, chelating agents, optionally anticaking agents, disintegrants, coating agents and optionally sweeteners such as natural and artificial, water soluble, and intense sweeteners. The sweetening agent is selected from but not limited to a group comprising dextrose, sucrose, maltose, dextrin, dried invert sugar, mannose, xylose, ribose, glucose, fructose, levulose, galactose, corn syrup, high fructose corn syrup, corn syrup solids, partially hydrolyzed starch, aspartame, neotame, cyclamates, glycyrrhizin, saccharin, sugar alcohols such as sorbitol, mannitol, xylitol, maltitol, isomalt, and hydrogenated starch hydrolysate or combinations thereof. Intense sweeteners such as dipeptide based intense sweeteners, monellin, thaumaoccous danielli, and L-aspartyl L-phenylalanine methyl ester and soluble saccharin salts may be incorporated as sweeteners and the like known to the art used either alone or in combination thereof. The diluents or fillers useful in the present invention are selected from but not limited to a group comprising maltodextrin, lactose, starch, mannitol, sorbitol, dextrose, microcrystalline cellulose, dibasic calcium phosphate, sucrose-based diluents, confectioner's sugar, monobasic calcium sulfate monohydrate, calcium sulfate, calcium lactate, dextrose, dextran, dextrates, inositol, hydrolyzed cereal solids, amylose, powdered cellulose, calcium carbonate, cellulose powder, starches, pregelatinized starch, sucrose, xylitol, lactitol, sorbitol, sodium chloride, polyethylene glycol, glycine, or bentonites, and the like. The lubricants used in the present invention are selected from but not limited to a

group comprising talc, magnesium stearate, calcium stearate, zinc stearate, stearic acid, hydrogenated vegetable oil, sodium stearyl fumarate, glyceryl behenate, waxes and the like. Preferably the lubricant used in the present invention does not produce a gritty or unpleasant feeling in the oral cavity such as, for example, sodium stearyl fumarate or the like. The anti-adherents or glidants are selected from but not limited to a group comprising talc, corn starch, DL-leucine, sodium lauryl sulfate, magnesium stearate, calcium stearate, sodium stearate, colloidal silicon dioxide, and the like. The stabilizers useful in the present invention are selected from but not limited to a group comprising antioxidants, buffers, acids, alkalis, and the like. The disintegrants used in the present invention are selected from but not limited to a group comprising croscarmellose sodium (e.g. Primellose®, Vivasol®), sodium starch glycollate, cross-linked sodium carboxymethylcellulose (e.g. Ac-di-sol®), starches, pregelatinized starch, celluloses, cross-linked carboxymethylcellulose, crospovidone, clays, alginates, gums and the like. The anticaking agents useful in the present invention are selected from but not limited to a group comprising silicates such as sodium aluminosilicate, calcium silicate, silicon dioxide, and the like or mixtures thereof.

In order to mask and/or enhance the taste of the dosage form in accordance with the present invention, at least one sweetener is preferably incorporated into the formulation. The sweetener may be a sugar, e.g., sucrose, fructose, or dextrose, or, more preferably, a non-sugar sweetening agent to reduce both caloric intake and the likelihood of dental caries. Sweeteners falling within the latter group include many well known artificial sweetening agents, such as, for instance, aspartame, saccharin, saccharin salts (e.g., sodium saccharin, calcium saccharin), sucralose, acesulfame-K (potassium acetosulfam), sorbitol, xylitol, stevioside, steviol, mannitol, erythritol, lactitol, alitame, miraculin, monellin, and thaumatin. When the dosage form composition in accordance with the present invention is in the form of buccoadhesive tablets or lozenges or gums or patches, the sweetener is preferably incorporated within the matrix, i.e., physically entrapped therein, while when the dosage form is in the form of buccoadhesive granules or powder, the sweetener is intimately mixed with the other components.

In another embodiment of the present invention, the compositions comprise at least one flavor for providing pleasant taste or to mask the unpleasant taste of the pharmaceutically active agent(s) or nutritional supplement(s) or food product(s) for better acceptability by the user. Flavors may be combined, as desired, to produce a particular flavor mix which is

compatible with a particular medication. Examples of flavors include but are not limited to a group comprising vanilla, mint, strawberry, cherry, spearmint, grape, coconut, chocolate, menthol, licorice, lemon, butterscotch, essential oils such as citrus oils e.g. lemon oil, lime oil, neroli oil, and orange oil, mint oils e.g. peppermint oil and spearmint oil, and other oils e.g. anise oil, cardamom oil, cinnamon oil, clove oil, coriander oil, eriodictyon fluidextract, eucalyptus oil, fennel oil, glycyrrhiza extract, lemongrass oil, and nutmeg oil, or the like, or suitable mixtures. Preferred flavors are those that, in an aqueous environment e.g., in the mouth gradually release the flavor(s).

In an embodiment, the compositions of the present invention may additionally comprise of a colorant in order to produce a desirable color. Coloring may also be important as a code to indicate the type and concentration of pharmaceutically active agent or nutritional supplement or food product present in a particular composition. Any type of color known to be 'FD&C' certified may be used to provide coloring to the product. Suitable colorants include natural colorants, i.e., pigments and dyes obtained from mineral, plant, and animal sources. Examples of natural colorants include red ferric oxide, yellow ferric oxide, annattenes, alizarin, indigo, rutin, and quercetin. Synthetic colorants may also be used, and will typically be an FD&C or D&C dye, e.g., an approved dye selected from the so-called 'coal-tar' dyes, such as a nitroso dye, a nitro dye, an azo dye, an oxazine, a thiazine, a pyrazolone, a xanthene, an indigoid, an anthraquinone, an acridine, a rosaniline, a phthalein, a quinoline, or a 'lake' thereof, i.e., an aluminum or calcium salt thereof. Particularly preferred colorants are food colorants in the 'GRAS' (Generally Regarded As Safe) category.

