International Journal of Pharmaceuticals and Health care Research (IJPHR)
IJPHR |Vol.12 | Issue 3 | Jul - Sept -2024
www.ijphr.com
DOI : https://doi.org/10.61096/ijphr.v12.iss3.2024.220-232
ISSN: 2306-6091

Research

Formulation And *In Vitro* Evaluation Of Atenolol Mucoadhesive Buccal Tablets

Piserla Teja [1*], Dr. D. Venkata Ramana, J. Pravalika

[1]Department of Pharmaceutics, Holy Mary Institute of Technology & Science (College of Pharmacy), Bogaram Village, Keesara Mandal, Hyderabad, Telangana, India.

*Author for Correspondence: Piserla Teja
Email: piserlateja1307@gmail.com

Published on: 28 Sept 2024

Published by:
DrSriram Publications

Abstract

Background: Atenolol is a widely used beta-blocker for managing hypertension and angina, traditionally administered via oral tablets. However, oral administration often leads to variable bioavailability and frequent dosing. Mucoadhesive buccal tablets offer a potential alternative by providing a controlled release mechanism and improving patient compliance.
Objective: The primary aim of this study was to formulate and evaluate mucoadhesive buccal tablets of Atenolol to enhance drug bioavailability and ensure sustained release.
Methods: Mucoadhesive buccal tablets of Atenolol were formulated using various mucoadhesive polymers, including Chitosan and Carbopol. The tablets were prepared by direct compression. The formulation process was optimized for tablet hardness, drug content uniformity, and mucoadhesive properties. In vitro evaluation included assessments of physical characteristics, mucoadhesive strength, and drug release profile.
Results: The formulated mucoadhesive buccal tablets exhibited desirable physical properties, including appropriate size, shape, and hardness. The in vitro mucoadhesive tests showed significant adhesion strength, ensuring prolonged residence in the buccal cavity. Drug release studies indicated a controlled and sustained release of Atenolol over an extended period, enhancing the potential for improved therapeutic efficacy.
Conclusion: The study successfully developed and evaluated Atenolol mucoadhesive buccal tablets with promising results. The formulation provides a controlled release of Atenolol, potentially improving bioavailability and patient adherence.

Keywords: Atenolol, Mucoadhesive Buccal Tablets

INTRODUCTION

The oral route of drug administration is the most common and preferred route for drug delivery, as it enables easy ingestion, self-medication, accurate dosage, flexible and controlled dosing schedule, and patient compliance with a low chance of administration difficulty .[1] It also has some major disadvantages such as the first-pass effect, gastrointestinal enzymatic degradation, and slow onset of action.[2] To overcome these disadvantages, mucoadhesive drug delivery and sublingual drug delivery could be better alternatives.

Mucoadhesive dosage forms are specially designed to adhere to the mucosal surface, thus intensifying retention of the drug at the site of application, while providing a controlled rate of drug release for better therapeutic outcome.[3] To mention, a few mucoadhesive drug delivery systems are adhesive patches, adhesive gels, adhesive tablets, adhesive films, adhesive discs, etc. Several regions such as the gastrointestinal (GI) tract, the urogenital tract, the ear, the nasal route, and the airways in the body are lined by the mucosal layer. These are either single-layered epithelium found in the GI tract, bronchi, and intestines or multilayered stratified epithelium found in the esophagus, vagina, and cornea and are the potential sites where mucoadhesive drug delivery systems can be useful.[4]

Buccal mucosa is one of such mucosal site which has a high extent of vascularization and enables direct drain of blood flow into the jugular vein, which helps to avoid the possible metabolism of drugs by the gastrointestinal route and liver. The buccal delivery thus implies the absorption of medication through the mucosal lining of the buccal cavity. Easier drug administration, the possibility of prompt termination in the condition of unpredicted side effects and emergencies, the possibility of incorporating enzyme inhibitor/permeation enhancer, etc. are other major advantages of this drug delivery system.[5]

Various mucoadhesive polymers (natural, semi-synthetic, and synthetic) used in this delivery system become adhesive on hydration, therefore can be used for targeting a drug to a particular region of the body. Initially, when the mucoadhesive product is in contact with the mucosal membrane, it swells and spreads, initializing deep contact with the mucosal layer and then mucoadhesive materials (polymers) are activated by the presence of moisture and drug releases slowly.[6]

Throughout the years, researchers in the advancement of drug studies are concentrating on other routes of administration to enhance pharmaceutical products, and to overcome the limitations of the oral route of administration. Buccal route of administration is a good alternative to the oral route due to its advantages in overcoming problems associated with oral administration. It has the advantage of avoiding the gastrointestinal tract (GIT), hepatic first pass effect and drug degradation in the GIT environment.[7]

The disadvantages of buccal route include low permeability of buccal membrane as compared to the sublingual membrane, short permanence time due to mechanical stress and swallowing and dilution of drug due to continuous secretion of saliva in the mouth. Nonetheless, the advantages and recent progress in drug delivery would outweigh the disadvantages involved.[8]To overcome the limitations of buccal route of administration, mucoadhesive dosage forms have gained interest. Mucoadhesion has the capacity to improve localization of drug delivery systems by retaining the drug dosage form at the site of intended action and in contact with the absorption site like the buccal cavity.Mucoadhesive formulations have been investigated for drug delivery into the oral cavity mucosa such as buccal, sublingual and gingival, eyes, nose, rectum and vagina. Among these systems, the buccal mucosa offers advantages, such as large absorption, accessibility, simple delivery devices, avoiding drug degradation and potential to incorporate drug as a controlled delivery system.[9]

