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DEVELOPMENT AND EVALUATION OF A HYALURONIC ACID-BASED BUCCAL PATCH FOR VALSARTAN DELIVERY

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Buccal patch, valsartan, hyaluronic acid, drug delivery

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ABSTRACT

The limitations of conventional oral dosage forms, such as poor patient compliance and reduced bioavailability, have driven the need for alternative drug delivery systems. Buccal drug delivery offers significant advantages, including bypassing first-pass metabolism, enhancing drug absorption, and ensuring a rapid onset of action. This study focuses on the development and evaluation of a valsartan-loaded buccal patch using hyaluronic acid (HA) as a bioadhesive polymer. Valsartan, an angiotensin II receptor blocker (ARB) used in the treatment of hypertension and heart failure, suffers from poor aqueous solubility and low bioavailability. Incorporating valsartan into a buccal patch aims to improve systemic absorption while reducing dose-related side effects. The formulated buccal patches were characterized for their mechanical properties, mucoadhesive strength, in-vitro drug release profile, and permeation efficiency. The inclusion of HA ensured prolonged adhesion to the buccal mucosa, enabling sustained drug release and enhanced therapeutic efficacy. Drug release studies indicated a controlled and predictable release pattern, while mucoadhesion tests confirmed adequate retention at the application site. The patches demonstrated desirable mechanical strength and elasticity, maintaining structural integrity throughout the administration period. The findings of this study suggest that a valsartan-loaded buccal patch formulated with hyaluronic acid offers an effective and patient-friendly alternative to conventional oral administration. This delivery system has the potential to enhance therapeutic outcomes, improve patient adherence, and minimize adverse effects associated with high oral doses. Future research may focus on in-vivo evaluations to validate the clinical applicability of this novel buccal drug delivery approach.

Introduction

The pharmaceutical industry has long relied on oral dosage forms, with tablets and capsules constituting the majority of marketed drugs. While effective, these traditional formulations often pose challenges for patient compliance, particularly among pediatric, geriatric, and psychiatric patients who experience difficulty swallowing. This issue can lead to improper dosing, reduced adherence, and suboptimal therapeutic outcomes, highlighting the need for alternative drug delivery systems that are both effective and patient-friendly. Buccal drug delivery has emerged as a promising approach, offering advantages such as bypassing first-pass metabolism, rapid drug absorption, and improved bioavailability. Among buccal drug delivery systems, buccal patches have gained attention due to their ease of application, prolonged retention, and controlled drug release, making them an attractive option for enhancing therapeutic efficacy. [1-6]

Valsartan, an angiotensin II receptor blocker (ARB), is widely prescribed for managing hypertension and heart failure. However, its poor aqueous solubility and low bioavailability necessitate higher oral doses, increasing the risk of side effects. Buccal administration presents an alternative that can circumvent hepatic metabolism, enhancing systemic drug absorption and reducing the required dosage. By formulating valsartan as a buccal patch, therapeutic efficacy can be improved while minimizing dose-dependent adverse effects, providing a patient-friendly approach to managing cardiovascular conditions. [7-11]

Hyaluronic acid (HA), a naturally occurring polysaccharide, has been recognized for its exceptional biocompatibility and mucoadhesive properties, making it an ideal bioadhesive polymer for buccal drug delivery. In addition to ensuring prolonged retention at the application site, HA offers controlled drug release, wound-healing properties, and anti-inflammatory benefits, enhancing both drug efficacy and patient comfort. These characteristics make HA a suitable excipient for buccal patch formulations, optimizing drug delivery performance while improving patient adherence. [12-17]

This study aims to develop and evaluate a buccal patch incorporating valsartan and hyaluronic acid as a bioadhesive polymer. The formulation will be systematically characterized to assess its mechanical properties, drug release profile, mucoadhesive strength, and in-vitro permeation. Parameters such as tensile strength, elasticity, and swelling properties will be analyzed to ensure structural integrity, while in-vitro drug release studies will provide insights into valsartan's release kinetics. By demonstrating the advantages of buccal drug delivery for drugs with poor solubility and bioavailability, this research may contribute to the development of more effective and patient-centric therapeutic options. Ultimately, the successful formulation of a valsartan-loaded buccal patch has the potential to enhance treatment outcomes and improve the quality of life for patients requiring long-term antihypertensive therapy. [18-24]