Other optional excipients that are useful in the present invention include but are not limited to release rate modifiers such as water soluble cellulosic polymers; ingestible solvents e.g. ethyl acetate, ethanol, glycerol, glycerol esters, etc.; adhesion modifiers e.g. ingestible solvents, mineral oil and vegetable oils and additional polymers and polymer compositions, including polymers typically used to form hydrogels e.g. ethylene vinyl acetate, polyvinyl alcohol, polyvinyl pyrrolidone, cellulose acetate, cellulose diacetate, and other cellulose esters; flavor stabilizers e.g. starches, etc.; pH-adjusting agents e.g. acids, bases, buffer systems, etc.; antioxidants; preservatives e.g. antimicrobial agents, etc. and any other excipient(s) known to or are obvious to a person skilled in relevant art, used either alone or

in combination thereof. It will be appreciated that certain excipients used in the present composition can serve more than one purpose.

In a further embodiment of the present invention is provided a composition which additionally may contain a cyclodextrin which may be an alpha, beta, or gamma cyclodextrin or cyclodextrin derivatives such as hydroxypropyl-.beta.-cyclodextrin, and acylated and modified cyclodextrins. In a preferred embodiment, the cyclodextrin is a beta.-cyclodextrin or derivative thereof, more preferably Hydroxypropyl beta cyclodextrin (HPβ-CD). The cyclodextrin used in the present invention functions as a taste masking agent and/or permeation enhancer and/or a channel forming agent depending on the type, nature and dose of the pharmaceutically active agent or nutritional supplement or food product used in the composition. In yet another embodiment, the compositions may contain optionally an ingestible acid component such as citric, tartaric, malic, maleic, fumaric, adipic, ascorbic, aspartic, succinic or alginic acids, or suitable mixtures thereof. Acid salts and anhydrides may also be used. In yet another embodiment, the compositions may contain optionally an ingestible base component, e.g. metallic oxides, hydroxides or carbonates like magnesium oxide, sodium hydroxide, sodium bicarbonate etc. Organic amines like triethanolamine etc. may also be used. In an aspect of the present invention, when either an acid or a base component exists, the said component renders the microenviromental pH of the hydrated dosage form to either acidic or basic pH. Also an optimum concentration of acidic or basic component is used in the composition to obtain a near-neutral or neutral pH, which triggers the drug release and also ensures the buccal retention of the dosage form.

In an embodiment, the compositions of the present invention comprises nutritional supplement in an amount that can be used to supplement the nutritional deficiencies observed in subjects afflicted with a disorder.

In a preferred embodiment of the present invention, the novel buccoadhesive compositions are in the form of matrix type sustained release dosage form. In an embodiment, the appropriate amount of any beneficial agent such as a pharmaceutically active agent(s) or a nutritional supplement(s) or a food product(s) in the dosage form will depend on the particular agent and/or the intended daily dose and/or the intended use. Unless explicitly indicated herein, it is to be understood that appropriate daily

doses for the various agents will be known to those of ordinary skill in the art of pharmaceutical formulation and pharmacology and/or can be found in the pertinent texts and literature. In another embodiment of the present invention, the novel buccoadhesive compositions are in the form of an inlay tablet where the pharmaceutically active agent(s) or the nutritional supplement(s) or the food product(s) exhibits a unidirectional release in a sustained manner for extended time period.

The sustained release dosage form may be in the form of tablets, patches and other dosage forms suitable for oral administration. In a preferred embodiment, the composition of the present invention is in the form of tablets. In the most preferred embodiments, the buccoadhesive sustained release oral dosage form may be in the form of matrix tablets, inlay tablets, bilayer layer tablets or the like. The tablets can be prepared by either direct compression, dry compression (slugging or compaction) or by granulation or a combination of compaction and direct compression. In a preferred embodiment of the present invention, the oral composition is prepared by compaction. The composition prepared by granulation technique is either aqueous or non-aqueous. The non-aqueous solvent used is selected from a group comprising ethanol, isopropyl alcohol or methylene chloride. In an embodiment, the compositions of the present invention are in the form of compacted tablets, compressed tablets, or moulded tablets prepared by extrusion or film cast technique or the like. The tablets might be optionally coated. The tablets may be formulated as layered tablets comprising at least two layers wherein the same bioactive agent is present in both or all the layers exhibiting different release profiles or one or more additional bioactive agent(s) is present in the layers exhibiting different release profiles. The layered tablet may comprise one layer comprising the bioactive agent(s) and at least one another layer which is a backing layer comprising at least one mucoadhesive agent.

In a preferred embodiment of the present invention, the matrix type composition comprises bioactive agent(s) in a range from about 0.5 % to about 75 % by weight of the composition, usually in the form of a complex with cyclodextrins in the ratio of about 1:10 to about 10:1 by weight of the composition. In further embodiment of the present invention, the buccoadhesive polymer is in the range from about 0.5 to about 70 % by weight of the composition. In another embodiment of the present invention, binders are preferably present in the range from about 1 % to about 20 % by weight of

the composition. In yet another preferred embodiment of the present invention, the water soluble sugar component is present in the range from about 2 % to about 70 % by weight of the composition. Further, the amount of lubricants in the composition are preferably used in an amount of from about 0 % to about 10 %, more preferably from about 0.5% to about 5% by weight of the composition. In another preferred embodiment of the present invention, the hydrophobic polymers that may be used in the present invention are in the range from about 2 % to about 50 % by weight of the composition. In another preferred embodiment, the amount of the swellable polymers preferably used in the formulation of inlay tablets are in the range of from about 1 % to about 60 % by weight of the composition. In another preferred embodiment, the solid oral dosage forms of the present invention may be in the form of compressed or compacted tablet.

In another embodiment is provided a process for preparation of such composition in accordance with the present invention which comprises of the following steps:

i) mixing the bioactive agent(s) with at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s),

ii) optionally adding one or more other excipients, and

iii) formulating the mixture into a suitable dosage form.

In a preferred embodiment of the present invention is provided a process for preparation of such composition which comprises of the following steps:

i) mixing the bioactive agent(s) or bioactive agent(s) complexed with HPβ-CD with filler(s), buccoadhesive polymer(s), binder(s), sweetener(s), sugar, color and flavor, optionally with other excipients,

ii) mixing the contents in step (i) with one part of lubricant(s) and roller compacting the blend to obtain compacts,

iii) crushing the compacts/slugs and passing the compacts through suitable sieve to obtain granules,

iv) mixing the granules with the remaining part of lubricant(s) optionally with other excipients, and

v) optionally compressing the blend of step (iv) into a suitable compressed dosage form.