Overview of oral mucosa

Structure

Majorly three distinctive layers composed the oral mucosa outermost stratified squamous epithelium below this lies basement membrane, lamina propria (connective tissue layer), followed by submucosa as innermostlayer (Figure 1.1).The epithelium acts as protective layer for the tissue beneath. It is classified as non-keratinized epithelium and keratinized epithelium. The former is found in mucosal lining of soft palate, the ventral surface of tongue, the floor of the mouth, vestibule, lips and cheeks, alveolar mucosa. The keratinized epithelium found in hard palate and non-flexible region of oral cavity. External carotid artery supplies the blood to oral mucosa. The blood supply to the lining of the cheek in the mucosal cavity derived from buccal artery, the posterior alveolar artery, some terminal branches of facial artery and the infraorbital artery.[10] The epithelium of buccal mucosa is about 40-50 cell layer thick, while that sublingual epithelium contain somewhat fewer.

Permeability

The permeability of buccal mucosa is 4-4000 times greater than that of skin. Due to the diverse structures and functions of the different oral mucosa leads difference in permeability between different regions of oral cavity. The permeability of oral mucosa depends on the thickness and degree of keratinization of tissue. According to this the permeability through sublingual is greater than buccal and buccal greater than palatal. Sublingual mucosa being relatively thin and non –keratinized, the buccal is thicker and non- keratinized and palatal intermediate in thickness but keratinized. Composition of epithelium is varies depending on sites in oral cavity. Ceramides and acylceramides are neutral lipids present in keratinized epithelia (gingivae, hard palates). These lipids associated with the barrier function because these are relatively impermeable to water. On the other hand acylceramides completely absent in non-keratinized epithelia (floor of the mouth and buccal epithelia) it only contains small amounts of Ceramides so non-keratinized epithelia are more permeable to water than keratinized epithelia.[11] Generally membrane coating granules, mechanism for penetration and enzymatic degradation are the barrier to drug permeability across the buccal epithelium.

Membrane Coating Granules

The permeability barrier property of the oral mucosa is due to the intracellular material called as membrane coating granules. It is found in both keratinized and non-keratinizedepithelia having spherical shape of diameter 100-300nm. These membrane coating granules also named as “corosula”, “small spherical shaped granules”, “small lamellated bodies”, “lamellated dense bodies”, “keratinosomes” and “cementosomes”. Membrane coating granules found in upper distal or superficial border of cell and a few occur near opposite border. Membrane coating granules forms a barrier to the permeability of various compounds by discharging their content into the intracellular space. Permeability barrier, cell desquamation, production of cell surface, cell adhesion and membrane thickening effect are the functions of membrane coating granules.[12]

Penetration Mechanism

Penetration of various substances are carried out by passive diffusion, carrier mediated diffusion, active transport and pinocytosis or endocytosis. Passive diffusion is primary mechanism for the transport of drug across buccal mucosa.

Paracellular

Transport of compounds through intracellular space between the cells. **Transcellula**r: Transport of compounds across the cell. Carrier mediated transport has been reported to have small role.

Enzymatic Degradation

Saliva contains moderate levels of esterases, carbohydrates and phosphatases. Some proteolytic enzymes have been found in buccal epithelium. It was reported that endopeptidases and carboxypeptidases were not present on the surface of porcine buccal mucosa, whereas aminopeptidases appear to be major enzymatic barrier to the buccal delivery of peptide drugs.

Environment

Intracellular ground substances and mucus covers the cell of oral epithelia. The major components of which are complexes made up of proteins and carbohydrates. These complexes either attached to certain region on cell surface or may be free of association. Matrix plays important role in cell-cell adhesion and act as lubricant. In oral mucosa mucus is secreted by the major and minor salivary glands whereas in rest of body where mucus is present it is secreted by the goblet cells of stratified squamous epithelium. Mucus network carries a negative charge at physiological pH because due to the presence of Sialic acid and Sulphate residue which plays important functions in the mucoadhesion. At this physiological pH strongly cohesive gel like structure is formed by mucus that will bind to epithelial cell surface as a gelation layer. The turnover time for the buccal epithelium has been reported 5-6 days and this is probably represents the oral mucosa. Depending on the site the oral mucosal thickness varies the buccal mucosa is about 500-800µm. The mucosal thickness of hard and soft palates, the ventral tongue, the floor of the mouth and gingivae is reported 100-200µm. Saliva is the protective fluid for all tissues of the oral cavity. Saliva is aqueous fluid contain 1% organic and inorganic materials. Flow rate is major determinant of the salivary composition which depends on the time of the day, the type of stimulus and the degree of stimulation. The salivary pH ranges from 5.5-7 depends upon flow rate. At high flow rates, the sodium and bicarbonate concentration increases leading to increase in the pH. The daily salivary volume is between 0.5 and 2 L. Hydrophilic polymer matrices forms the water rich environment of the oral cavity due to this reason they are mainly selected for transmucosal drug delivery system.[13]