Material & Methods

Selection of Drug and Excipients

Valsartan, an angiotensin II receptor blocker (ARB) with low oral bioavailability (~23%) due to first-pass metabolism, is an ideal candidate for buccal drug delivery. Buccal administration bypasses hepatic metabolism, ensuring controlled drug release. Hyaluronic acid (HA) was selected as the bioadhesive polymer due to its mucoadhesive, permeation-enhancing, and biocompatible properties, facilitating improved absorption and patient compliance.

Preformulation Study

Preformulation studies were conducted to evaluate the physical, chemical, and compatibility properties of valsartan and

excipients. Organoleptic characterization, melting point, solubility, UV-visible spectroscopy, Fourier Transform Infrared Spectroscopy (FTIR), X-ray Diffraction (XRD), and Differential Scanning Calorimetry (DSC) analyses were performed to ensure drug stability and formulation feasibility.

Preparation of Valsartan-Loaded Buccal Patch

Buccal patches were prepared using valsartan, HA, polyethylene glycol (PEG), and distilled water. The polymeric solution was stirred at 800 rpm, followed by drug incorporation. The mixture was poured into petri plates and dried at room temperature for 24–48 hours. The dried films were cut into 2×2 cm^2 patches and stored in aluminum foil. Drug loading was calculated as Drug Loading (mg/cm^2) = Total Drug Amount (mg) / Total Surface Area (cm^2).

Evaluation of Buccal Patch

The patches were evaluated for:

General Appearance: Transparency, color, and texture.

Thickness & Weight Variation: Measured using a digital caliper and weighing balance.

Surface pH: Assessed by placing the patch in water and recording pH using a pH meter.

Moisture Loss: Measured after storage in a desiccator for three days.

Folding Endurance: Determined by manually folding the patch until breakage.

Disintegration Time: Evaluated in phosphate buffer (pH 6.8).

In-vitro Dissolution Study: Conducted using USP Apparatus I at 37°C, analyzing drug release via UV spectrophotometry at 250 nm.

Stability Study

The optimized batch was stored for three months under ambient conditions. Physical appearance, pH, thickness, disintegration time, and drug release properties were monitored to assess stability.

Results & Discussion

Selection of Drug and Excipients

Valsartan, hyaluronic acid, and polyethylene glycol (PEG) are chosen for the buccal patch formulation because of their complementary capabilities to distribute medication. Valsartan, an angiotensin II receptor blocker, is used to treat hypertension and heart failure. It was chosen for the buccal patch to circumvent hepatic first-pass metabolism, which increased bioavailability and speeded action. Hyaluronic acid is a bioadhesive polymer because of its mucoadhesive, biocompatible, and moisture-retaining qualities. It prolongs patch occupancy on buccal mucosa, promoting prolonged medication release and improved mucosal membrane absorption. Plasticiser polyethylene glycol (PEG) gives the patch flexibility and improves its mechanical characteristics. PEG modulates the polymeric matrix to increase drug penetration and control Valsartan release. Valsartan, hyaluronic acid, and PEG form a durable, flexible, and effective buccal patch with longer drug release, enhanced bioavailability, and patient compliance.

Drug Authentication

Organoleptic Properties

Table 1: Organoleptic Properties

Observation	Inference
Physical State	Crystalline
Colour	White
Odour	Odourless

To confirm its physical qualities, Valsartan was examined organoleptically. Crystalline medicine indicates a well-defined solid structure. The white powder indicates pure Valsartan and no obvious contaminants. Valsartan is odourless, which improves patient acceptability in pharmaceutical formulations. These organoleptic parameters match Valsartan's standard properties, confirming its purity and quality.

