DEVELOPMENT EVALUATION AND CHARACTERIZATION OF BUCCAL PATCHES CONTAINING ATENOLOL USING HYDROPHILIC POLYMERS

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ABSTRACT

Objective: The present investigation focused on fabrication and evaluation of atenolol releasing buccal patches comprising mucoadhesive hydrophilic polymers like sodium alginate and tamarind seed polysaccharide with a drug-free backing layer (6 % ethylcellulose).

Methods: Solvent evaporation technique being employed in the development of atenolol comprising buccal patches using mucoadhesive hydrophilic polymers. The prepared buccal patch formulations were tested for thickness, weight variation, folding endurance, drug content, moisture content, moisture absorption, % swelling, surface pH, *in vitro* residence time and mucoadhesion studies. The drug permeation through goat buccal mucosal membrane was conducted with the use of Franz diffusion cell in phosphate buffer saline, pH 6.8 and was subjected to FT-IR and SEM characterization. Stability study was performed as per ICH guidelines.

Results: For all the buccal patch formulations, the average weight, thickness, drug content, moisture content, moisture absorption, % swelling, surface pH study exhibited satisfactory results. Out of 7 different buccal patches, the formulation FA-1 revealed the highest mucoadhesive strength (31.36±0.95 g), the force of adhesion (0.31±0.04 N), maximum swelling index (341±0.83 %) and more than 24 h *in vitro* residence time. The buccal patch formulation FA-1 indicated highest drug permeation (97.51 %) in 24 h and was found to be stable. FT-IR examination confirms lack of drug polymer interaction. SEM investigation reveals a smooth surface of the buccal patch.

Conclusion: The developed buccal patches comprising atenolol can be very promising in increasing patient compliance and reducing dosing frequency.

Keywords: Tamarind seed polysaccharide, Buccal patches, Mucoadhesion, Atenolol, *Ex vivo* permeation

INTRODUCTION

The peroral mode of drug administration is a convenient and popular path of medication delivery accepted universally. However, the difficulties associated with the oral route such as presystemic metabolism, drug degradation in the gastrointestinal environment, poor bioavailability of certain group of drugs necessitate the development of some other non-invasive route like buccal, transdermal, rectal, inhalation route of drug administration [1, 2]. Drug administration through the mucosal surface present on the interior aspect of the buccal cavity can be regarded as buccal drug delivery system [3, 4].

The buccal route is preferred over other noninvasive routes on the basis of the following reasons:

The drug administration via buccal route provides, bypassing of presystemic metabolism, improve bioavailability, sustained manner drug delivery, rapid onset of action, easy termination of therapy as per requirement, increased ease of drug administration and improved patient acceptance [5-7].

Atenolol is a β1 selective receptor antagonist extensively employed in the therapy of hypertension, myocardial infarction, angina pectoris and heart failure. Atenolol is sparingly soluble in water, daily dose is 25 mg to 100 mg, suffering from short biological half life of 6 to 7 h with low bioavailability of 40 %. Atenolol due to small dose, substantial first-pass metabolism, less half-life and low oral bioavailability, makes it a suitable candidate for delivery by buccal path [8, 9].

The oral disintegrating films of atenolol were prepared by solvent casting technique exhibit an optimal drug release profile and effective disintegration time [10].

The formulated and evaluated bilayered buccal adhesive tablets of atenolol possessed an increased drug bioavailability and unidirectional drug release property [11].

The floating matrix tablets of atenolol have been devised to prolong the gastric residence time and its release rate using different polymers [12].

The objectives of the present research work were to develop and evaluate various mucoadhesive buccal patch formulations of Atenolol with mucoadhesive polymers like sodium alginate and tamarind seed polysaccharide (TSP) for a sustained therapy of hypertension.

MATERIALS AND METHODS

Materials

Atenolol was a gift item from M/S. P. D. I. L, India. Tamarind seed polysaccharide was obtained from Tamarind (*Tamarindus indica)* seeds*.* Glycerine was acquired from Loba Chemie Pvt. Ltd., India. Ethylcellulose was secured from Matrix Laboratories, India. Dibutyl phthalate was purchased from Ranbaxy Laboratories, India. All other reagents used were of analytical grade.