Mucus

Mucus is translucent and viscid secretion, which forms a thin continuous gel blanket covering the epithelial cell of buccal mucosa. The thickness of this layer is ranging from 40-300 µm. The goblet cells lining of the epithelia or by special exocrine gland with the mucus cell acini secrets mucus.[14] The main component of mucus is water (95%), glycoprotein knows as mucin (1-5%), inorganic salts (1%) and free protein (0.5-1%). The mucin having molecular mass ranging from 0.5 to over 20 MDa. Mucin contains large amount of carbohydrate. Mucus plays a major role in adhesion of mucoadhesive drug delivery system and also acts as lubricant allowing the cell to move relative to one another. It is also protective in function.

Mucoadhesive Polymer

First generation mucoadhesive materials are hydrophilic macromolecules containing numerous hydrogen bonds forming group. The very first use of mucoadhesive was as denture fixers. Adhesion is occurring due to presence of hydroxyl, carboxyl or amine group on the molecule. Such groups are activated by moistening and will adhere nonspecifically to many surfaces called as wet adhesive.[15] These polymers can be subdivided in three main classes Cationic, Anionic and Nonionic.

Cationic

Cationic molecule can interact with mucus surface, since it is negatively charged at physiological pH. Examples are Chitosan, Aminodextran, and Trimethylated Chitosan. Mucoadhesion of Chitosan occurs because of the electrostatic interaction of their amino group with the sialic groups of mucin in the mucus layer.[16]

Anionic

Mucoadhesion of anionic polymer can be occur by physical or chemical process, such as hydrophobic interaction, hydrogen and van der waals bonds which are control by pH and ionic composition. Examples are Carboxymethylcellulose, Sodium alginate, Xanthan gum, Pectin.

Non-ionic

Non-ionic polymer present a weaker mucoadhesion forces as compared to anionic polymers. Examples are Hydroxylethyl starch, Hydroxypropyl cellulose, Poly (ethylene oxide), Seleroglucan.

MATERIALS AND METHODS

Atenolol-Provided by SURA LABS, Dilsukhnagar, Hyderabad, Chitosan-Panchi Chemicals Pvt Ltd, Mumbai, Carbopol-Alkem Labs Pvt, Ltd, Mumbai, Lactose-Sd fine Chem.Ltd. Mumbai, Magnesium stearate-SD Fine chemicals, Mumbai, Talc-Qualigens fine chemicals, Mumbai., Aspartame-SD Fine chemicals, Mumbai.

Methodology

Pre formulation studies

Analytical method used in the determination of Atenolol

Preparation of pH 6.8 phosphate buffer

Preparation of 0.2 M sodium hydroxide solution: Accurately weighed 8 g of sodium hydroxide pellets were dissolved in 1000 mL of distilled water and mixed.

Dissolved 6.805 g of potassium dihydrogen orthophosphate in to 800mL of Purified water and mixed. Added 112mL of 0.2M NaOH solution in to this solution, diluted to volume with purified water. Then adjusted the pH of this solution to 6.8 with 0.2M NaOH solution.

Preparation of pH 7.4 phosphate buffer: Accurately measured 250 mL of 0.2M potassium dihydrogen ortho phosphate and 195.5 mL of 0.2M NaOH was taken into the 1000 mL volumetric flask. Volume was made up to 1000 mL with distilled water.

Preparation of standard graph in phosphate buffer pH 6.8

100 mg of Pure drug was dissolved in small amount of Methanol (5-10 ml), allowed to shake for few minutes and then the volume was made up to 100ml with phosphate buffer pH 6.8, from this primary stock (1mg/ml), 10 ml solution was transferred to another volumetric flask made up to 100 ml with phosphate buffer pH 6.8. From this secondary stock 0.5, 1.0, 1.5, 2.0, 2.5 ml was taken separately and made up to 10 ml with phosphate buffer pH 6.8 to produce 5, 10, 15, 20, 25µg/ml respectively. The absorbance was measured at 254 nm using a UV spectrophotometer. Standard calibration curve values were shown in Table (9.1). The standard calibration curve of Atenolol in phosphate buffer pH 6.8 was shown in fig 9.1.

Preparation of standard graph in phosphate buffer pH 7.4

100 mg of drug was dissolved in small amount of phosphate buffer and make the volume up to 100ml with phosphate buffer pH 7.4, from this primary stock(1mg/ml), 10 ml solution was transferred to another volumetric flask made up to 100 ml with phosphate buffer pH 7.4. From this secondary stock 0.5, 1.0, 1.5, 2.0, 2.5ml were taken separately and made up to 10 ml with phosphate buffer pH 7.4, to produce 5, 10, 15, 20, 25µg/ml respectively. The absorbance was measured at 254 nm using a UV spectrophotometer. Standard calibration curve values were shown in Table (9.2). The standard calibration curve of Atenolol in phosphate buffer pH 7.4 was shown in fig 9.2.