In another preferred embodiment of the present invention, the process for preparation of the novel compositions of the present invention comprises of the following steps:

A) Core layer:

i) mixing the bioactive agent(s) or bioactive agent(s) complexed with HPβ-CD, with filler(s), buccoadhesive polymer(s), binder(s), sweetener(s), sugar, color and flavor, optionally with other excipients,

ii) mixing the contents in step (i) with one part of lubricant(s) and roller compacting to obtain compacts,

iii) crushing the compacts/slugs and passing the compacts through suitable sieve to obtain granules, and

iv) mixing the granules with the remaining part of lubricant(s) optionally with other excipients.

B) Backing layer:

i) mixing the hydrophobic polymer(s), binder(s), pH independent polymer(s) and a part of lubricant(s) optionally with other excipients followed by sifting through suitable sieve,

ii) mixing the contents in step (i) with part of lubricant(s) and roller compacting the contents to obtain compacts,

iii) crushing the compacts/slugs and passing the compacts through suitable sieve to obtain granules,

iv) mixing the granules with the remaining part of lubricant(s), optionally with other excipients, and

compressing the granules of step A (iv) and step B (iv) into suitable dosage form.

The formulation of the dosage form in the present invention follows an easy and convenient manufacturing procedure, requiring no sophisticated equipments or process controls. In an embodiment, particularly the sustained/extended delivery of the pharmaceutically active agent ensures reduction in administration frequency, better patient compliance and decrease in plasma level fluctuations. Furthermore, the buccoadhesive dosage form releases the bioactive agent in the mouth of the user followed by absorption through the mucosal tissues of the mouth, thereby bypassing the hepatic metabolism. This results in increased bioavailability and thus a reduction in

total drug dose. The bioactive agent is released primarily by the erosion mechanism from the novel compositions of the present invention.

In a preferred embodiment of the present invention, when Ondansetron is used as the active agent, the ondansetron is first complexed with HPβ-CD. The said complex is preferably prepared by dissolving or dispersing both the components in about 1:10 to 10:1 ratio (w/w), in an aqueous medium or aqueous/solvent system followed by spray drying or lyophilizing to get free flowing solid powder, which is then further processed with at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s), optionally adding one or more other excipients, and formulating of the mixture into a suitable dosage form.

In another aspect, the process of preparation of composition of the present invention involves complexation of the bioactive agent(s) with cyclodextrins resulting in the formation of an inclusion complex which aims at masking the bitter taste of the bioactive agent(s). The other embodiment of the present invention dealing with the tablets having an inlaid portion, are developed with an aim to prevent the loss of the bioactive agent into the saliva and ensuring a higher absorption through the buccal mucosa because of the unidirectional release of the bioactive agent from the exposed surface of the inlaid portion. In a still further embodiment, the combination of the buccoadhesive polymer with the binders enhances the intactness of the dosage form, preferably a tablet. The tablet shape is retained up to at least 3-6 hours or more in vitro with the total drug release in about 5-10 hours in the selected dissolution media. The in vivo retention (retention in the oral cavity) is for more than about 3 hours, preferably for a period of 5-12 hours with no bitter aftertaste and no substantially insoluble residues in the mouth of the user. In an embodiment, the compositions of the present invention is capable of releasing the active agent at a constant rate in a linear fashion up to the complete release of the active agent as evidenced in phosphate buffer pH 6.0 media. The dissolution media is chosen taking into consideration the pH conditions of the buccal cavity.

Buccoadhesion of a dosage form is believed to occur in three stages namely wetting, interpenetration and mechanical interlocking between mucin and polymer used to formulate the dosage form composition. It is thus important to realize that a balanced adhesive and cohesive property is essential for a polymer for its application in a transmucosal drug delivery system, especially for the removable devices. Hence, it is evident that the rate of hydration of

the device shall determine the initial degree of mucoadhesiveness of the dosage form and, in turn, determines the buccal residence time of the dosage form. In the present invention, the ratio of the bioadhesive polymer(s) and the water soluble sugar component(s) used to formulate the composition produces optimum hydration of the dosage form within a short period of contact with the buccal tissue so as to produce the desired degree of buccoadhesiveness and the duration of the buccal retention. Further the ratio of the bioadhesive polymer and the water soluble sugar component determines the hydration rate, rate of swelling and rate of erosion of the dosage form in the oral cavity, which, in turn, governs the efficiency of the buccoadhesive dosage form and patient compliance. In an aspect of the present invention, the buccoadhesive dosage form are intended to be used in the day time or in the night, preferably before bed time, depending on the use of the active agent(s) in the device.

In the present invention, the buccoadhesive dosage forms are small and flexible enough to be accepted by the patient, and do not cause irritation. These requirements are met by using a bioadhesive polymer which is preferably a hydrogel-forming polymer such as a cellulosic polymer that is capable of swelling in aqueous media. These polymer(s) swell, and the component molecules dissolve from the surface of the matrix. The active agent then releases through the spaces or channels within the gel or gel-like network as well as through the dissolution and/or the disintegration of the matrix. Primarily the hydrogel-forming polymers have numerous large-size pores, wherein most of the pores inside are interconnected to form an open channel system. In the dry state, the pores remain tightly connected to each other forming no capillary channels. Because of this, such polymers cannot swell extremely fast upon contact with water. Hence, the presence of a water soluble sugar component hydrates the dosage form faster and thus provides the desired mechanical and elasticity properties initially so that the dosage form sticks at the desired site of the oral mucosa.

The compositions of the present invention comprises optimum concentration of bioadhesive polymer and water soluble sugar component which provides desired water uptake/swelling so that the swelled mass erodes slowly in the buccal cavity without leaving any residual swollen mass or gritty particles that may result in an unpleasant feeling in the oral cavity. The rate of hydration of the dosage form largely depends on the ratio of bioadhesive polymer and water soluble sugar component. The optimum

ratio between the polymer and water soluble sugar component, which is preferably between about 1:10 to about 10:1 provides the initial hydration of the dosage form, which determines the buccoadhesiveness of the dosage form. Further the ratio of the polymer and the water soluble component determines the hydration rate, rate of swelling and rate of erosion of the dosage form in the oral cavity, which improves the patient compliance. The molecular weight of the bioadhesive polymer also plays a significant role with respect to buccal residence time of the dosage form; higher the molecular weight, greater is the retention time of the dosage form containing equal quantity of water soluble sugar component. However, even the dosage form containing the lower molecular weight bioadhesive polymer with optimal concentration will give higher buccal residence time. In the present invention, the use of optimum ratio of polymer with the water soluble channel formers provides the desired buccal adhesivity in less than about 2-3 minutes, preferably in less than a minute holding time at the contact surface, and the dosage form is retained in the contact surface for a prolonged period of time to release the active agent. In the buccal sustained release matrix systems of the present invention, the active agent is incorporated into a matrix comprising of hydrophilic polymer optimally with water soluble additives optionally with water insoluble additives/polymers. The predominant mechanism of drug release from these systems is by diffusion, erosion, or a combination of both mechanisms.