Methods

Extraction of tamarind seed polysaccharide

To remove the outer cover tamarind seeds were immersed in hot water. Then the seeds were crushed gently to form the powder. About 20 g of powdered seed was immersed with 200 ml of double-distilled water for 24 h to make slurry. Then the slurry was poured in 800 ml steaming distilled water for 20 min on a water bath for obtaining a clear solution and was kept overnight under normal storage condition. The attenuated transparent solution was centrifuged for 20 min at 6000 rpm to segregate all the foreign matter. The supernatant liquid was separated and poured into the double volume of 95 % ethanol accompanied by continuous stirring. The precipitate thus obtained was kept in the hot air oven at 40 °C for 12 h to dry the sample. The dried tamarind seed polysaccharide was then powdered and kept in desiccators until use [13-17].

Preparation of backing membrane

Backing membrane in the present investigation was developed by pouring 6 % ethylcellulose in a blend of acetone: isopropyl alcohol (65:35) using dibutyl phthalate 10 % as plasticizer in a 38 cm²petridish and was dried for 12 h at room temperature [18].

Preparation of buccal patches

A series of buccal patches composed of mucoadhesive polymeric layers of sodium alginate, tamarind seed polysaccharide (TSP) containing atenolol 25 mg/cm², 10 % w/w of glycerinewere developed by solvent evaporation process. The mixture solution containing atenolol, sodium alginate and tamarind seed polysaccharide were mixed properly with the help of magnetic stirrer and then homogenized employing a homogenizer stirrer for 15 min. Glycerine 10 % w/w of dry weight of polymers was incorporated within these mixture solutions as a plasticizer. For removing air bubbles the solution was then sonicated for 30 min and then poured in a petridish of 38 cm² containing backing membrane and was dried at 50 °C for 24 h. Then, the dried buccal patches were taken out from the petridish, and kept in a desiccator until use. Table 1: represents the composition of different atenolol comprising buccal patches [19, 20].

Table 1: Formulation design of atenolol buccal patches

FC	Sodium alginate (mg)	Tamarind seed polysaccharide (mg)	Drug (mg/cm²)	Glycerine (%)	Double distilled water (ml)
FA-1	700	100	25	10	30
FA-2	600	200	25	10	30
FA-3	500	300	25	10	30
FA-4	400	400	25	10	30
FA-5	100	700	25	10	30
FA-6	200	600	25	10	30
FA-7	300	500	25	10	30

FC-Formulation code

Compatibility study of atenolol with different polymers used in the investigation

To determine the possible interaction if any between the drug atenolol and various excipients employed in the present investigation and also to confirm the identity of the drug, the compatibility study was carried out in FT-IR spectrophotometer. The IR spectrum of pure drug Atenolol and physical mixture of drug and various polymers were determined by mixing the samples employing KBR and the spectra was attained by scanning in the wavelength range of 500-3500 cm⁻¹ [21, 22].

Determination of average weight

The buccal patch formulations (n=3) were individually weighed employing a digital balance and the average weights were determined [23, 24].

Measurement of thickness

Thickness gauze was used for the measurement of thickness of the three randomly selected patches for each formulation at six different points [25, 26].

Determination of folding endurance

The prepared buccal patches were examined for folding endurance value and were obtained manually by repeatedly folding a patch at the same position till it broke or folded upto 300 times without breaking. The number of times the patch folded at the same location without cracking or breaking represents the folding endurance value [27].

Determination of drug content

For determination of drug content, saline phosphate buffer solution 100 ml was taken and 1 cm²of the patch was dissolved in it and was agitated at room temperature for 24 h. After 24 h filtration of the solution was carried out using Whatman filter paper (No. 42) and was analysed by UV-VIS spectrophotometer (UV-1700 Double beam spectrophotometer, SHIMADZU Corporation, Japan) at 274 nm against a blank. The calibration curve of atenolol was formulated between 1 to 5 μg/ml concentration ranges. The method was validated for linearity, accuracy, and precision. The regression equation for the calibration curve was Y = 0.048 X+0.002, R² = 0.9990 [28, 29].

