A Review on Aspirin Buccal Patches for Antiplatelet use

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Abstraction

Extensive research efforts have recently been focused on placing a drug delivery system in a particular region of the body for maximizing biological drug availability and minimizing dose-dependent side effects. Buccal delivery of drugs provides an attractive alternate to other conventional methods of systemic drug administration, since buccal mucosa is relatively permeable with rich blood supply and acts as an excellent site for the absorption of drugs .The buccal patches of nitroglycerin were prepared by using solvent casting method. Weighed accurately amount of polymer Dispersed in a beaker containing distilled water with stirring on magnetic stirrer. Add Poly ethylyne glycol (PEG)-400 to the polymeric solution during addition of plastisizer continuous stirring is necessary to prevent lump formation. Weigh accurately amount of nitroglycerin and dissolve in distilled water which gives the suspension of nitroglycerin. Add the nitroglycerin suspension to the solution of polymer and plastisizer with continuous stirring. FT-IR spectra for pure nitroglycerin and Different polymers acquired at room temperature using FT-IR spectrophotometer in transmittance mode. The samples were ground in a mortar, mixed with Nujol and placed between two plates of KBr and compressed to form a thin film. The sandwiched plates were placed in the infrared spectrometer and the spectra were obtained. Scanning was performed between wave numbers 4000-400 cm-1.

Kye words – Nitro-glycerine **,** Buccal Patches, Hydroxy propyl methyl cellulose

INTRODUCTION

Extensive research efforts have recently been focused on placing a drug delivery system in a particular region of the body for maximizing biological drug availability and minimizing dose-dependent side effects. Buccal delivery of drugs provides an attractive alternate to other conventional methods of systemic drug administration, since buccal mucosa is relatively permeable with rich blood supply and acts as an excellent site for the absorption of drugs(.1) However, oral route presents some problems for few drugs. The enzymes in the GI fluids, GIT-pH conditions, and the enzymes bound to GIT membranes are the few factors responsible for the bioavailability problems. The blood that drains the GIT carries the drug directly to the liver leading to first-pass metabolism resulting in poor bioavailability.The inherent problems associated with the drug, in some cases, can be solved by modifying the formulation or by changing the routes of administration. Parenteral, mucosal, and transdermal routes circumvent hepatic first-pass metabolism and offer alternative routes for the systemic delivery of drugs(2) A buccal patch for systemic administration of acyclovir in the oral cavity was developed using polymers hydroxy propyl methyl cellulose (K4M), hydroxy propyl methyl cellulose (K15M), sodium carboxy methyl cellulose and, plasticizer poly ethylene glycol (400). The films were evaluated in terms of swelling, residence time, mucoadhesion, release, and organoleptic properties.(3)Therefore the Oral mucosal drug delivery system is widely applicable as novel site for administration of drug for immediate

And controlled release action in various body cavities, like the nasal, buccal, ocular, rectal and vaginal mucosae has the benefit of bypassing the hepatic first-pass elimination associated with oral administration. Because of the dual biophysical and biochemical nature of these mucosal membranes drugs with hydrophilic and lipophillic nature can be rapidly absorbed.

MATERIAL AND METHODS

The nitroglycerin drug, Hydroxyl propyl methyl cellulose (HPMC K15) , Polyethylene glycol (PEG)- 400

PREPARATION OF MUCOADHESIVE BUCCAL PATCHES

The buccal patches of nitroglycerin were prepared by using solvent casting method. Weighed accurately amount of polymer Dispersed in a beaker containing distilled water with stirring on magnetic stirrer. Add Poly ethylyne glycol (PEG)-400 to the polymeric solution during addition of plastisizer continuous stirring is necessary to prevent lump formation. Weigh accurately amount of Aspirin and dissolve in distilled water which gives the suspension of Aspirin. Add the Aspirin suspension to the solution of polymer and plastisizer with continuous stirring. The solution was mixed continuously on the magnetic stirrer to get semisolid consistency. The resulting solution was casted on to glass ring kept on the surface of mercury in petri-plates and allowed to dry in oven. The dried films were cut into 2×2cm diameter pieces and kept in desiccator till further use.

EVALUATION OF FORMULATED BUCCAL PATCHES

Compatibility of nitroglycerin to excipient

FT-IR

FT-IR spectra for pure nitroglycerin and Different polymers acquired at room temperature using FT-IR spectrophotometer in transmittance mode. The samples were ground in a mortar, mixed with Nujol and placed between two plates of KBr and compressed to form a thin film. The sandwiched plates were placed in the infrared spectrometer and the spectra were obtained. Scanning was performed between wave numbers 4000-400 cm-1.

Physical appearance and surface texture-

It includes visual inspection of patches and evaluation of texture by feel or touch.