A study was carried out on two compositions namely Ondansetron buccoadhesive tablets 8 mg (as described hereinafter under Example-1) and Ondansetron buccoadhesive tablets 16 mg (as described hereinafter under Example-2) in order to evaluate buccal retention and patient acceptability for the dosage form in a randomized double blind two way cross over study in eight human volunteers. The study was done in two periods (Period I and Period II) wherein Period II was initiated after 7 days of wash out period of Period I. One buccoadhesive tablet of Ondansetron was placed in buccal cavity tissue underneath the upper lip, opposite to either left or right canine gingival after wiping of excess saliva in the buccal tissue placement site. The two formulations were evaluated for their buccal retention, taste and feel in the patient's mouth on a score scale of 0-10 (1-4: poor taste and feel, 4-6: good taste and feel, 6-8: very good taste and feel and 8-10: excellent taste and feel). Result is summarized in table-1 as follows:

Table-1: Dosage form comfort rating - Ondansetron Buccoadhesive tablets

Volunteer No.	Product tested	Period I Rating (Hourly)						Product tested	Period II Rating (Hourly)					
		1 hr	2 hr	3 hr	4 hr	5 hr	6 hr		1 hr	2 hr	3 hr	4 hr	5 hr	6 hr
1	Example-1	7	7	6	6	--	--	Example-2	6	6	6	6	5	5
2	Example-2	6	6	6	6	6	6	Example-1	7	7	7	6	5	--
3	Example-1	7	7	7	6	--	--	Example-2	6	6	5	5	4	4
4	Example-2	7	7	6	6	6	5	Example-1	6	6	5	5	--	--
5	Example-1	7	7	7	6	5	--	Example-2	7	6	6	6	5	5
6	Example-2	6	6	6	5	5	5	Example-1	6	6	5	5	4	--
7	Example-1	8	7	7	6	--	--	Example-2	8	8	7	7	6	6
8	Example-2	7	6	6	6	5	5	Example-1	7	6	5	5	5	--

Results showed that Ondansetron buccoadhesive tablets 8 mg (Example-1) were retained for about 4-4.5 hours and Ondansetron buccoadhesive tablets 16 mg (Example-2) were retained for about 7-8 hours in oral cavity. Further, it was observed that both formulations (Example-1 and Example-2) stuck to the buccal mucosa in less than 30 seconds after administration. It was also concluded that the patient acceptability ranged from very good to good with a good taste and mouth feel and no experience of gritty/insoluble residues or bitter aftertaste. Furthermore, no localized or systemic side effects were noticed thereafter.

In a further embodiment, the compositions of the present invention comprising pharmaceutically active agent(s) were subjected to in vitro dissolution study in a dissolution media having a pH ranging from 1 to 9, preferably having a pH of about 6. About 0-40% of the active agent(s) was released within 2 hours and greater than 50% of the active agent(s) was released after 8 hours of test. In a still further embodiment, the compositions of the present invention are studied in healthy human volunteers. The time taken to reach the peak plasma concentration (C_{max}) by the compositions of the present invention is in the range of 0.5-16 hours (T_{max}), preferably in the range of 1-14 hours. However, it might be emphasized that the selection of the in vitro dissolution study media, the parameters and apparatus is made in such a manner so as to provide a scientific rationale to the intended study and/or a logical correlation to the in vivo data as understood by a person skilled in art, and any modifications in such study either in vitro or in vivo is within the purview of the present invention.

In a still further embodiment, the present invention also provides method of using such compositions which comprises administering to a subject in need thereof an effective amount

of the composition. In one aspect, the compositions of the present invention comprising ondansetron are useful predominantly in the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy. The composition comprising domperidone is useful for treatment of nausea and vomiting and as a gastroprokinetic. The composition comprising carvedilol is useful for the treatment of mild-to-severe heart failure of ischemic or cardiomyopathic origin. The composition comprising sumatriptan is useful for acute treatment of migraine attacks with or without aura in adults.

The present dosage form compositions are also useful in pediatric applications, i.e., in the administration of cough and cold medications to children. In this way, the need for medicated tablets, which children often find difficult to swallow, is avoided. Beneficial bioactive agents are cold remedies, agents for combating halitosis, local anesthetics, local anti-infective agents, diet aids, fluoride-releasing compounds and other agents exhibiting utility in the dental context. The compositions of the present invention are also useful as lozenge or gum for reducing sore throat pain, insofar as such compounds exhibit antiviral activity. It will be appreciated that these dosage forms are also useful in treating and/or reducing pain associated with local viruses of the mouth, which are often manifested as sores or lesions e.g., those associated with herpes infection, or with various disorders of the tongue. The dosage forms of the invention are also useful in treating oral sores, including cold sores and oral mucositis. The compositions of the present invention are also used to prevent or treat drug-induced, alcohol-induced, biologically-induced, trauma-induced or pain-induced nausea, vomiting, dizziness and other adverse effects arising from but not limited to motion sickness, cancer therapy, and pregnancy. Dry mouth conditions associated with certain illnesses such as cancer, extreme medical procedures such as chemotherapy and post operative dry mouth sensation can also be alleviated by the preparations. Also, the compositions comprising nicotine can be used to treat withdrawal symptoms associated with cessation of smoking. The conditions amenable to treatment with the compositions of the present invention also include, but are not limited to oral infections, lesions, low or high blood pressure, Helicobacter infections, pain, cough, migraine, vomiting, nausea, sleep apnoea, gastroesophageal reflux disease (GERD), reflux disease, and inflammation, yeast infections, periodontal diseases, snoring, oral ulcers or other lesions.

The examples given below serve to illustrate embodiments of the present invention. However they do not intend to limit the scope of the present invention.