Measurement of surface pH

The surface pH of the prepared buccal patch formulations of atenolol were determined to conduct an investigation about the chances of side effect in the buccal cavity results from alteration in pH that may cause buccal mucosal surface irritation. Surface pH of prepared patches were measured by placing 1 cm²of a patch in a petridish comprising 1 ml of distilled water and was allowed to swell for a period of 2 h at room temperature and pH was quantified by making a contact of the swellen patch with the electrode of the pH meter and was allowed to equilibrate for 1 minute. The examination was repeated three times and mean were reported [30].

Measurement of moisture content

Moisture content of the prepared buccal patches was obtained by storing accurately weighed buccal patches in the desiccator containing anhydrous calcium chloride. After 3 d, the buccal patches were removed and reweighed. The percentage moisture content was estimated by percentage moisture loss calculation applying the formula [31, 32]:

$$\text{Moisture content (\%)} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Determination of percentage moisture absorption

The examination was carried out to check the physical stability of the prepared atenolol buccal patches at excessive humid conditions. In this study three 1 cm²buccal patches of each formulation were cut out, accurately weighed and stored in a desiccator comprising saturated solution of aluminium chloride, maintaining relative humidity of 76% within the desiccator for 3 d. After 3 d, the buccal patches were removed, reweighed, and percentage moisture absorption was calculated applying the formula [33, 34]:

$$\text{Moisture absorption (\%)} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Measurement of bioadhesive strength

Mucoadhesion is known as the involvement between two materials out of which one must be a biological surface for extended period of time. Mucoadhesive strength is the weight in gram required to separate the patch formulation from the buccal mucosal surface. The two pans of the physical balance were removed. The right side pan was displaced with a lighter base and the left pan having a Teflon ring held with a copper wire. On the opposite side of the ring using a copper wire a Teflon cylinder was hanged. A glass beaker was accommodated in between by arranging the height of the total framework. The two sides of the balance were balanced in such a way that the right side was exactly 5 grams heavier than the left. The buccal mucosal tissue of goat was cleaned with phosphate buffer saline pH 6.8, so that the buffer solution just gets contact with the

tissue surface and maintains it moist. A 2 cm²buccal patch formulation was moistened with 1 ml of phosphate buffer saline solution pH 6.8 for initial hydration and swelling. By uplifting the cylinder a contact of hydrated buccal patch formulation with buccal mucosa was done. The balance was maintained in this position for 3 min and then weights were increased slowly on the right side pan until the patch was separated from the buccal mucosa. Mucoadhesive strength of the buccal patch formulation was determined by deducting a weight of 5 gram from the total weight that was the required weight for the separation of the patch from the mucosal surface. At the end of each examination, the buccal mucosa was gently and thoroughly cleaned with phosphate buffer saline, pH 6.8 and left for 5 min before the next examination. Caution must be given for the use of fresh buccal mucosa for each formulation and a broken mucosal membrane should not be used [35, 36].

Determination of *in vitro* residence time

In the present investigation USP disintegration apparatus was employed for determination of *in vitro* residence time of the prepared buccal patch formulations. Phosphate buffer saline, pH 6.8 kept at 37±0.5 °C filled in 800 ml disintegration medium. A piece of (4 cm) excised goat buccal mucosa was attached to the surface of glass slab with adhesive. The buccal patch formulation of 2 cm diameter was moistened with phosphate buffer saline, pH 6.8 and was made in association with the surface of the mucosal layer. An up and down movement of the apparatus was permitted in such a way that near the lowest point the patch formulation was utterly submerged in buffer solution and at the highest point patch was outside the solution. The time needed for absolute erosion or detachment of the buccal patch from surface of the mucosal membrane was recorded, known as the *in vitro* residence time of the buccal patch formulation. For each formulation the experiment was conducted in triplicate and the mean value was reported [37, 38].