Weight variation test

From each formulation, five films of similar specifications have been chosen and subjected to weight variation test as per the IP procedure using Shimadzu digital balance. The average weight of five buccal films was subtracted from individual film weight. The mean ± SD values were calculated for all the formulations.(5)

Measurement of Folding Endurance

The folding endurance was determined manually for the prepared films by repeatedly folding the film at the same place until it broke. The number of times the film could be folded at the same place without breaking or cracking gave the value of folding endurance.(6)

Drug content uniformity of the patches

The patches were tested for the content.Uniformity. A patch of size 1×1 cm2 was cut and Placed in a beaker. Ten ml of a 0.1 N Hydrochloric acid solution was added. The Contents were stirred in a cyclo-mixer to dissolve The film. The contents were transferred Volumetric flask (10 ml). The absorbance of the Solution was measured against the corresponding Blank solution at 248 nm.(7)

Surface pH study

The surface pH of the buccal patches was determined in order to investigate the possibility of Any side effects in-vivo. As an acidic or alkaline pH may cause irritation to the buccal mucosa, it Was determined to keep the surface pH as close to neutral as possible. A combined glass Electrode was used for this purpose. The buccal patch was

allowed to swell by keeping it in Contact with 1 ml of distilled water for 1 h at room temperature. The pH was measured by Bringing the electrode in contact with the surface of the patch and allowing it to equilibrate for 1 Min. The experiment was performed in triplicate, and average values were reported.(8)

Water absorption capacity test

Circular Patches, with a surface area of 2.3 cm2 are allowed to swell on the surface of agar plates prepared in simulated Saliva (2.38 g Na2HPO4, 0.19 gKH2PO4, and 8 g NaCl per litter of distilled water adjusted with phosphoric acid to pH 6.7), and kept in an incubator maintained at 37°C ± 0.5°C. At various time intervals (0.25, 0.5, 1, 2, 3, and 4 hours), Samples are weighed (wet weight) and then left to dry for 7 days in a desiccators over anhydrous calcium chloride at Room temperature then the final constant weights are recorded. Water uptake (%) is calculated using the following

Equation21.

Water uptake(%)= (WW-Wf) x 100

Wf

Where,

Ww is the wet weight and Wf is the final weight. The swelling of each film is measured(9)

Swelling studies

Buccal films of 1 cm2 area from each formulation, accuratelyWeighed by using digital weighing balance (W1), were placedIn a Petri dish containing 50 ml distilled water. After a timeInterval of 5 min up to 30 min, films were removed and Blotted between filter paper and weighed (W2). The swelling index was calculated by the following formula (Pavankumar

Et al., 2005):Swelling index ¼ ð Þ W2 – W1 =W2 ——————————————————————————————— 100: (10)

Measurement of tensile strength (TS) and Percentage

Elongation (E/B) The mechanical property was evaluated using instron universal Testing instrument (Model 1121, instron Ltd., japan, NITK, Surathkal, India) with a 5 kg load cell. Film strips in special dimension and free From air bubbles or physical imperfections were held between two Clamps positioned at a distance of 3 cm. During the measurement, The strips were pulled by the top clamp at a rate of 100 mm/min, And then the force and elongation were measured when the filmBroke. Results from the film samples, which broke at and notBetween the clamps, were not included in the calculations. Measurements were run in triplicate for each film. Two mechanical Properties, namely, TS and % E/B were computed for the evaluation Of the film. TS is the maximum stress applied to a point at which the Film specimen breaks and was computed from the applied load at Rupture as a mean of three measurements and cross sectional area Of fractured film as described from the following equation.

Tensile strength of the patches

Tensile strength of the patch was determined with Digital Tensile Tester (DY-20, Adamulthomargy, France (12)

In vitro drug release study

For in vitro release study, goat buccal mucosa membrane is used as a barrier membrane with Phosphate buffer (pH 7.4) as a medium. The patches are evaluated for drug release using franz diffusion cells. Buccal mucosa membrane is mounted between the donor and receptors compartments. The patches are placed on the mucosal membrane. The diffusion cell is placed in simulated saliva maintained at 37±2°C.The receptor compartment is filled with 50 mL phosphate buffer (pH 7.4) and hydrodynamics is maintained by stirring with a magnetic bead at 300 rpm. Five mL sample are withdrawn and replaced with 5 mL fresh medium to maintain the sink condition. The samples are analyzed in U.V. spectrophotometer at 226 nm. (13)

Advantages of buccal Patches

(1) The buccal mucosa is widely vascularized, making it possible to quickly swallow medications.

(2) Prevents the drugs from entering the gastrointestinal fluids and gets around the first pass effect.

(3) The area of buccal membrane is

(4) Sufficiently large to allow a delivery System to be placed at different occasion Additionally; there are two areas of buccal Membranes per mouth, which would Allow buccal drug delivery systems to be Placed, alternatively on the left and right Buccal membranes.

(5) The performance of the drug is enhanced by close contact with the mucosa

Disadvantage of buccal Patches

1) i. The buccal route cannot be used to administer mucosa-bothering or strongly-flavored medications.
2) Small dose medications can only be given.
3) Saliva production is constant, causing drugs to be quickly eliminated.
4) Little area for absorption.
5) Involuntary salivation gulping causes a sizable portion of the delivered drug to disintegrate or suspend And be removed from the site of retention. The delivery system itself could also be swallowed, which is Another risk.

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