EXAMPLES

Example-1:

S. No.	Ingredient	mg/tablet
1.	Ondansetron: HPβ-CD complex (equivalent to 8mg of ondansetron base)	24.36
2.	Sodium carboxymethylcellulose (Blanose® 7H4XF)	15.00
3.	Copovidone (Plasdone® S630)	5.00
4.	Maltodextrin	10.00
5.	Sucrose	13.16
6.	Aspartame	1.00
7.	Sodium stearyl fumarate	0.70
8.	Lake of erythrosine	0.07
9.	Strawberry flavor	0.70
Total weight		70.00
Hardness		87±5 N
Thickness		2.13±0.05 mm
Punch shape and size		5.5 mm, round, flat punch on both sides

Preparation of Ondansetron- HPβ-CD complex:

i) HPβ-CD was dissolved in the aqueous medium.

ii) Ondansetron was dispersed in the material of step (i) by sonication.

iii) The solution of step (ii) is freeze dried to obtain a complex in the form of a dry powder.

Procedure:

i) Ondansetron: HPβ-CD complex, Maltodextrin, Sodium carboxymethylcellulose, Copovidone, Aspartame, Sucrose, Lake of erythrosine and Strawberry flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Sodium stearyl fumarate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with the remaining part of Sodium stearyl fumarate.

v) The granules in step iv) were compressed to obtain tablets.

Example-2:

S. No.	Ingredient	mg/tablet
1.	Ondansetron: HPβ-CD complex (equivalent to 16mg of ondansetron base)	49.28
2.	Sodium carboxymethylcellulose (Blanose® 7H4XF)	23.20
3.	Copovidone (Plasdone® S630)	8.00
4.	Maltodextrin	9.00
5.	Sucrose (NuTab™ 4000)	17.34
6.	Aspartame	1.00
7.	Sodium stearyl fumarate	1.00
8.	Lake of erythrosine	0.08
9.	Strawberry flavor	1.10
Total weight		70.00
Hardness		100±5 N
Thickness		2.55±0.05 mm
Punch shape and size		6.5 mm, round, flat punch on both sides

Preparation of Ondansetron- HPβ-CD complex:

i) HPβ-CD was dissolved in the aqueous medium.

ii) Ondansetron was dispersed in the material of step (i) by sonication.

iii) The solution of step (ii) is freeze dried to obtain a complex in the form of a dry powder.

Procedure:

i) Ondansetron: HPβ-CD complex, Maltodextrin, Sodium carboxymethylcellulose, Copovidone, Aspartame, Sucrose, Lake of erythrosine and Strawberry flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Sodium stearyl fumarate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with the remaining part of Sodium stearyl fumarate.

v) The granules in step iv) were compressed to obtain tablets.

Example-3:

S. No.	Ingredient	mg/tablet
1.	Domperidone maleate (equivalent to 10mg of domperidone base)	12.79
2.	Sodium carboxymethylcellulose (Blanose® 7MXF)	11.90
3.	Hydroxypropyl cellulose (Klucel® EXF)	13.60
4.	Maltodextrin	90.00
5.	Sugar IP	32.01
6.	Sodium deoxycholate	3.00
7.	Aspartame	2.50
8.	Sodium stearyl fumarate	1.70
9.	Lake of quinoline yellow	1.00
10.	Strawberry flavor	1.50
Total weight		170.00
Hardness		55±5 N
Thickness		2.13±0.05 mm
Punch shape and size		9.0 mm, round, standard concave punch on one side and flat punch on other side

Procedure:

i) Domperidone maleate, Maltodextrin, Sodium carboxymethylcellulose, Hydroxypropyl cellulose, Aspartame, Sugar IP, Lake of quinoline yellow and Strawberry flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Sodium stearyl fumarate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with remaining part of Sodium stearyl fumarate.

v) The granules in step iv) were compressed to obtain tablets.

Example-4:

S. No.	Ingredient	mg/tablet
1.	Carvedilol	12.55
2.	Sodium carboxymethylcellulose (Blanose® 7MXF)	11.90

3.	Hydroxypropyl cellulose (Klucel EXF)	13.60
4.	Maltodextrin	90.00
5.	Sugar IP	35.25
6.	Aspartame	2.50
7.	Sodium stearyl fumarate	1.70
8.	Lake of quinoline yellow	1.00
9.	Strawberry flavor	1.50
Total weight		170.00
Hardness		50±5 N
Thickness		2.4±0.05 mm
Punch shape and size		9.0 mm, round, standard concave punch on one side and flat punch on other side

Procedure:

i) Carvedilol, Maltodextrin, Sodium carboxymethylcellulose, Hydroxypropyl cellulose, Aspartame, Sugar IP, Lake of quinoline yellow and Strawberry flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Sodium stearyl fumarate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with remaining part of Sodium stearyl fumarate.

v) The granules in step iv) were compressed to obtain tablets.

Example-5 :

S. No.	**Ingredient**	**mg/tablet**
1.	Ondansetron hydrochloride	8.00
2.	Sodium carboxymethylcellulose (Blanose® 7H3SXF)	10.00
3.	Copovidone (Plasdone® S 630)	5.00
4.	Maltodextrin	10.00
5.	Sugar® DC	17.77
6.	Aspartame	1.00
7.	Sodium stearyl fumarate	0.50
8.	Lake of quinoline yellow	0.25

9.	Cherry flavor	0.50

Procedure:

i) Ondansetron Hydrochloride, Maltodextrin, Sodium carboxymethylcellulose, Copovidone, Aspartame, Sugar® DC, Lake of quinoline yellow and Cherry flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Sodium stearyl fumarate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#30 and retained on sieve#60.

iv) The granules in step iii) were mixed with remaining part of Sodium stearyl fumarate.

v) The granules in step iv) were compressed to obtain tablets.

Example-6:

S. No.	Ingredient	mg/tablet
1.	Domperidone Maleate (equivalent to 10mg of domperidone base)	12.78
2.	Sugar (Nutab 4000 (#80 passed))	30.42
3.	Dextran	10.5
4.	Hydroxyethyl cellulose	7.0
5.	Polycarbophil	2.0
6.	Sorbitol	1.1
7.	Calcium stearate	0.7
8.	Vanilla flavor	0.7
9.	Color lake of quinoline yellow	0.35
10.	Citric acid	3.5
11.	Sodium deoxycholate	0.95

Procedure:

i) Domperidone maleate, Dextran, Hydroxyethyl cellulose, Polycarbophil, Sorbitol, Sugar, Citric acid, Sodium deoxycholate ,Color lake of quinoline yellow and Vanilla flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Calcium stearate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with remaining part of Calcium stearate.

v) The granules in step iv) were compressed to obtain tablets.