Swelling index study

The swelling index of different buccal patch formulations were measured by the consequence of increase in weight results from swelling. For investigation of swelling index the drug loaded patches (n=3) of 1×1 cm were accurately weighed and kept in a petridish comprising 50 ml of phosphate buffer saline pH 6.8. At an interval of 1h up to 6 h theswollen patches were carefully withdrawn from the petridish, surplus water was out of the patch by filter paper, reweighed and % swelling index was obtained by the following formula [39, 40]:

$$(\%) \text{ Swelling index} = \frac{\text{Wet weight} - \text{Dry weight}}{\text{Dry weight}} \times 100$$

Ex vivo drug permeation study

Franz diffusion cell of 40 ml capacity with effective diffusion area 1.74 cm²was employed to conduct *ex vivo* drug permeation examination of various atenolol containing buccal patches. The receptor compartment containing saline phosphate buffer solution pH 6.8 and 37±0.5 °C temperature was maintained. The buccal mucosa was mounted between the donor and receptor medium of the diffusion cell. The buccal patch was placed over the mucosal membrane in such a way that the drug releasing portion of the patch formulation facing towards the mucosal membrane and the drug impermeable backing layer facing towards the donor compartment. A stirring speed of 50 rpm was employed using a magnetic stirrer for simulating buccal cavity environment. At regular intervals, five millilitres of the sample was withdrawn from the receptor compartment and replaced immediately

with an equal volume of phosphate buffer saline, pH 6.8. The quantity of drug (atenolol) permeated into the receptor medium was estimated by using UV–VIS spectrophotometer (UV-1700 Double beam spectrophotometer, SHIMADZU Corporation, Japan) at 274 nm for atenolol buccal patches against a blank [41, 42].

Stability studies

The purpose of stability testing is to make available confirmation on how the quality of a drug substance changes with time when exposed to a variety of environmental factors including temperature, humidity and light, and therefore validate recommended storage conditions. In the present investigation, the stability testing was conducted according to ICH guidelines. The selected drug formulation was supplied in borosilicate glass bottles, flushed with nitrogen, and conserved in stability chamber at 40 °C/75% RH for six months. A known quantity of sample from the formulations subjected to stability study was analyzed at pre determined time intervals for drug content and *ex vivo* drug permeation through the goat buccal mucosa [43-45].

Scanning Electron Microscopy (SEM) study

The SEM examination generally performed for demonstrating surface texture and to check the morphology of the fractured or sectioned surface. It is employed for producing three dimensional surface relief images obtained from secondary electrons. The surface examination of formulation containing drug and polymer can present essential information regarding the micro texture of appliance [46].

RESULTS

The present study was an attempt to develop, evaluate and characterize atenolol (an anti hypertensive drug) comprising buccal patches consisting drug in a mucoadhesive polymeric layer of sodium alginate and tamarind seed polysaccharide and a drug free backing membrane composed of 6% ethyl cellulose employing solvent evaporation technique.

Average weight

The average weight of different atenolol buccal patch formulations as a whole (38 cm²) was observed in the range of 1.67±0.06 g (FA-7) to 1.79±0.04 g (FA-5) (table 2).

Thickness

The thickness was measured for different buccal patches employing thickness gauge. For atenolol buccal patch formulations, FA-1 to FA-7, the thickness were determined in the range of 0.54±0.03 mm (FA-1) to 0.63±0.05 mm (FA-5) (table 2).

Folding endurance

The folding endurance value of the prepared buccal patches was measured manually. It was observed that folding endurance was measured to be highest with formulation, FA-1 (186±2) and lowest with formulation FA-4 (159±2), (table 2). The folding endurance examination signifies flexibility of the prepared buccal patch formulations [47].

Drug content

The drug content uniformity of the prepared buccal patch formulations FA-1 to FA-7 was determined in 1 cm²of each buccal patch. The drug content of the buccal patches were found in the range of 99.06±0.09 % (FA-6) to 99.62±0.08 % (FA-1) (table 2). Drug content investigation indicating uniformity with respect to drug content.