Melting Point Determination

The melting point of the valsartan by capillary fusion method was found in between 116-117°C.

Table 2: Melting point determination of Valsartan

Method Used	Observed Value	Mean±SD Value	Standard Value
Capillary Fusion	116°C	116.67±0.58°C	116-117°C
Capillary Fusion	117°C		
Capillary Fusion	117°C		

To verify Valsartan's purity and identification, capillary fusion was used to ascertain its melting point. The melting point was 116-117°C, which matches the literature value. The mean melting point was 116.67 ± 0.58°C, demonstrating limited fluctuation and consistent results. The drug's purity and conformity with pharmaceutical standards are confirmed by the tiny deviation within the standard range.

Solubility Determination

Formulation design depends on valsartan's multisolvent solubility. The BCS Class II medication valsartan is highly permeable and poorly soluble. Water, buffer solutions, and organic solvents like ethanol, methanol, and DMSO are tested for valsartan solubility. Poor water solubility hinders oral absorption. Buffers and organic solvents dissolve it better than water. Solubility may improve using solvents and surfactants. Valsartan's solubility in each solvent is analysed. Formulations benefit from solvent-soluble excipients.

UV-Visible Spectroscopy

The maximum wavelength of absorption (λmax) of Valsartan was determined using a UV spectrophotometer. Valsartan exhibited its highest absorption in ethanol at 250 nm, which is closely aligned with the standard value, as illustrated in the figure 1. Calibration curve values of valsartan in pH 6.8 phosphate buffer: Ethanol (50:50)

Table 3: Calibration curve of valsartan

Concentration(ug/ml)	Absorbance(nm)
0	0
2	0.071
4	0.148
6	0.251
8	0.273
10	0.369

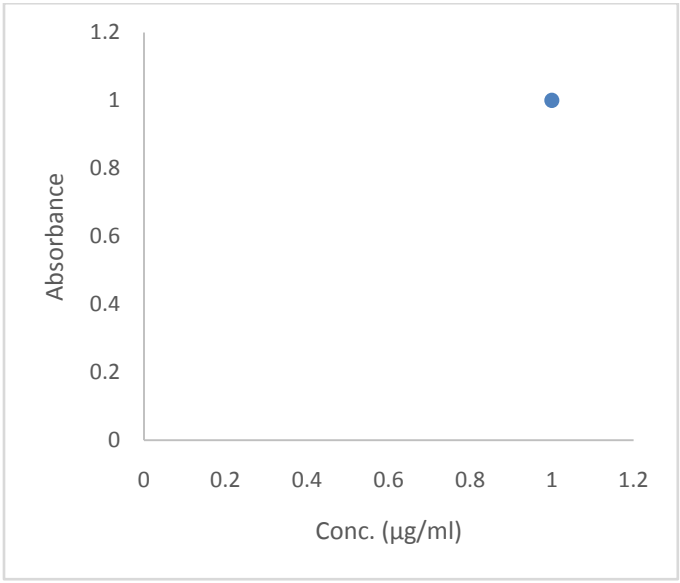

Figure 1: Calibration curve of valsartan in pH 6.8 phosphate buffer: Ethanol (50:50)

Fourier Transform Infrared Spectroscopy

Valsartan's FTIR spectrum was studied by Bruker. The spectrum in Figure 3 was thoroughly studied to find Valsartan's functional group peaks. FTIR research demonstrated that the pure drug exhibited all expected molecular structure peaks without loss, shift, or addition. The absence of pollutants or chemical degradation is shown. Unique peaks prove Valsartan's purity and structure. Spectral pattern analysis determines medication quality and consistency since

divergence may suggest contamination, degradation, or drug interactions.

