WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 13, Issue 2, 373-379. Review Article ISSN 2277–7105

REVIEW ON BUCCAL PATCHES CONTAINING PERINDOPRIL AND HYDROCHLOROTHIAZIDE

Manisha P.*

Lecturer Department of Pharmaceutics Malik Deenar College of Pharmacy, Kasaragod.

Article Received on
28 November 2023,

Revised on 18 Dec. 2023,
Accepted on 08 Jan. 2024

DOI: 10.20959/wjpr20242-31013

***Corresponding Author**
Manisha P.
Lecturer Department of Pharmaceutics Malik Deenar College of Pharmacy, Kasaragod.

ABSTRACT

The objective of this study was to formulate and evaluate buccal patches containing hydrochlorothiazide (HCZ) and perindopril for sustained release. Films were fabricated by solvent casting using combinations of mucoadhesive polymers such as hydroxypropyl methyl cellulose (HPMC), hydroxypropyl cellulose (HPC), polyvinyl alcohol (PVA), polyvinyl pyrolidone (PVP) and ethyl cellulose (EC) as a backing layer. The patches were evaluated for physicochemical characteristics such as weight, thickness, surface pH, folding endurance, bioadhesive strength, swelling index, drug content, tensile strength, elongation at break and mucoadhesive time and *ex-vivo* permeation studies. The FT-IR spectral studies showed no interaction between drug and polymer. Physicochemical characteristics of all the formulations were satisfactory. The stability studies did not show any significant difference in external appearance, drug content, swelling index and *ex-vivo* drug permeation after a storage period of 2 months.

INTRODUCTION

Buccal patches are designed to deliver drugs systemically or locally via, buccal mucosa. The buccal mucosa provides readily accessible route for transmucosal delivery. Absorption through the buccal mucosa overcomes premature drug degradation due to the enzyme activity and pH of gastro intestinal tract.[1]

Buccal patches have unique characteristics including flexibility, relative rapid onset of drug delivery, sustained drug release and rapid decline in the serum drug concentration when the patch is removed. The patch is confined to the buccal area over which it is attached and

therefore the absorption profile may have less inter and intra individual variability. The most promising and challenging routes appear to be the nasal, sublingual and buccal.[2]

Transmucosal routes of drug delivery (i.e., the mucosal linings of the nasal, rectal, for systemic drug delivery. These advantages include possible bypass of first pass effect, avoidance of presystemic elimination within the GI tract and depending on the particular drug, a better enzymatic flora for drug absorption.[3]

Perindopril and hydrochlorothiazide (HCZ) in combination is usually prescribed in hypertension. Perindopril (PL), a drug widely used in the treatment of hypertension. However, its first pass metabolism results in poor bioavailability. HCZ, a thiazide diuretic commonly used to treatment for edema, hypertension, diabetes insipidus and hyperparathyroidism. To overcome all the shortcomings in conventional tablet dosage forms, there is a need to formulate mucoadhesive buccal patches which provide good advantages of easy accessibility and needle free drug application without necessity of a trained personnel facilitating self - medication. The objective of this study was to formulate and evaluate buccal patches containing hydrochlorothiazide (HCZ) and perindopril (PL) for mucoadhesive drug delivery.

MATERIALS AND METHODS

Hydrochlorothiazide and Perindopril was procured from Yarrow Chemicals Mumbai, India, HPMC K15M, Polyvinyl alcohol, Polyvinyl pyrolidone were procured from S.D. Fine Chem. Ltd, Mumbai, India. All the chemicals and reagents were used are of analytical grade.

Formulation of HCZ and PL Buccal Patches

Buccal patches were prepared by solvent casting method. Weighed amount of drug is dissolved in Dimethyl sulphoxide (DMSO) and PVP K-30 was added, Stirred well and ethanol was added to the mixture and HPMC K15/HPC was dissolved in it. Propylene glycol was added as plasticizer. Also buccal patches of (PVP: PVA) were prepared in specified amount of hot water (80-100°C) with stirring to produce a clear solution, incorporated into cooled gel solution and make up the volume with ethanol. The above mixtures in both the solutions was covered with aluminum foil and allowed to stand overnight to remove air bubbles. The solution was then poured into glass moulds of diameter 9 cm and kept aside covered with funnel to allow for controlled evaporation. The dried patches were cut into circular patches of 1.5 cm diameter, so that each patch contains about 12.5 mg of perindopril

and 12.5 mg of HCZ. Buccal patches of PVP K-30 and HPMC K15 in wereprepared in the ratios of 1:1, 1:1.5 and 1:2, Buccal patches of PVP – PVA were prepared ratio in the ratios of 9:1, 8:2, 7:3.[7]

Preparation of ethyl cellulose backing layer

Ethanol (5ml) was taken in a beaker containing 10 ml of acetone. Ethyl cellulose (1g) was dissolved in the above solvent with 0.35 ml of tri ethyl citrate as plasticizer. The polymer solution was kept for deaeration and then poured into 9.5 cm diameter petridish with an aluminum foil spread over the surface. The solution was kept for controlled evaporation of the solvents at room temperature. The dried layer was carefully removed from the aluminum foil and cut into films of 1.5 cm diameter.