Solubility Studies

The solubility of Atenolol in phosphate buffer solution pH 6.8 was determined by phase equilibrium method. An excess amount of drug was taken into 20 ml vials containing 10 ml of phosphate buffers (pH 6.8). Vials were closed with rubber caps and constantly agitated at room temperature for 24 hr using rotary shaker. After 24 hr, the solution was filtered through 0.2µm Whattman's filter paper. The amount of drug solubilized was then estimated by measuring the absorbance at 254 nm using a UV spectrophotometer.

The standard curves for Atenolol were established in phosphate buffers (pH 6.8) and from the slope of the straight line the solubility of Atenolol was calculated. The studies were repeated in triplicate (n = 3), and mean was calculated.

Evaluation of pre-compression blend

The quality of tablet, once formulated, by rule is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characterization of blends produced. Prior to compression, granules were evaluated for their characteristic parameter such as Tapped density, Bulk density, Carr's index, Angle of repose, Hausner's ratio. Compressibility index was calculated from the bulk and tapped density using a digital tap density apparatus. The various characteristics of blends tested are as given below:

Angle of repose

The angle of repose of granules was determined by the funnel method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the granules. The granules were allowed to flow through funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

tan□ = h/r

Where, □ = angle of repose

h = height of the cone

r = radius of the cone base

The relationship between the angle of repose and flowability is as follows:

Table 1: Angle of repose values

S.No	Angle of Repose	Flowability
1.	<25	Excellent
2.	25-30	Good
3.	30-40	Passable
4.	>40	Poor flow

Bulk density

Density is defined as weight per unit volume. Bulk density ρb, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping and storage of raw material and blend. It is also important in size blending equipment. 30 gm of powder blend introduced into a dry 100 mL cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume V_0, was read. The bulk density was calculated using the formula:

$\rho b = M/V_0$

Where, ρb= Apparent bulk density.

M=Weight of the sample.

V=Apparent volume of powder.

Tapped density

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides a fixed drop of 14±2 mm at a nominal rate of 300 drops per minute. The cylinder was tapped 500 times initially followed by an additional tap of 750 times until difference between succeeding measurement is less than 2% and then tapped volume, V_f was measured, to the nearest graduated unit. The tapped density was calculated, in gm per mL, using the formula:

$\rho_{tap} = M/V_f$

Where, ρ_{tap}= Tapped density.

M = Weight of the sample.

V_f= tapped volume of the powder.

Carr's index

The compressibility index (Carr's index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measure of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials,

there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the compressibility index which is calculated using the following formula:

Carr's index = $[(\rho_{tap}-\rho b)]/\rho_{tap}]\times100$

Where, ρb= bulk density

ρ_{tab}= tapped density

Table 2: Carr's index values

S.No	Carr's Index	Flowability
1.	5-12	Free Flowing
2.	13-16	Good
3.	18-21	Fair to Passable
4.	23-35	Poor
5.	33-38	Very Poor
6.	>40	Extremely Poor

Hausner's ratio

It is the ratio of tapped density to the bulk density. Hausner's found that this ratio was related to interparticle friction and, as such, could be used to predict powder flow properties. Generally a value less than 1.25 indicates good flow properties, which is equivalent to 20% of Carr's index.

Hausner's Ratio = $\rho_{tap}/\rho b$

Where, ρ_{tap} = Tapped density.

ρb = Bulk density.

Table 3: Hausner's ratio values

S.No	Hausner's Ratio	Flowability
1.	0-1.2	Free flowing
2.	1.2-1.6	Cohesive powder

Preparation of Tablets

1. The ingredients were weighed.
2. All the ingredients except Magnesium stearate, Chitosan, Carbopol, PVP K90 and IPA were sieved and hand mixed together.
3. Then PVP K 90 was dissolved in sufficient quantity of IPA was added slowly in small quantities to the previous blend and it was hand mixed thoroughly.
4. The wet mass was air dried to remove the IPA.
5. The dried mass was then passed through sieve no. 30 to obtain granules.
6. The granular mixture was then compacted using a 10 station punching machine using 7mm punch tooling with an average weight of 150mg per tablet.

Table 4: Formulation Chart

Ingredients (MG)	FORMULATION CODES							
	A1	A2	A3	A4	A5	A6	A7	A8
Atenolol	25	25	25	25	25	25	25	25
Chitosan	5	10	15	20	-	-	-	-
Carbopol	-	-	-		5	10	15	20
Lactose	149	144	139	134	149	144	139	134
Magnesium stearate	5	5	5	5	5	5	5	5
Talc	6	6	6	6	6	6	6	6
Aspartame	10	10	10	10	10	10	10	10
Total weight	200	200	200	200	200	200	200	200

RESULT AND DISCUSSION

Solubility Studies

Table 5: Solubility studies

S.No	Medium	Amount present (µg/mL)
1	Phosphate pH 6.8 buffer	98.18
2	Phosphate pH 7.4 buffer	96.71

Saturation solubility of Atenolol in various buffers were studied and shown in the Table 9.1. The results revealed that the solubility of the Atenololwas increased from pH 6.8 to 7.4. The solubility of the Atenolo lin phosphate buffer pH 6.8 is 98.18µg/mL and it was selected as the suitable media for the release studies because the pH of the phosphate buffer pH 6.8 is nearer to that of buccal mucosa pH.