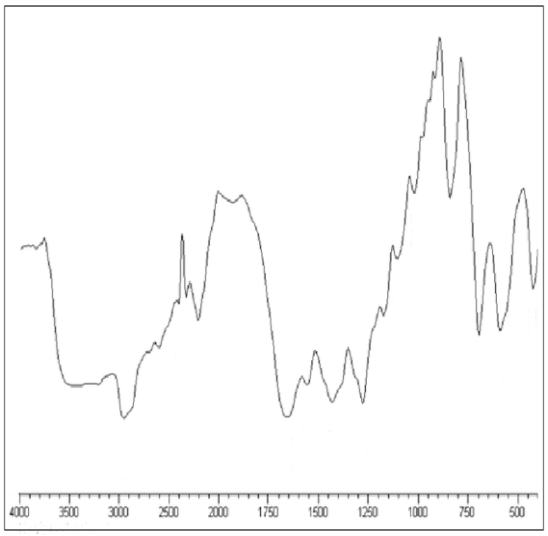

Figure 2: FTIR of Valsartan

Valsartan's FTIR spectrum identifies its functional groups and molecular structure through bond vibrations. Key absorption peaks include: 3300-3500 cm^{-1} (O-H stretching), 3100-3000 cm^{-1} (C-H stretching), 1700-1750 cm^{-1} (C=O stretching), 1600-1500 cm^{-1} (C=C stretching), 1250-1300 cm^{-1} (C-N stretching), and 1000-1300 cm^{-1} (C-O stretching). Analyzing pure Valsartan ensures expected peaks without additional bands, confirming purity and structural integrity. Comparing FTIR spectra with reference data validates its identity, essential for pharmaceutical quality control.

XRD Study

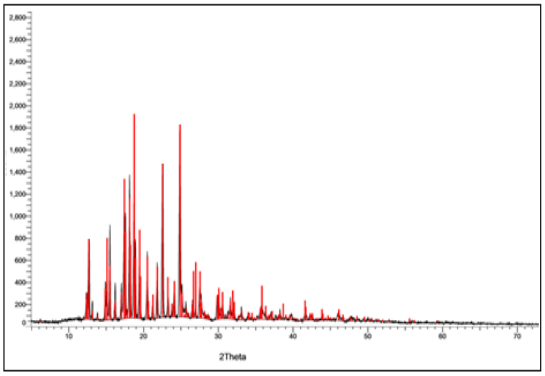

Figure 3: XRD of Valsartan

X-ray diffraction (XRD) analysis determines Valsartan's crystalline nature, polymorphic form, and purity. Sharp, well-defined peaks in its XRD pattern confirm crystallinity. Specific 2θ values indicate an orderly crystal lattice. Comparing the peak intensity and position with standard XRD data verifies Valsartan's identity and purity.

DSC Study

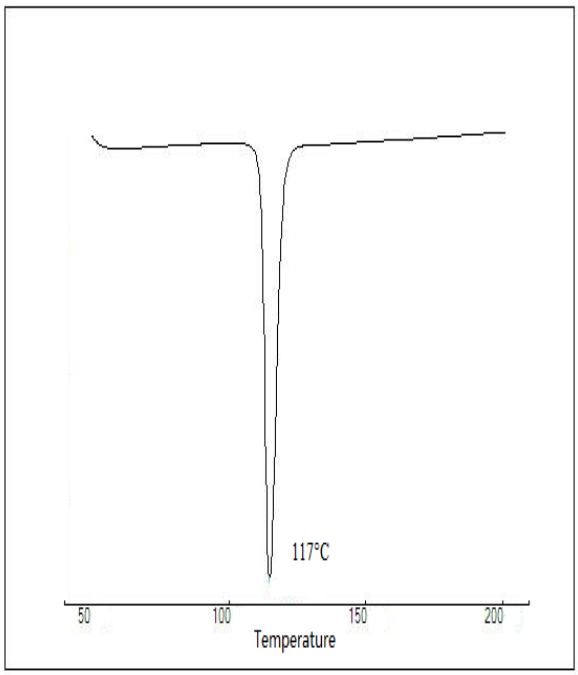

Figure 4: DSC of Valsartan

Differential scanning calorimetry (DSC) analyzes Valsartan's thermal behavior, including melting point, phase transitions, and stability. A sharp endothermic peak at 117°C confirms crystallinity. The absence of additional thermal events indicates high purity and no polymorphic transitions or impurities.