Table 2: Physico-chemical parameters of atenolol buccal patches

FC	Weight variation (g) n=3	Thickness (mm) n=3	Drug content (%) n=3	Folding endurance n=3	Surface pH n=3
FA-1	1.68±0.03	0.54±0.03	99.62±0.08	186±2	6.59±0.02
FA-2	1.71±0.02	0.58±0.02	99.36±0.11	175±3	6.66±0.01
FA-3	1.76±0.05	0.61±0.05	99.45±0.06	182±1	6.69±0.02
FA-4	1.74±0.08	0.59±0.06	99.48±0.09	159±2	6.55±0.03
FA-5	1.79±0.04	0.63±0.05	99.26±0.12	167±2	6.79±0.02
FA-6	1.70±0.05	0.57±0.06	99.06±0.09	169±3	6.63±0.01
FA-7	1.67±0.06	0.56±0.04	99.11±0.12	181±1	6.61±0.01

FC-Formulation code, Data represent mean±SD

Surface pH

The estimation of surface pH of the prepared patches is important for improvement of drug permeation and mucoadhesion, as an acidic or alkaline pH may cause buccal mucosal irritation. In the present investigation effort has been made to maintain the surface pH as close to the buccal/salivary pH as possible by selecting appropriate polymers for formulation of patches. The surface pH of the buccal patch formulations FA-1 to FA-7 were found in the range of 6.55±0.03 (FA-4) to 6.79±0.02 (FA-5) (table 2) (convenient to buccal pH). The surface pH study illustrates absence of any irritation to the buccal tissue as the buccal patches thus prepared reported pH range close to buccal pH [48].

Determination of percentage moisture content and percentage moisture absorption

The different buccal patch formulations of atenolol was investigated for percentage moisture content and percentage moisture uptake to examine the physical stability of the prepared patches at high humid conditions and patch integrity at dry conditions. The percentage moisture content of the prepared buccal patch formulations of atenolol, FA-1 to FA-7 was observed to be within the range of 1.31±0.02 (FA-1) to 1.92±0.04 % (FA-5). The moisture absorption (%) study results for atenolol buccal patch formulations, FA-1 to FA-7 were recorded in the range of 5.35±0.04 (FA-1) to 6.89±0.06% (FA-5) (table 3). The moisture uptake study indicates that the moisture uptake of the prepared patches was observed to be enhanced with the more hydrophilic character of the polymers. The low moisture content protects them well from microbial contamination and also provides stability from brittleness. For each formulation experiment was repeated for three times and mean value was tabulated [49].

Swelling index study

A high swelling characteristics is needed for mucoadhesive application by a polymer. When mucoadhesive polymers come in proximity with aqueous vehicle they absorb water and swell to form a gel. The rate and extent of water absorption by a polymer is an important determinant in relation to its relative mucoadhesive strength. The swelling index examination indicates that the percentage swelling of the buccal patch formulations FA-1 to FA-7 were obtained in the order of FA-1>FA-2>FA-3>FA-7>FA-6>FA-4>FA-5. Among the various Atenolol buccal patch formulations highest swelling index of 341±0.83 % was observed with formulation FA-1 and lowest swelling index of 292±1.54 % was found with formulation FA-5 (table 3). The swelling index study demonstrates swelling of patches significantly very with the polymer composition.

In vitro residence time

The different atenolol buccal patches has recorded the highest *in vitro* residence time of greater than 24 h with formulations FA-1 and FA-2 while the lowest *in vitro* residence time of 18.28±1.1 h with formulation FA-5 (table 4). *In vitro* residence time study demonstrates very good association of the prepared buccal patches with the buccal membrane for a sufficiently longer time period [50].

Ex vivo mucoadhesion study

The *ex vivo* mucoadhesion study findings has demonstrated that among the atenolol buccal patch formulations, FA-1 to FA-7, the maximum mucoadhesive strength of 31.36±0.95 g was observed with formulation FA-1 while minimum mucoadhesive strength of 19.45±0.82 g with formulation FA-5 and the mucoadhesive strength of different buccal patch formulations were found in the order of FA-1>FA-2>FA-3>FA-7>FA-6>FA-4>FA-5. The highest force of adhesion was observed with formulation FA-1 (0.31±0.04 N) and the lowest force of adhesion with formulation FA-5 (0.19±0.04 N) (table 31). The *ex vivo* mucoadhesion study result indicates strong bonding between the mucoadhesive polymers and mucosal tissue [51, 52].