Evaluation of buccal patches

1. **Uniformity of weight**

The individual weight of 10 samples of each formulation was determined and the average weight was calculated.

2. **Patch thickness**

The thickness of 10 patches of each formulation was determined using micrometer screw gauge and average was determined.

3. **Folding endurance**

This test indicates the ability of the films to sustain mechanical handling as well as pliability during use in the buccal cavity. The folding endurance was determined by repeatedly folding one patch at the same place till it broke or folded up to 300 times which is considered satisfactory to reveal good patch properties. The number of times the patch could be folded at the same place without breaking gives the value of the folding endurance.

4. **Surface pH of the buccal patches**

The patch to be tested was placed in petridish and was moistened with 0.5 ml of distilled water and kept for 30 seconds. The pH was noted after bringing the electrode of pH meter in contact with the surface of the formulation and allow to equilibrating for 1 min.

5. **Measurement of swelling index**

The buccal patch sample was weighed and placed in a pre weighed Stainless steel wire sieve of approximately 800 µm mesh. The mesh containing the patch sample was submerged into

15 ml of simulated salivary medium contained in a petridish. At definite time interval the stainless steel mesh was removed, excess moisture removed by carefully wiping with absorbent tissue and reweighed. Increase in weight of the patch was determined at each time interval until a constant weight was observed.

The degree of swelling was calculated using the formula
Swelling Index = Wt -W0/W
Where
Wt is the weight of the patch at time t and W_0 is the weight of the patch at time zero.[8]

6. Uniformity of drug content

This parameter was determined by dissolving one patch of 1.5 cm diameter designed to contain 12.5 mg of HCZ and 12.5 mg of Perindopril by homogenization in a mixture of 5 ml of ethyl alcohol and 2ml of DMSO for 5 hr with agitation and diluted to 50 ml with distilled water. After filtration to remove insoluble residue, 1 ml of the filtrate was diluted to 10 ml with simulated saliva of pH 6.8. The absorbance was measured at 272 nm and 268 nm using a UV spectrophotometer. The experiments were carried out in triplicate for all formulations.[7]

7. Tensile strength measurement

Tensile strength is the maximum stress (applied at one point) required to break the patch. This mechanical property was evaluated using 'Tensile strength apparatus'. Patch strips in special dimension and free from air bubbles or physical imperfections were held between two clamps positioned at a distance of 20 mm. During measurement, the strips were pulled by the down clamps at a rate of 5 mm/min, the force and elongation was measured when the patch broke. Two mechanical properties, namely, tensile strength and percentage elongation were computed for the evaluation of the patch.

Tensile strength = Force at break / Initial cross section area of the sample (mm^2).[9]

8. Percentage elongation

Percentage elongation to break = increase in length × 100 / original length.

9. Compatibility studies

FT-IR spectra matching approach was used for detection of any possible chemical interaction between the drugs and polymers. The individual sample of drugs and polymer powder and the three different drugs: polymer combination patches were prepared and mixed with

potassium bromide. It was scanned from 4000 - 600 cm^{-1} in Bruker FTIR spectrophotometer. The IR spectrums of the formulations were compared with those of pure drugs and matching was done to detect any appearance or disappearance of peak.

10. *In-Vitro* drug release

A patch of 1x 1 cm^2 size was cut and attached to a glass slide with a few drops of phosphate buffer (pH 6.8). This slide was kept in a dissolution apparatus containing 200 ml phosphate buffer (pH 6.8) solution and temperature was maintained at 37ºC. A non-agitated system was selected to eliminate any effect of turbulence on the release rate. Samples were withdrawn periodically. The solution was stirred with a glass rod and 5 ml of sample was withdrawn using a graduated pipette, whose tip was attached to a tube with glass wool (as a filter). 5 ml of the buffer was replaced immediately. The samples were taken periodically and analyzed for drug content at 272 and 268 nm by simultaneous estimation method.

DISCUSSION

FTIR studies indicates that no interaction between drug and the polymers. The IR spectrum of the HCZ shows the characteristic peaks at 3362.04 cm^{-1} (NH stretching group), 750.33 cm^{-1} (-NH bending group), 1604.83 cm^{-1} (C-C stretching group), 1244.13 cm^{-1} (SO_2 stretching) and 2360 cm^{-1} (-CH_2 group).The IR spectrum of Perindopril exhibited the principle peak at 3353.2 cm due to N-H stretching around 3557.85cm^{-1}, O-H stretching around 3300 cm^{-1}, aromatic C-H stretching around 3200 cm^{-1}, sp3C-H stretching 2957 cm^{-1}, C=O stretching around 1700 cm^{-1} and C-O stretching around 1045 cm^{-1}.