Preparation of Valsartan loaded buccal patches

Table 4: Valsartan loaded buccal patches

Batches	Hyaluronic acid (mg)	PEG 400 (ml)
B1	1000	10
B2	1250	10
B3	1500	10
B4	1000	20
B5	1250	20
B6	1500	20
B7	1000	30
B8	1250	30
B9	1500	30

Valsartan-loaded buccal patches were formulated in nine batches (B1–B9) with varying hyaluronic acid (1000, 1250, 1500 mg) and PEG 400 (10, 20, 30 ml) concentrations. This systematic variation enabled evaluation of their effects on mechanical, physicochemical, and drug release properties.

Evaluation of Buccal Patch

General appearance

The general appearance of all nine batches was assessed through visual observation and sensory evaluation. Parameters such as transparency, odor, color, and texture were carefully examined, and the findings are presented in the table below.

Table 5: General Appearance of Patches

Formulation	Visual Appearance	Odor	Color	Texture
B1	Semi-transparent	Odorless	White	Smooth
B2	Semi-transparent	Odorless	White	Smooth
B3	Semi-transparent	Odorless	White	Smooth
B4	Semi-transparent	Odorless	White	Smooth
B5	Semi-transparent	Odorless	White	Smooth
B6	Semi-transparent	Odorless	White	Smooth
B7	Semi-transparent	Odorless	White	Smooth
B8	Semi-transparent	Odorless	White	Smooth
B9	Semi-transparent	Odorless	White	Smooth

Thickness

The thickness of the patch was measured using calibrated digital Vernier caliper. Multiple measurements were taken at different locations on the patch, and the average thickness was calculated. The thickness was found to range between 0.20 mm to 0.25 mm.

Table 6: Thickness of the patches

Formulation	Thickness
B1	0.241 ±0.24
B2	0.247±0.21
B3	0.237±0.20
B4	0.224±0.18
B5	0.239±0.14
B6	0.236±0.27
B7	0.240±0.17
B8	0.223±0.19
B9	0.243±0.27

Weight variation

The weight variation ranged from 140 to 150 mg for batches B1 to B9.

Table 7: Weight Variation of patches

Formulation	Weight Variation (mg)
B1	140.13 ±0.35
B2	147.71 ±0.61
B3	144.33 ±0.26
B4	147.12 ±0.63
B5	148.21 ±0.25
B6	146.23 ±0.26
B7	147.32 ±0.18
B8	147.51 ±0.23
B9	150.0 ±0.21

Surface pH

The surface pH of all the patches was evaluated and found to be within the normal pH range of the oral mucosa. For the prepared batches B1 to B9, the surface pH ranged from 6.0 to 6.9, indicating that the patches are unlikely to cause skin irritation. This is significant as extremely acidic or basic pH levels can lead to irritation. The surface pH values of all film batches are summarized in the table below.

Table 8: Surface pH of patches

Formulation	Surface pH
B1	6.64 ±0.03
B2	6.67 ±0.02
B3	6.69 ±0.02
B4	6.64 ±0.05
B5	6.68 ±0.02
B6	6.70 ±0.03
B7	6.64 ±0.21
B8	6.66 ±0.03
B9	6.70 ±0.03

% Moisture Loss

Table 9: % Moisture loss of the patches

Formulation	% Moisture loss
B1	1.92±0.063
B2	2.12±0.084
B3	2.21±0.064
B4	1.33±0.026
B5	1.54±0.041
B6	1.17±0.052
B7	2.37±0.033
B8	2.24±0.034
B9	1.95±0.026

The percentage moisture loss of Valsartan-loaded buccal patches was assessed for stability and moisture retention. Batch B4 showed the lowest moisture loss (1.33 ± 0.026%), while B7 had the highest (2.37 ± 0.033%). Other batches exhibited values ranging from 1.17% to 2.24%. The results indicate good structural integrity and stability, with variations attributed to differences in polymer composition and formulation techniques.