Table 3: Moisture content (%), Moisture uptake (%), swelling index study of different atenolol buccal patches

FC	Moisture content (%) n=3	Moisture uptake (%) (76%RH) n=3	Swelling Index (%) 6h n=3
FA-1	1.31±0.02	5.35±0.04	341±0.83
FA-2	1.48±0.02	5.89±0.03	338±0.63
FA-3	1.59±0.05	6.38±0.02	319±1.12
FA-4	1.71±0.06	6.55±0.05	305±0.39
FA-5	1.92±0.04	6.89±0.06	292±1.54
FA-6	1.88±0.02	6.81±0.08	308±1.19
FA-7	1.78±0.02	6.22±0.02	313±0.39

FC-Formulation code, Data represent mean±SD

Table 4: In vitro residence time, ex vivo mucoadhesion study of different atenolol buccal patches

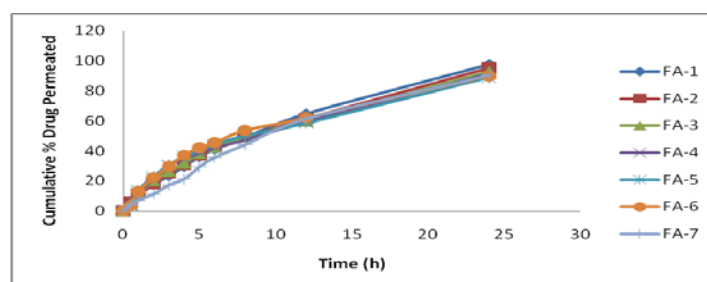| FC	In vitro residence time (h) n=3	Mucoadhesive strength (g) n=3	Force of adhesion (N) n=3
FA-1	24±1.4	31.36±0.95	0.31±0.04
FA-2	24±1	29.42±0.39	0.29±0.05
FA-3	23.16±1.2	25.59±0.85	0.25±0.02
FA-4	21.33±1	22.33±0.63	0.22±0.03
FA-5	18.28±1.1	19.45±0.82	0.19±0.04
FA-6	20.15±1.13	23.19±0.91	0.23±0.02
FA-7	20.55±1.1	24.86±0.58	0.24±0.03

FC-Formulation code, Data represent mean±SD

Fig. 1: Mean e*x vivo* drug permeation comparative study of different atenolol buccal patch

Ex vivo **drug permeation study**

Table 5: *Ex vivo* drug permeation study of different atenolol buccal patch formulations

| Time (h)	FA-1 % CDP	FA-2 % CDP	FA-3 % CDP	FA-4 % CDP	FA-5 % CDP	FA-6 % CDP	FA-7 % CDP
0	0	0	0	0	0	0	0
0.5	5.12±0.05	5.98±0.11	4.39±0.08	3.65±0.11	3.25±0.16	3.71±0.03	4.19±0.12
1	10.35±0.89	11.26±0.52	11.91±0.25	12.35±0.15	13.65±0.33	12.88±0.09	7.06±0.28
2	17.68±0.58	18.19±0.26	20.15±0.33	21.44±0.58	23.12±0.21	22.36±0.12	11.35±0.43
3	23.34±0.25	25.08±0.49	26.32±0.51	29.98±0.64	30.59±0.19	29.68±0.19	17.29±0.68
4	29.66±0.63	30.98±0.18	31.85±0.69	34.83±0.31	36.38±0.65	37.24±0.25	21.25±0.85
5	36.15±0.19	37.11±0.57	38.31±0.34	38.56±0.49	40.24±0.58	42.18±0.75	29.31±0.59
6	41.09±0.38	43.36±0.08	42.44±0.29	41.95±0.92	44.12±0.61	45.49±0.68	35.62±0.79
8	48.84±1.02	48.96±0.14	49.35±0.72	47.38±0.38	50.09±0.86	53.76±0.83	44.16±0.84
12	64.61±0.85	61.36±0.9	59.99±0.48	59.36±0.26	58.46±0.88	62.14±0.95	61.38±0.98
24	97.51±1.15	95.18±0.94	92.96±1.01	91.43±1.04	88.89±1.12	90.06±1.08	90.48±1.21