Example-7 :

S. No.	Ingredient	mg/tablet
1.	Domperidone Maleate (equivalent to 10mg of domperidone base)	12.78
2.	Inositol	31.37
3.	Lactose	10.5
4.	Hydroxypropyl cellulose	7.0
5.	Polyethylene oxide	2.0
6.	Aspartame	1.1
7.	Zinc stearate	0.7
8.	Strawberry flavor	0.7
9.	Color lake of quinoline yellow	0.35
10.	Citric acid	3.5

Procedure:

i) Domperidone maleate, Lactose, Hydroxypropyl cellulose, Polyethylene oxide, Aspartame, Inositol, Citric acid, Color lake of quinoline yellow and Strawberry flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Zinc stearate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with remaining part of Zinc stearate.

v) The granules in step iv) were compressed to obtain tablets.

Example-8:

S. No.	Ingredient	mg/tablet
1.	Carvedilol	12.55
2.	Sodium carboxymethylcellulose (Blanose® 7H4F)	15.00
3.	Polycarbophil	5.00
4.	Maltodextrin	10.00

5.	Sugar (Nutab 4000 (#80 passed))	25.20
6.	Saccharin	1.00
7.	Sodium stearyl fumarate	0.500
8.	Lake erythrosine	0.250
9.	Butterscotch flavor	0.500

Procedure:

i) Carvedilol, Maltodextrin, Sodium carboxymethylcellulose, Polycarbophil, Saccharin, Sugar, Lake erythrosine and Butterscotch flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Sodium stearyl fumarate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with remaining part of Sodium stearyl fumarate.

v) The granules in step iv) were compressed to obtain tablets.

Example-9: Inlay tablets

S. No.	**Ingredient**	**mg/tablet**
Core Layer		
1.	Ondansetron- HPβ-CD complex (equivalent to 8mg of ondansetron base)	26.90
2.	Methyl cellulose	15.00
3.	Gum Arabic	5.00
4.	Microcrystalline cellulose	10.00
5.	Xylose	10.65
6.	Glycyrrhizin	1.00
7.	Glyceryl behenate	0.500
8.	Lake of ponceau	0.136
9.	Lake of brilliant blue	0.014
10.	Talc	0.100
11.	Strawberry flavor	0.700
Backing layer		
12.	Ethyl cellulose	34.00

13.	Copovidone (Plasdone® S 630)	5.00
14.	Hydroxyethyl cellulose	10.00
15.	Sodium stearyl fumarate	1.00

Preparation of Ondansetron- HPβ-CD complex:

i) HPβ-CD was dissolved in the aqueous medium.

ii) Ondansetron was dispersed in the material of step (i) by sonication.

iii) The solution of step (ii) is spray dried or freeze dried to obtain a complex in the form of a dry powder.

Procedure:

A) Core layer:

i) Ondansetron- HPβ-CD complex, Microcrystalline cellulose, Methyl cellulose, Gum arabic, Glycyrrhizin, Xylose, Lake of ponceau, Lake of brilliant blue, Talc, Strawberry flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Glyceryl behenate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with remaining part of Glyceryl behenate.

B) Backing layer:

i) Ethyl cellulose, Copovidone, Hydroxyethyl cellulose were mixed together with portion of Sodium stearyl fumarate and passed through sieve#40.

ii) The blend of step i) was mixed with one part of Sodium stearyl fumarate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules obtained in step iii) were mixed with remaining part of Sodium stearyl fumarate.

The granules of step A iv) and step B iv) were compressed together to obtain inlay tablets.

Example-10:

S. No	**Ingredients**	**mg/tablet**
1.	Sumatriptan succinate (equivalent to 10mg of sumatriptan)	14.00

2.	Fructose	12.0
3.	Mannitol	12.0
4.	Sodium alginate	14.0
5.	Copovidone (Plasdone® S 630)	5.0
6.	Maltitol	1.1
7.	Stearic acid	0.7
8.	Strawberry flavor	0.7
9.	Color lake of quinoline yellow	0.35

Procedure:

i) Sumatriptan, Mannitol, Sodium alginate, Copovidone, Maltitol, Fructose, Color lake of quinoline yellow and Strawberry flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Stearic acid and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with remaining part of Stearic acid.

v) The granules in step iv) were compressed to obtain tablets.

Example-11:

A) Fast release layer:

S. No	**Ingredients**	**mg/tablet**
1.	Cetirizine	12.5
2.	Sodium carboxymethylcellulose (Blanose® 7H3SXF)	15.5
3.	Copovidone (Plasdone® S 630)	6.0
4.	Maltodextrin	12.5
5.	Maltose	10
6.	Saccharin	1.00
7.	Lake of ponceau	0.12
8.	Strawberry flavor	0.80
9.	Croscarmellose sodium (Ac-Di-Sol®)	1.5
10.	Calcium stearate	0.80

Procedure:

i) Cetirizine, Maltodextrin, Sodium carboxymethylcellulose, Copovidone, Saccharin,

Maltose, Croscarmellose sodium, Lake of ponceau and Strawberry flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Calcium stearate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with remaining part of Calcium stearate.

B) Sustained release layer:

Core composition:

S. No	Ingredients	mg/tablet
1.	Ondansetron	16.5
2.	Hydroxypropyl cellulose	15.5
3.	Polycarbophil	6.0
4.	Lactose	12.5
5.	Inositol	10
6.	Saccharin	1.00
7.	Strawberry flavor	0.70
8.	Sodium stearyl fumarate	0.80
9.	Lake of ponceau	0.35

Procedure:

i) Ondansetron, Lactose, Hydroxypropyl cellulose, Polycarbophil, Saccharin, Inositol, Lake of ponceau and Strawberry flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Sodium stearyl fumarate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with remaining part of Sodium stearyl fumarate.

The material of step A (iv) was compressed with the material of step B (iv) to obtain bilayered tablets.