Folding Endurance

Table 10: Folding endurance the patches

Formulation	Folding Endurance
B1	52 ±0.64
B2	56 ±0.04
B3	59 ±0.66
B4	87 ±0.17
B5	102 ±0.18
B6	105 ±0.23
B7	114 ± 0.61
B8	118 ±0.03
B9	126 ±0.14

The folding endurance of Valsartan-loaded buccal patches assessed mechanical strength and flexibility. B1 showed moderate flexibility (52 ± 0.64), while B9 exhibited the highest endurance (126 ± 0.14), indicating excellent strength. Endurance increased with higher polymer content, enhancing flexibility and durability.

Disintegration Time

Table 11: Disintegration time of the patches

Formulation	Disintegration time (Sec)
B1	30 ±0.24
B2	25 ±0.22
B3	32 ±0.15
B4	35±0.32
B5	29 ±0.13
B6	34±0.15
B7	32±0.21
B8	34±0.15
B9	36±0.31

The disintegration time of Valsartan-loaded buccal patches ranged from 25 ± 0.22 seconds (B2) to 36 ± 0.31 seconds (B9). Batches with lower polymer content disintegrated faster, indicating quicker drug release. All formulations showed acceptable disintegration times for buccal patches.

***In-vitro* dissolution studies**

Table 12: *In-vitro* dissolution studies

Formulation	% drug release after 10 min
B1	86.21±1.26
B2	88.28±1.92
B3	90.01±1.93
B4	92.74±1.27
B5	94.95±1.31
B6	97.02±1.52
B7	94.32±1.22
B8	95.64±1.52
B9	95.94±1.23

In-vitro dissolution studies showed drug release ranging from 86.21 ± 1.26% (B1) to 97.02 ± 1.52% (B6) after 10 minutes. Higher polymer concentrations enhanced drug release due to increased hydration, swelling, and diffusion, ensuring efficient dissolution.

Stability study

Table 13: Stability studies

Parameter	Initial	After 1 month	After 2 months	After 3 months
Thickness (mm)	0.24	0.24	0.24	0.24
pH	6.6	6.5	6.5	6.4
Folding Endurance	114	104	97	93
Disintegration Time	34	36	40	42
In vitro dissolution (%) after 10 min	97.02	96.16	95.13	93.45

A three-month stability study of Valsartan patches showed consistent thickness (0.24 mm) and slight pH reduction (6.6 to 6.4), remaining within the acceptable range. Folding endurance decreased from 114 to 93, indicating minor flexibility loss. Disintegration time increased from 34 to 42 seconds, and drug release slightly declined from 97.02% to 93.45%. Despite minor changes, the patches maintained good stability and efficacy for buccal drug delivery.

Conclusion

Valsartan, an angiotensin II receptor blocker, was formulated into buccal patches using hyaluronic acid as a bioadhesive polymer and polyethylene glycol (PEG) as a plasticizer to enhance flexibility and drug permeation. Preformulation studies confirmed the drug's identity, purity, and stability through melting point analysis (116-117°C), UV-visible spectroscopy (λmax 250 nm), FTIR, XRD, and DSC studies. Nine batches (B1–B9) were prepared with varying polymer concentrations and evaluated for physicochemical properties. The patches were semi-transparent, smooth, with uniform thickness (0.20-0.25 mm) and weight (140-150 mg). Surface pH (6.0-6.9) ensured minimal irritation, while moisture loss (1.17-2.37%) indicated stability. Mechanical properties improved with higher polymer concentrations, with B9 exhibiting the highest folding endurance (126). Disintegration time ranged from 25-35 seconds, ensuring rapid drug release. Overall, the formulated buccal patches showed promising mechanical and drug release properties for effective Valsartan delivery.