% CDP-% Cumulative Drug Permeated, Data represent mean±SD, n=3

Formulations (FA-1 to FA-7)

The ex vivo permeation study of atenolol from different buccal patches through goat buccal mucosa is shown in table 5 and fig. 1.

Among the Atenolol buccal patch formulations FA-1 to FA-7, the ex vivo permeation was maximum with formulation FA-1 (97.51±1.15 %) through goat buccal mucosa in 24 h and minimum with formulation FA-5 (88.89±1.12 %) as evident from table 4 and fig. 2. The drug permeation profile of formulation FA-1 to FA-7 was observed in the order of FA-1>FA-2>FA-3>FA-4>FA-7>FA-6>FA-5. The *ex vivo* drug permeation study demonstrated a slow and steady manner drug permeation profile. The examination revealed a better drug permeation profile observed with higher swelling of the polymers. The results of *ex vivo* permeation examination of atenolol reveals that atenolol easily permeated through the excised buccal mucosal membrane of goat for a period of 24 h and could possibly permeate through the human buccal membrane [53].

Drug-polymer compatibility study

Pure drug   Formulation FA-1
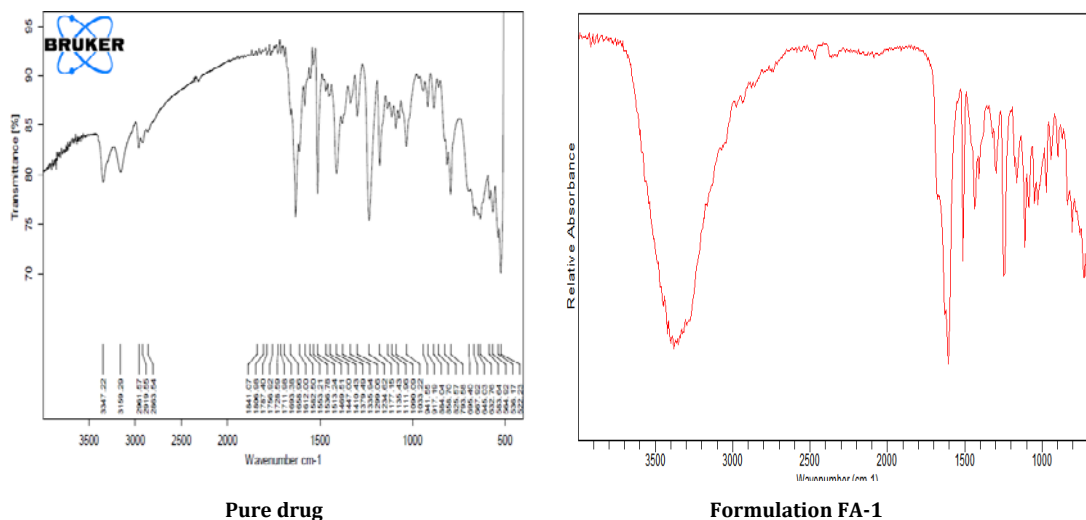
Fig. 2: FT-IR spectra of pure drug atenolol and atenolol containing buccal patch formulation, FA-1

The FT-IR spectra of atenolol and atenolol containing buccal patch formulation FA-1 are shown in fig. 2. The FT-IR spectra of pure drug, atenolol exhibited characteristic peaks of atenolol at 3347.22 cm[1] due to O-H (stretching), at 2961.57 cm[1] due to C-H (stretching), at 3159.29 cm[1] due to N-H (stretching), at 1513.24 cm[1] due to C=C, at 1693.38 cm[1] due to C=O, at 825.57 cm[1] due to C-H aromatic stretching as expected. The FT-IR investigation demonstrated compatibility between pure drug atenolol and physical mixture of atenolol with excipients like sodium alginate, tamarind seed polysaccharide, employed in the investigationas all the characteristic peaks of pure drug atenolol emerged in the spectrum of atenolol comprising buccal patch formulation, FA-1.