Standard graph in phosphate buffer pH 6.8 (λ_{max} 280 nm)

Standard graph of Atenolol was plotted as per the procedure in experimental method and its linearity is shown in Table 9.2 and Fig 9.1**.** The standard graph of Atenolol showed good linearity with R^2 of 0.998, which indicates that it obeys "Beer- Lamberts" law.

Table 6: Standard graph values of Atenolol in pH 6.8 phosphate buffer

Concentration (µg/mL)	Absorbance
0	0
5	0.118
10	0.231
15	0.339
20	0.447
25	0.565

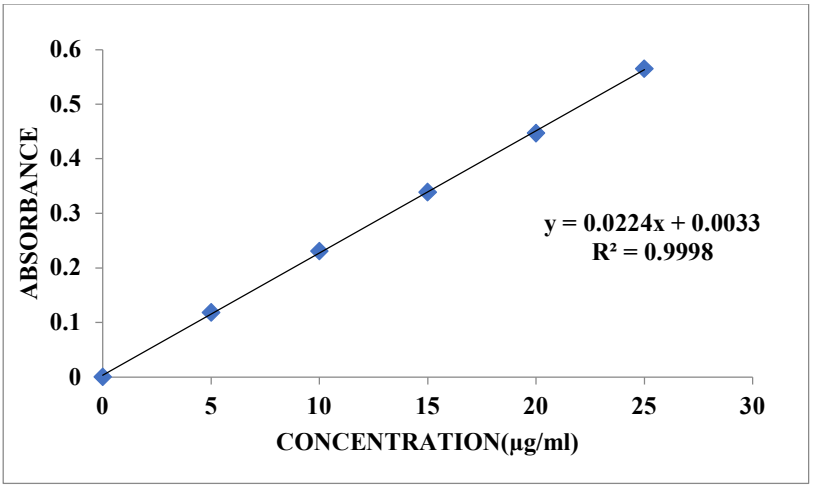

Fig 1: Standard graph of Atenolol in pH 6.8 phosphate buffer

Standard graph in phosphate buffer pH 7.4 (λ_{max} 280 nm)

Standard graph of Atenolol was plotted as per the procedure in experimental method and its linearity is shown in Table 9.3 and Fig 9.2. The standard graph of Atenolol showed good linearity with R^2 of 0.999, which indicates that it obeys "Beer- Lamberts" law.

Table 7: Standard graph values of Atenolol in pH 7.4 phosphate buffer

Concentration (µg/mL)	Absorbance
0	0
5	0.111
10	0.228
15	0.335
20	0.448
25	0.563

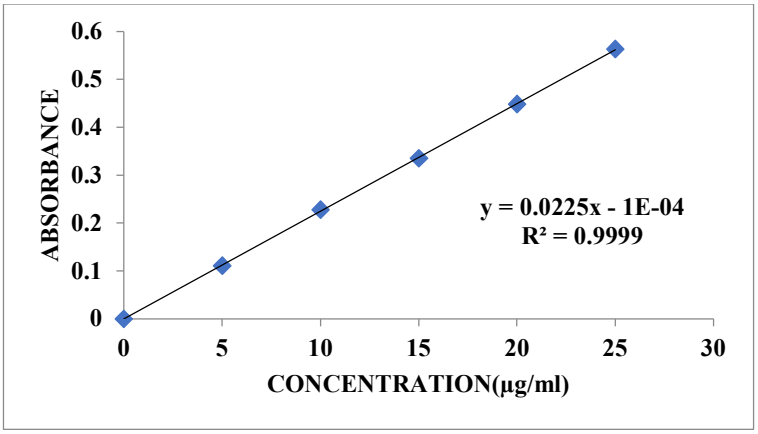

Fig 2: Standard graph of Atenolol in pH 7.4 phosphate buffer

Evaluation

Characterization of pre-compression blend

The pre-compression blend of Atenololbuccal tablets were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio**.** Angle of repose was less than 23.45º, Carr's index values were less than 14.7 for the pre-compression blend of all the batches indicating good to fair flowability and compressibility. Hausner's ratio was less than 1.24 for all the batches indicating good flow properties.

Table 8: Physical properties of pre-compression blend

Formulation Code	Angle of repose (Ɵ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's Index (%)	Hausner's ratio
A1	18.8	0.38	0.43	11.6	1.13
A2	19.6	0.39	0.44	11.3	1.12
A3	19.4	0.42	0.47	10.6	1.11
A4	21.9	0.40	0.45	11.1	1.12
A5	17.5	0.41	0.46	10.8	1.12
A6	19.2	0.37	0.43	13.9	1.16
A7	19.5	0.38	0.46	17.3	1.21
A8	21.3	0.39	0.45	13.3	1.15

Evaluation of buccal tablets

Physical evaluation of Atenolol buccal tablets

The results of the weight variation, hardness, thickness, friability and drug content of the tablets are given in Table 9.5. All the tablets of different batches complied with the official requirement of weight variation as their weight variation passes the limits. The hardness of the tablets ranged from 4.0 to 5.6 kg/cm^2 and the friability values were less than 0.77 % indicating that the buccal tablets were compact and hard. The thickness of the tablets ranged from 4.01 – 4.92 mm. All the formulations satisfied the content of the drug as they contained 95.38-99.82 % of Atenolol. Thus all the physical attributes of the prepared tablets were found to be practically within control limits.