References

1. Patel VF, Liu F, Brown MB. Advances in oral transmucosal drug delivery. J Control Release. 2011;153(2):106-16.
2. Shojaei AH. Buccal mucosa as a route for systemic drug delivery: a review. J Pharm Pharm Sci. 1998;1(1):15-30.
3. Senel S, Kremer MJ. Buccal drug delivery systems for local and systemic applications. Expert Opin Drug Deliv. 2012;9(6):615-27.
4. Smart JD. Buccal drug delivery. Expert Opin Drug Deliv. 2005;2(3):507-17.
5. Gavini E, Bonferoni MC, Rassu G, et al. Buccal drug delivery systems and their use in the management of hypertension. Int J Pharm. 2021;599:120435.
6. Patel VM, Prajapati BG, Patel MM. Design and characterization of chitosan-based buccal adhesive drug delivery system of

propranolol hydrochloride. Acta Pharm. 2007;57(1):61-72.
7. Sohi H, Sultana Y, Khar RK. Taste masking technologies in oral pharmaceuticals: recent developments and approaches. Drug Dev Ind Pharm. 2004;30(5):429-48.
8. Rathbone MJ, Senel S, Pather I. Oral Mucosal Drug Delivery and Therapy. New York: Springer; 2015.
9. Lavanya K, Gomathi T, Rajasekar R, et al. Hyaluronic acid as a versatile polymer in transdermal drug delivery systems – A review. Int J Biol Macromol. 2020;143:290-303.
10. Bai L, Liu F, Hu K, et al. Buccal film as an alternative for oral delivery of valsartan: development, characterization, and pharmacokinetic evaluation. Drug Deliv. 2022;29(1):591-601.
11. Senel S, Hincal AA. Drug permeation enhancement via buccal route: possibilities and limitations. J Control Release. 2001;72(1-3):133-44.
12. Nafee NA, Ismail FA, Boraie NA, Mortada LM. Mucoadhesive buccal patches of miconazole nitrate: in vitro/in vivo performance and effect of aging. Int J Pharm. 2003;264(1-2):1-14.
13. Rathbone MJ, Drummond BK, Tucker IG. The oral cavity as a site for systemic drug delivery. Adv Drug Deliv Rev. 1994;13(1-2):1-22.
14. Harris D, Robinson JR. Drug delivery via the mucous membranes of the oral cavity. J Pharm Sci. 1992;81(1):1-10.
15. Peh KK, Wong CF. Polymeric films as vehicle for buccal delivery: swelling, mechanical, and bioadhesive properties. J Pharm Pharm Sci. 1999;2(2):53-61.
16. Perioli L, Ambrogi V, Angelici F, Ricci M, Giovagnoli S, Rossi C. Development of mucoadhesive patches for buccal administration of ibuprofen. J Control Release. 2004;99(1):73-82.
17. Squier CA, Wertz PW. Structure and function of the oral mucosa and implications for drug delivery. J Pharm Sci. 1996;85(1):1358-66.
18. Nafee NA, Boraie NA, Ismail FA, Mortada LM. Design and characterization of mucoadhesive buccal patches containing cetylpyridinium chloride. Acta Pharm. 2003;53(3):199-212.
19. Singh S, Jain S, Muthu MS. Tiwari S. Preparation and evaluation of buccal bioadhesive films containing clotrimazole. AAPS PharmSciTech. 2008;9(2):660-7.
20. Semalty A, Semalty M, Kumar G. Formulation and characterization of mucoadhesive buccal films of glipizide. Indian J Pharm Sci. 2008;70(1):43-8.
21. Shojaei AH. Buccal mucosa as a route for systemic drug delivery: a review. J Pharm Pharm Sci. 1998;1(1):15-30.
22. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: An innovative drug delivery system and dosage form. Int J ChemTech Res. 2010;2(1):576-83.
23. Patel VM, Prajapati BG, Patel MM. Formulation, evaluation, and comparison of bilayered and multilayered mucoadhesive buccal devices of propranolol hydrochloride. AAPS PharmSciTech. 2007;8(1):E147-54.
24. Kulkarni AS, Deokate UA. Natural polymers in drug delivery systems. Int J Pharm Sci Res. 2011;2(1):59-65.

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