Example-12:

S. No.	Ingredient	mg/tablet
1.	Ondansetron	16.5
2.	Sodium carboxymethylcellulose (Blanose® 7H4F)	15.00

3.	Polycarbophil	5.00
4.	Maltodextrin	10.00
5.	Vitamin B	10.65
6.	Sugar® DC	25.20
7.	Neotame	1.00
8.	Sodium stearyl fumarate	0.500
9.	Lake erythrosine	0.250
10.	Chocolate flavor	0.500

Procedure:

i) Ondansetron, Maltodextrin, Sodium carboxymethylcellulose, Polycarbophil, Neotame, Sugar® DC, Vitamin B, Lake erythrosine and Chocolate flavor were mixed together.

ii) The mixture in step i) was mixed with one part of Sodium stearyl fumarate and roller compacted to obtain compacts.

iii) The compacts in step ii) were broken into granules which passed through sieve#20 and retained on sieve#40.

iv) The granules in step iii) were mixed with remaining part of Sodium stearyl fumarate.

v) The granules in step iv) were compressed to obtain tablets.

We claim:

1. A novel buccoadhesive composition comprising at least one bioactive agent(s), at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s), optionally with other excipients, wherein the said composition has improved cohesiveness, enhanced intactness and improved adhesion at the desired site of the mucosa for substantially longer duration and releases the bioactive agent(s) in a sustained manner in the oral cavity for extended time period.

2. A composition according to claim 1, which releases the bioactive agent(s) in the oral cavity of the subject such that the bioactive agent is absorbed through the mucosal tissues of the oral cavity thereby bypassing the hepatic metabolism and resulting in increased bioavailability.

3. A composition according to claim 1, wherein the bioactive agent(s) is selected from a group comprising pharmaceutically active agent(s) or its salts, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms, derivatives or mixtures thereof; nutritional supplement(s) and food product(s), or combinations thereof.

4. A composition according to claim 1, wherein the composition additionally comprises at least one taste masking agent(s), one or more hydrophobic polymers and/or taste masking agents and/or permeation enhancers and/or sweeteners.

5. A composition according to claim 1, wherein the bioactive agent(s) is formulated as spray dried or lyophilized complex with a cyclodextrin.

6. A composition according to claim 3, wherein the bioactive agent is selected from a group comprising pharmaceutically active agents that show poor bioavailability primarily due to presystemic metabolism and/or have a bitter taste and/or required to exhibit a sustained release drug release profile.

7. A composition according to claim 6, wherein the pharmaceutically active agent useful in the present invention is selected from a group comprising abortifacients; ACE inhibitors; alpha-adrenergic agonists; beta-adrenergic agonists; alpha-adrenergic blockers; adrenocortical steroids; adrenocorticotrophic hormones; alcohol deterrents; aldose reductase inhibitors; aldosterone antagonists; anabolics; analgesics; androgens; angiotensin II

receptor antagonists; anorexics; anthelmintics; antiallergics; antiamoebics; antiarrhythmics; antiarthritics/antirheumatics; antiasthmatics; antibacterials; anticholinergics; anticoagulants; anticonvulsants; antidepressant; antidiabetic; antidiarreal; antidiuretic; antidyskinetic; antiemetic; antifungal; antihistaminic; antihyperlipoproteinemic; antihypertensive; antihypotensive; anti-inflammatory/analgesic; anticancer drugs; antifungal; anti-malarial; antiarrhythmics; antimigraine; antiparkinsonian; antipsychotic; antipyretic; antispasmodic; antitussive; antiulcerative; anxiolytic; bronchodilator; calcium channel blocker; cardiotonics; cholinergics; CNS stimulants; diuretic; dopamine receptor antagonist; enzymes; gastroprokinetic; glucocorticoid; leukotriene antagonist; mineralcorticoids; monoamine oxidase inhibitors; muscle relaxants; narcotic antagonist; progestogen; prolactin inhibitor; prostaglandin/prostaglandin analogs; peptide or protein drugs or polysaccharides; antivirals; sedative/hypnotic; serotonin noradrenaline reuptake inhibitor; serotonin reuptake agonist; serotonin receptor antagonist; serotonin uptake inhibitor; vasodilators; vasoconstrictor; vitamins; breath fresheners; tooth-whitening agents; tooth-desensitizing agents or their pharmaceutically acceptable salts, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms, derivatives or mixtures thereof used either alone or in combinations thereof.

8. A composition according to claim 7, wherein peptide or protein is selected from a group comprising enzymes, heparin, antigens, calcitonin, cyclosporin, insulin, oxytocin, tyrosine, enkephalin, tyrotropin releasing hormone (TRH), follicle stimulating hormone (FSH), luteinizing hormone (LH), growth hormone, clotting factor VIII & IX, glucocerebrosidase, vasopressin and vasopressin analogs, catalase, superoxide dismutase, interleukin-II (IL2), interferon, colony stimulating factor (CSF), tumor necrosis factor (TNF) or melanocyte-stimulating hormone, erythropoietin, thrombopoietin, etanercept, or mixtures thereof.

9. A composition according to claim 3, wherein the nutritional supplement is selected from a group comprising vitamins, peptide, polypeptides, proteins, carbohydrates, lipids and minerals or mixtures thereof and the food product is selected from a group comprising caffeine, chocolates, breath fresheners,

flavors, agents that provide cooling effect in the oral cavity, sugars or sugar alcohols, herbal products having a pleasant taste, or mixtures thereof.

10. A composition according to claim 1, wherein the bioadhesive polymer is selected from a group comprising cellulosic polymers; enteric and non-enteric cellulose esters; low molecular weight polyvinyl alcohol; medium viscosity polyvinyl alcohol; polyoxyethylene glycols; alginates; polyethylene oxide; vinyl polymers or copolymers; polyacrylic acid (PAA) used either alone or in combination thereof.

11. A composition according to claim 10, wherein the cellulosic polymer is selected from a group comprising sodium carboxymethylcellulose, methylcellulose, low molecular weight hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose or mixtures thereof.

12. A composition according to claim 1, wherein the water soluble sugar component is selected from a group comprising directly compressible sugar; mixture of sucrose, invert sugar and magnesium stearate; maltodextrin, starch, sucrose, sucrose-based diluents, confectioner's sugar, dextrin, dextrose, dextran, dextrates, inositol, amylose, cellulose, maltose, dried invert sugar, lactose, mannose, xylose, ribose, glucose, fructose, levulose, galactose, corn syrup, high fructose corn syrup, partially hydrolyzed starch, saccharin, sorbitol, mannitol, xylitol, maltitol, isomalt, hydrogenated starch hydrolysate or combinations thereof.