Table 9: Physical evaluation of Atenolol buccal tablets

Formulation code	Weight variation (mg)	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Content uniformity (%)
A1	199.25	3.14	4.15	0.28	99.38
A2	198.12	3.56	4.96	0.63	97.42
A3	200.89	3.91	4.11	0.42	98.69
A4	201.43	3.11	4.98	0.82	99.27
A5	197.22	3.57	4.21	0.59	99.14
A6	199.67	3.82	4.98	0.39	98.89
A7	198.58	3.41	4.01	0.51	99.03
A8	201.35	3.87	4.28	0.72	97.51

Swelling Index

Table 10: Swelling Index and Mucoadhesive strength (G)

S.NO.	Formulations	Swelling Index (%)	Mucoadhesive strength(G)
1	A1	0.82	11.82±0.82
2	A2	1.19	13.28±0.85
3	A3	2.26	12.44±0.92
4	A4	2.96	15.72±0.79
5	A5	1.25	14.20±1.44
6	A6	2.31	18.23±1.11
7	A7	3.10	19.23±1.09
8	A8	4.21	15.24±1.75

Swelling index is an important parameter in judging the mucoadhesion property, at least in the initial stages, since water uptake is important for the polymers to uncoil and interact with the mucin. The swelling indices of the Atenolol buccal tablets reveals that while the buccal tablet formulations are all made of different materials, the extent of swelling differs based on the individual tablet composition. The Swelling indices of the first three formulations are quite low because of the fact that they started to disintegrate and lose mass soon after placing them upon the Petri-dish. The formulations containing higher levels of the polymers Carbopol displayed the highest swelling index.

***In vitro* release studies**

In vitro drug release studies were conducted in phosphate buffer pH 6.8 and the studies revealed that the release of Atenololfrom different formulations varies with characteristics and composition of matrix forming polymers.

Table 11: *In vitro* dissolution data for formulations A1 – A8

TIME (H)	Cumulative percente of drug release							
	A1	A2	A3	A4	A5	A6	A7	A8
0	0	0	0	0	0	0	0	0
0.5	22.86	29.44	33.26	21.43	26.11	31.27	29.27	39.58
1	29.12	34.35	48.45	36.92	32.28	39.43	36.19	48.97
2	34.28	42.48	53.36	45.41	44.15	47.12	44.95	59.66
3	48.73	46.46	61.68	51.82	53.22	52.62	58.28	63.29
4	54.94	58.19	65.46	58.95	59.23	62.33	66.88	71.87
5	68.16	64.18	78.37	64.24	67.18	64.28	68.16	77.61
6	72.24	67.26	86.98	77.23	72.21	71.43	77.51	84.34
7	85.95	79.14	94.29	83.22	79.32	84.12	86.25	91.54
8	91.62	93.98	99.85	89.12	87.51	91.41	93.96	96.82

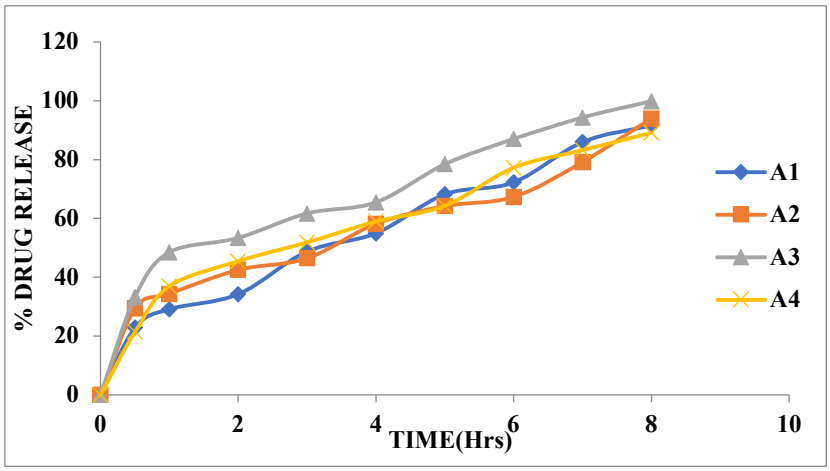

Fig : *In vitro* dissolution data for formulations A1 – A4 by using Chitosan polymer

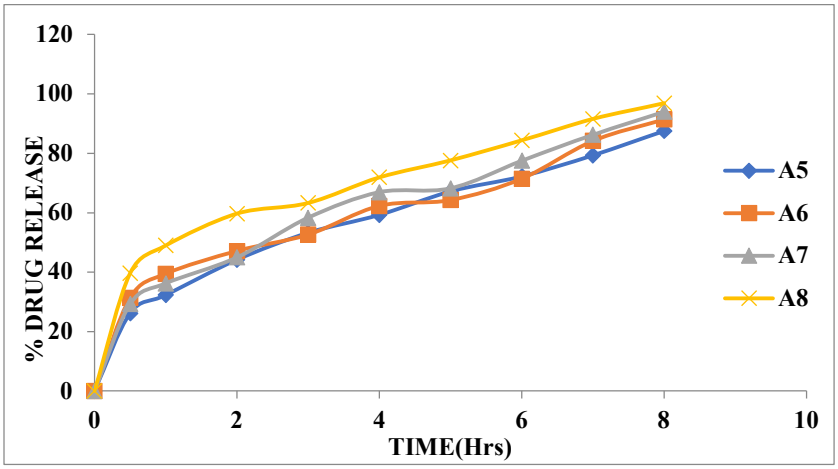

Fig 3: *In vitro* dissolution data for formulations A5 –A8 by using Carbopol polymer