Stability studies

Table 6: Stability study of atenolol buccal patch formulation FA-1 for six months

Time	Drug content (%) (n=3)	Cumulative % drug permeation (n=3)
Initial	99.62±0.06	97.51±1.3
1 Mo	99.14±0.08	96.14±0.8
3 Mo	98.39±0.09	95.98±1.2
6 Mo	97.81±0.12	95.06±1.2

Data represent mean±SD

Among all the 7 different atenolol buccal patch formulations, the formulation FA-1 (atenolol-25 mg/cm², sodium alginate-700 mg, tamarind seed polysaccharide-100 mg, glycerine-10% w/w), was the best formulation as possessed highest drug content, best drug release profile *ex vivo*, highest swelling index, maximum *in vitro* residence time, maximum mucoadhesive strength was subjected to stability test. The formulation FA-1 supplied in borosilicate glass bottles, flushed with

nitrogen, and conserved in stability chamber at 40 °C/75% RH for six months. A known amount of sample from the stored formulations subjected to stability testing was analyzed at pre determined time intervals for estimation of drug content, *ex vivo* drug permeation through the goat buccal mucosa. The results of the stability study indicated no significant change in drug content and *ex vivo* drug permeation, thus demonstrating stability of the buccal patch formulation FA-1.
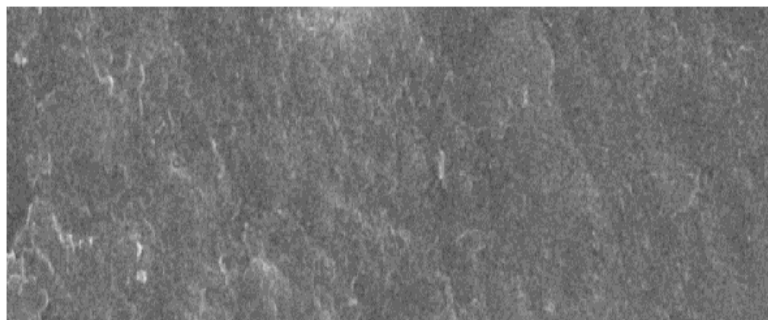
Surface morphology study

Fig. 3: SEM study of atenolol buccal patch formulation, FA-1

The SEM photographs of the atenolol buccal patch formulation, FA-1 (atenolol-25 mg/cm², sodium alginate-700 mg, tamarind seed polysaccharide–100 mg, glycerine-10% w/w) revealed a nearly smooth surface and good lamination of the mucoadhesive polymers like sodium alginate and tamarind seed polysaccharide on the ethyl cellulose backing membrane. It indicates atenolol being uniformly dispersed in the polymeric matrix of buccal patches and confirms perfect binding between the drug-containing mucoadhesive layer and the adhesive layer of backing membrane.

CONCLUSION

In the present research work effort was made for developing an antihypertensive novel buccal patch formulation for drug delivery. From the research study, it was revealed that the buccal patch formulations of atenolol, FA-1 was the best formulation among all the seven buccal patch formulations on the basis of different evaluation parameters. Further, it was found that the formulation FA-1 was devoid of any interaction with the polymers used and was stable under various storage conditions as per ICH guidelines. The above investigation can be concluded with a remark that the feasibility of developing novel mucoadhesive bilaminated buccal patches using various mucoadhesive hydrophilic polymers are safe, stable and can sustain drug release through buccal mucosa. Hence they can be very effective in the treatment and prophylaxis of hypertension.

AUTHORS CONTRIBUTIONS

The corresponding author has mainly designed the article with the support of co author. The corresponding author is the Ph. D. research scholar at Biju Patnaik University of Technology, Odisha, India.

CONFLICT OF INTERESTS

Declared none

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