The weight of the patches ranges from 34.08 to 36.33 mm, weight of the patch is increases when the concentration of the polymers is increased. The films with increased polymer content showed a marginal increase in thickness and ranges from 0.67 to 0.75 mm. Folding endurance for all the formulations shows greater than 300 which indicates the flexibility of the film. It was found that among the formulations FA and FB, those with more HPMC and HPC respectively (FA3 and FB1) showed more bioadhesive force compared to other formulations.

The rate of swelling affects the duration of adhesion with faster swelling resulting in adhesion of shorter duration studies have shown that excessive hydration can lead to a weakening of the adhesive bond due to dilution of functional groups responsible for the adhesive interaction between the bioadhesive film and mucosa.

Formulations FA and FB, the tensile strength and % elongation increased with increase in the percentage of mucoadhesive polymer, HPMC K15M and PVP respectively. Proportions of PVP higher than that used in these films make them weaker. In the case of PVA films (FC3) TS and E/B is the greatest for FC3 and least for FC1, indicated that the inclusion of PVP decreased the tensile strength. Formulation FC showed high tensile strength (TS) compared to FA and FB which increased with increased amount of PVA which showed that PVA gives good TS to buccal patches compared to HPMC or PVP. Therefore such patches are tough. Mucoadhesive force also increases which results in longer mucoadhesion time among FA and FB formulations FA3 and FB3 show longer mucoadhesion time.

It was observed that mucoadhesion time was more with formulation containing PVA, the mucoadhesion time increased as the PVA content increase with a maximum of 7.15 hours in case of FC3. It was because as PVA content increased its mucoadhesive force also increased which results in longer mucoadhesion time. Among FA and FB formulations FA3 and FB1 showed longer mucoadhesion time.

The drug release from the patches varies with respect to the polymer ratio. An increase in drug release from the buccal patches was found with increase in concentration of polymers that are hydrophilic in nature. Among all formulations, the maximum drug release was observed in FA formulations, which contains different ratios of HPMC and PVP over a period of 7 hr.

The *ex-vivo* drug permeation across the porcine buccal mucosa for HCZ and PL delayed by half an hour while comparing the *in-vitro* drug release for the optimized FA formulation. The *in vitro* release data were fitted to zero order, first order, Higuchi matrix and Korsmeyer Peppas model and the correlation coefficients are compared and it is found to follow first order kinetics. The results of stability studies of HCZ and PL buccal patches showed no significant change with respect to physical appearance, drug content, surface pH, swelling index for a period of 60 days when stored in 30°C / 75% RH.

CONCLUSION

Buccal patches of HCZ and PL are prepared using polymers such as HPMC, HPC, PVA, PVP, in different ratio and combinations and showed satisfactory physiochemical and mucoadhesive characteristics. The concentration of polymers used in various formulations have influence on drug release from the prepared HCZ and PL buccal patches. From the

present study it is concluded that buccal patches of HCZ and PL provides sustained buccal delivery in the treatment of hypertension, which is a alternate to hepatic by pass metabolism.

ACKNOWLEDGEMENT

First of all, I thank God for giving me the strength to keep going. MY sincere thanks to all faculties and friends to all faculties and friends of Malik Deenar College of Pharmacy, for providing facilities for finishing my work.

REFERENCES

1. Jain N K. Controlled and novel drug delivery. CBS Publishers, New Delhi, 2000; 1.
2. Siddiqui N M D, Garg G, Sharma P K. A short review on novel approach in oral fast dissolving drug delivery system and their patents. Advances in Biological Research, 2011; 5(6): 291-303.
3. Vishwkarma D K, Tripathi A K, Yogesh P and Maddheshiyab B. Review article on mouth dissolving film. Journal of Global Pharma Technology, 2011; 3(1): 1-8.
4. Shojaei A H. Buccal mucosa as a route for systemic drug delivery: A review. Journal of Pharmacy and Pharmaceutical Sciences, 1998; 1(1): 15-30.
5. Wright D, Tomlin S. How to help when patients cannot swallow. The Pharmaceutical Journal, 2011; 286(5): 271-274.
6. Abang P, Momin M, Inamdar M, Kar S. Transmucosal drug Delivery-An overview. Drug Delivery Letters, 2014; 4: 26-37.
7. Patel N, Prabhu P, Dubey A, Kamath J V. Design and evaluation of buccal patch containing combination of hydrochlorothiazide.