From the dissolution studies observed Total Eight Formulation are prepared. The formulations prepared with Chitosan in different concentrations. The formulation TS2 was maximum drug released 92.69 % in 8 h. Concentration of polymer increased the drug release was decreased. The formulation was prepared with Carbopol the drug release was observed, the formulation TS6 was showed 99.58 % maximum drug release in 8 hours. Among all formulations TS6 was showed maximum drug r release in 8 hrs. So Formulation TS6 was selected as optimised formulation.

Table 12: Moisture absorption, surface pH of selected formulations

Formulation Code	Moisture absorption	Surface pH
A2	92	6.19
A6	98	6.01

The moisture absorption studies give important information of the relative moisture absorption capacities of polymers and it also give information regarding whether the formulations maintain the integrity or not. Among the selected formulations TS6 formulation shown good moisture absorption.

The surface pH of the buccal tablets was determined in order to investigate the possibility of any side effects. 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. The surface pH of the selected formulations was found to be 6.01 to 6.19 and the pH was near to the neutral. These results suggested that the polymeric blend identified was suitable for oral application and formulations were not irritant to the buccal mucosa.

Release kinetics

Data of *in vitro* release studies of formulations which were showing better drug release were fit into different equations to explain the release kinetics of Atenololrelease from buccal tablets. The data was fitted into various kinetic models such as zero, first order kinetics; higuchi and korsmeyer peppas mechanisms and the results were shown in below table.

Table 12: Release kinetics and correlation coefficients (R^2)

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
33.26	0.5	0.707	1.522	-0.301	1.824	66.520	0.0301	-0.478	66.74	4.642	4.056	0.585
48.45	1	1.000	1.685	0.000	1.712	48.450	0.0206	-0.315	51.55	4.642	3.722	0.920
53.36	2	1.414	1.727	0.301	1.669	26.680	0.0187	-0.273	46.64	4.642	3.600	1.042
61.68	3	1.732	1.790	0.477	1.583	20.560	0.0162	-0.210	38.32	4.642	3.371	1.270
65.46	4	2.000	1.816	0.602	1.538	16.365	0.0153	-0.184	34.54	4.642	3.257	1.385
78.37	5	2.236	1.894	0.699	1.335	15.674	0.0128	-0.106	21.63	4.642	2.786	1.855
86.98	6	2.449	1.939	0.778	1.115	14.497	0.0115	-0.061	13.02	4.642	2.353	2.289
94.29	7	2.646	1.974	0.845	0.757	13.470	0.0106	-0.026	5.71	4.642	1.787	2.854
99.85	8	2.828	1.999	0.903	-0.824	12.481	0.0100	-0.001	0.15	4.642	0.531	4.110

This formulation was following Higuchi release mechanism with regression value of 0.973.

Drug – excipient compatibility studies by physical observation

Atenololwas mixed with various proportions of excipients showed no color change at the end of two months, proving no drug-excipient interactions.

FTIR

FTIR spectra of the drug and the optimized formulation were recorded. The FTIR spectra of pure Atenololdrug, drug with polymers (1:1) shown in the below figures respectively. The major peaks which are present in pure drug Atenololare also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug. There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