13. A composition according to claim 1, wherein the binder is selected from a group comprising vinyl polymers or copolymers or mixtures thereof.

14. A composition according to claim 13, wherein the vinyl polymer or copolymer is selected from a group comprising polyvinyl pyrrolidone, vinyl acetate, starch, cellulosic polymers, polycarbophil, polyethylene oxide, arabic gum or mixtures thereof.

15. A composition according to claim 4, wherein the hydrophobic polymer is selected from a group comprising acrylic polymers, acrylic acid and methacrylic acid copolymers, hydrophobic cellulosic material, or mixtures thereof.

16. A composition according to claim 15, wherein the acrylic acid and methacrylic acid copolymer is selected from a group comprising Eudragit®, methyl methacrylate copolymers, ethoxyethyl methacrylates, cyanoethyl methacrylate,

aminoalkyl methacrylate copolymer, poly(acrylic acid), poly(methacrylic acid), methacrylic acid alkylamide copolymer, poly(methyl methacrylate), poly(methacrylic acid) (anhydride), methyl methacrylate, polymethacrylate, poly(methyl methacrylate), poly(methyl methacrylate) copolymer, polyacrylamide, aminoalkyl methacrylate copolymer, poly(methacrylic acid anhydride), glycidyl methacrylate copolymers or mixtures thereof.

17. A composition according to claim 15, wherein the hydrophobic cellulosic material is ethylcellulose or alkyl cellulosic polymer.

18. A composition according to claim 4, wherein the permeation enhancer is selected from a group comprising sodium cholate, sodium glycocholate, sodium glycodeoxycholate, taurodeoxycholate, sodium deoxycholate, sodium lithocholate chenocholate, chenodeoxycholate, ursocholate, ursodeoxy-cholate, hyodeoxycholate, dehydrocholate, glycochenocholate, taurochenocholate, taurochenodeoxycholate, sodium dodecyl sulfate, dimethyl sulfoxide, sodium lauryl sulfate, salts and other derivatives of saturated and unsaturated fatty acids, surfactants, bile salt analogs, derivatives of bile salts, medium chain monoglyceride, medium chain fatty acid esters, small polar solvents, glycerol monooleate, azone, glycol, pyrrolidone, fatty alcohol, fatty acid and ester thereof, propylene glycol monolaurate, propylene glycol, oleic acid, lauric acid, oleyl alcohol, lauryl alcohol, vitamin E TPGS, methyl sulfonyl methane, used either alone or in combination thereof.

19. A composition according to claim 1, wherein the excipients are selected from a group comprising diluents or fillers, binders, stabilizers, lubricants, anti-adherents or glidants, antioxidants, vehicles, buffers, preservatives, complexing agents, colorants, flavorants, flavor stabilizers, pH-adjusting agents, channel formers, viscosifiers, gelling agents, tonicity modifiers, lipid components, plasticizers, organic solvents, stabilizers, chelating agents, anticaking agents, disintegrants, coating agents, sweeteners, antioxidants, preservatives, release rate modifiers, ingestible solvents, adhesion modifiers, used either alone or in combination thereof.

20. A composition according to claim 1, wherein the buccoadhesive compositions are in the form of matrix type sustained release dosage form.

21. A composition according to claim 1, wherein the composition comprises

bioactive agent(s) in a range from about 0.5 % to about 75 % by weight of the composition, buccoadhesive polymer(s) in the range from about 0.5 to about 70 % by weight of the composition, binder(s) in the range from about 1 % to about 20 % by weight of the composition and water soluble sugar component(s) present in the range from about 2 % to about 70 % by weight of the composition.

22. A process for preparation of composition in accordance with claim 1, which comprises of the following steps:

i) mixing the bioactive agent(s) with at least one bioadhesive polymer(s), at least one water soluble sugar component(s) and at least one binder(s),

ii) optionally adding one or more other excipients, and

iii) formulating the mixture into a suitable dosage form.

23. A process for preparation of composition in accordance with claim 1, which comprises of the following steps:

i) mixing the bioactive agent(s) or bioactive agent(s) complexed with HPβ-CD, with filler(s), buccoadhesive polymer(s), binder(s), sweetener(s), sugar, color and flavor, optionally with other excipients,

ii) mixing the contents in step (i) with one part of lubricant(s) and roller compacting the blend to obtain compacts,

iii) crushing the compacts/slugs and passing the compacts through suitable sieve to obtain granules,

iv) mixing the granules with the remaining part of lubricant(s) optionally with other excipients, and

v) optionally compressing the blend of step (iv) into a suitable compressed dosage form.

24. A process for preparation of composition in accordance with claim 1, which comprises of the following steps:

A) Core layer:

i) mixing the bioactive agent(s) or bioactive agent(s) complexed with HPβ-CD, with filler(s), buccoadhesive polymer(s), binder(s), sweetener(s), sugar, color and flavor, optionally with other excipients,

ii) mixing the contents in step (i) with one part of lubricant(s) and roller compacting to obtain compacts,

iii) crushing the compacts/slugs and passing the compacts through suitable sieve to obtain granules, and

iv) mixing the granules with the remaining part of lubricant(s) optionally with other excipients.

B) Backing layer:

i) mixing the hydrophobic polymer(s), binder(s), pH independent polymer(s) and a part of lubricant(s) optionally with other excipients followed by sifting through suitable sieve,

ii) mixing the contents in step (i) with part of lubricant(s) and roller compacting the contents to obtain compacts,

iii) crushing the compacts/slugs and passing the compacts through suitable sieve to obtain granules,

iv) mixing the granules with the remaining part of lubricant(s), optionally with other excipients, and

compressing the granules of step A (iv) and step B (iv) into suitable dosage form.

25. A method of using the pharmaceutical composition according to claim 1, which comprises administering to a subject in need thereof an effective amount of the composition.

26. Use of a composition according to claim 1, for the manufacture of a medicament for administering to a subject in need thereof.

27. The pharmaceutical composition and the process for preparation of the pharmaceutical composition substantially as herein described and illustrated by the examples.