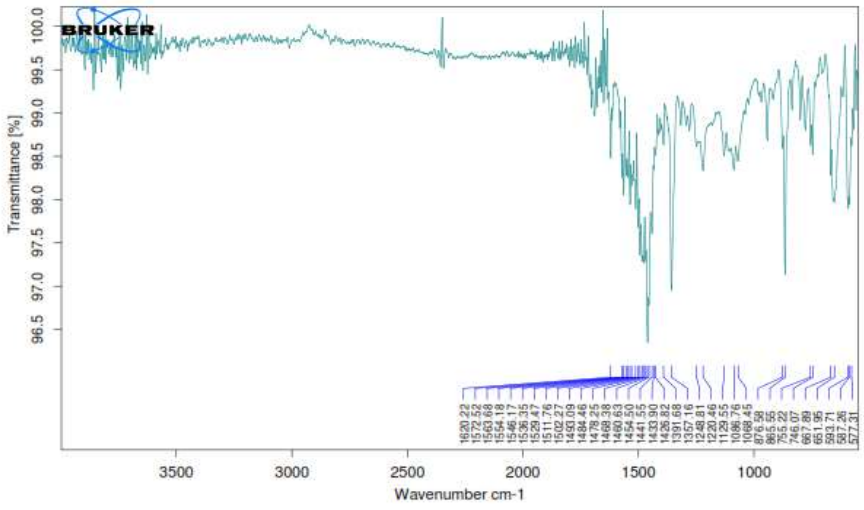

Fig 4: FTIR Peak of pure drug Atenolol

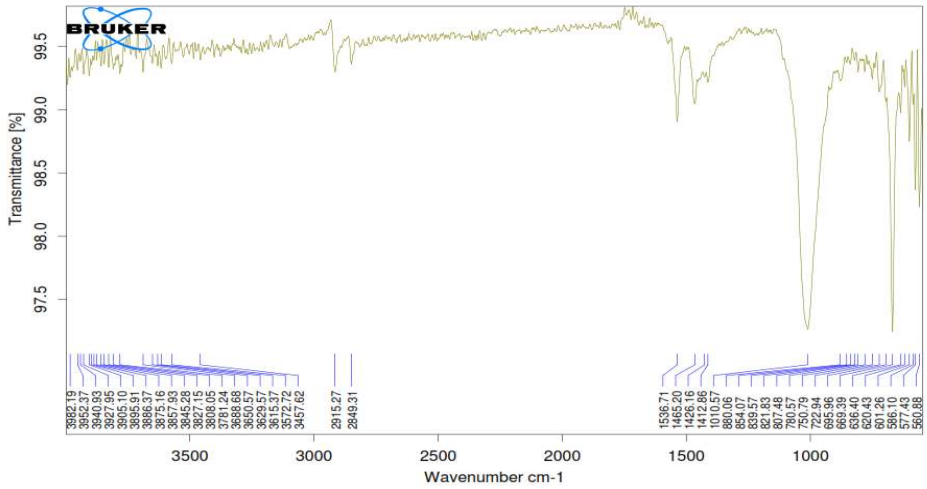

Fig 5: FTIR Peak of Optimised formulation

CONCLUSION

The study successfully developed Atenolol mucoadhesive buccal tablets with the aim of enhancing drug bioavailability and ensuring controlled release. The formulation process involved selecting suitable mucoadhesive polymers and excipients to optimize tablet properties and performance. The in vitro evaluations demonstrated that:

Formulation Success: The mucoadhesive buccal tablets exhibited favorable physical characteristics, including appropriate size, shape, hardness, and drug content uniformity, aligning with the designed specifications.

Mucoadhesive Properties: The tablets demonstrated significant mucoadhesive strength, which is essential for prolonged residence time in the buccal cavity, thereby potentially improving drug absorption and therapeutic efficacy.

Controlled Drug Release: The in vitro dissolution studies confirmed a sustained and controlled release profile for Atenolol from the buccal tablets. This indicates that the formulation effectively maintains drug levels over an extended period, which could enhance therapeutic outcomes and reduce dosing frequency.

REFERENCES

1. Gilhotra R.M., Ikram M., Srivastava S., Gilhotra N. A clinical perspective on mucoadhesive buccal drug delivery systems. J. Biomed. Res. 2014;28(2):81–97.
2. Bhowmik D., Chiranjib B., Pankaj K., Chandira R.M. Fast dissolving tablet: an overview. J. Chem. Pharm. 2009;1(1):163–177.
3. Shaikh R., Singh T.R.R., Garland M.J., Woolfson A.D., Donnelly F.D. Mucoadhesive drug delivery systems. J. Pharm. Bioall. Sci. 2011;3(1):89–100.
4. Alexander A., Ajazuddin S., Tripathi D.K., Verma T., Mayura J., Patel S. Mechanism responsible for mucoadhesion of mucoadhesive drug delivery system: a review. Int. J. Appl. Biol. Pharmaceut. Technol. 2011;2(1):434–445.
5. mart J.D. Buccal drug delivery. Expet. Opin. Drug. Deliv. 2005;2(3):507–517.
6. Boddupali B.M., Mohammed Z.N.K., Nath R.A., Bhanji D. Mucoadhesive drug delivery system: an overview. J. Adv. Pharm. Technol. Res. 2010;1(4):381–387.
7. Chinna, Chaitanya, Madhusudan, 2011; Velmurugan, Srinivas, 2013.
8. Russo et al., 2016; Salamat-Miller, Chittchang, Johnston, 2005.
9. Padsala, Desai, Swamy, 2014.
10. Miller NS, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. Advanced Drug Delivery Reviews, 2005; 57:1666– 1691.
11. Madhav N, Shakya AK, Shakya P, Singh K. Orotransmucosal drug delivery systems: A review. Journal of Controlled Release, 2009; 140: 2–11.
12. Miller NS, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. Advanced Drug Delivery Reviews, 2005; 57:1666–91.

13. Shojaei AH. Buccal Mucosa as A Route for SystemicDrug Delivery: A Review. J Pharm Pharmaceut Sci, 1998; 1(1): 15-30.
14. Alexander A, Ajazuddin, Tripathi DK, Verma T, Swarna, Maurya J, Patel S. Mechanism responsible for Mucoadhesion of Mucoadhesive drug delivery system: A review. Int. J. Applied Biology and Pharmaceutical Technology,2011; 2(1):434-45.
15. Smart JD. The basics and underlying mechanisms of Mucoadhesion. Advanced Drug Delivery Reviews, 2005; 57: 1556–68.