GSC Biological and Pharmaceutical Sciences

eISSN: 2581-3250 CODEN (USA): GBPSC2

Cross Ref DOI: 10.30574/gscbps

Journal homepage: https://gsconlinepress.com/journals/gscbps/

(RESEARCH ARTICLE)

Check for updates

Development and evaluation of buccal patches of theophylline

Kapil Kumar *, Gurleen Kaur, Seema, Deepak Teotia and Ikram

Department of Pharmaceutics, Global Institute of Pharmaceutical Education and Research, Kashipur- 244713, Uttarakhand, India.

GSC Biological and Pharmaceutical Sciences, 2021, 16(03), 235–240

Publication history: Received on 20 August 2021; revised on 27 September 2021; accepted on 29 September 2021

Article DOI: https://doi.org/10.30574/gscbps.2021.16.3.0287

Abstract

Buccal patches are the types of formulations in which the drug is administered through buccal mucosa. these patches are or placed in between the gums and the for the pharmacological response. The main advantage of these patches is there is no first pass metabolism takes place and easily absorb in systemic circulation through themucosa .the main objective of this drug delivery system is to elevate or increase the bioavailability of the drug. the review informs about the steps involve in the preparation of buccal patch and to promote the awareness towards this type of drug delivery system. This article intends to analyze the overall profile of Buccal Patches and scope of future advances.

Keywords: Buccal mucosa; Buccal patch; Bio adhesive; Asthma; Theophylline

1. Introduction

Amidst the several routes of drug delivery, Buccal route of drug delivery is a great substitute [1].Buccal drug delivery is very beneficial because its ample blood supply in buccal mucosa, avoiding the liverwort effect and reachability [2] Nevertheless peroral management of drugs has drawbacks for instance hepatic first pass metabolism and enzymatic degradation within the GI tract, that forbid oral management of convinced classes of drugs especially peptides and proteins. Subsequently, other absorptive mucosae are measured as possible sites for drug managemen [3] Oral cavity is examined for various applications as well as for the handling of periodontal disease, aphthous and dental stomatitis, bacterial and fungal infection. For the past twenty years mucoadhesion has become matter of curiosity because of its efficient delivery by retaining a construction intimate contact with buccal cavity [4] The term bio adhesion is used to describe the add-on of a synthetic natural mucoadhesion to a biological tissue for a prolonged period of time. Mucoadhesion occurs when a substrate in a mucosal system stick to and intermingles mainly with the mucus layer.5 Such drug delivery platforms have adhesive properties which can decrease the enzymatic degradation because of the rising intimacy between the delivery vehicle and the absorbing membrane [6]

In buccal drug delivery, the use of mucoadhesive polymers has a greater application. Recently numerous mucoadhesive devices have been developed including tablets, disks, films, strips, ointments, patches, and gels. Nevertheless, buccal patch gives more flexibility and relief than the other devices. Since the gels are effortlessly washed away by saliva, a patch can avoid the problem of the comparatively short dwelling time of oral gels on mucosa. Buccal route of drug delivery delivers the straight contact to systematic circulation through jugular vein circumventing the first pass hepatic metabolism leading to high bioavailability [7]

Unifacial mucoadhesive buccal patches containing theophylline were developed in the current study to ensure sufficient drug release, avoid 1st-pass metabolism, there fore enhance bioavailability of results.

* Corresponding author: Kapil Kumar
Department of Pharmaceutics, Global Institute of Pharmaceutical Education and Research, Kashipur- 244713, Uttarakhand, India.

2. Method Of Preparation

2.1. Preparation of buccal patches

B.P contains Theophylline and different additive in different proportion HEC ,HPMC E15, PVA, and PG are manufacture with the solvent casting method. Drug and polymer are dissolved respectively in 5ml methanol and in a separate container with distilled water with distilled water 20ml with consrant stirring upto 4 hrs. After it blend both medicament and polymers plasticizer like P.G in it. Solution obtained is kept aside for a nyt to get a bubble free clear sol. , pour the sol. in the petridish and allow to dried (40°C). Carefully remove the patch . Take one piece of it (1mm) and check any imperfection in it, then they are pack in Al. foil and kept on dessicator for retaining the elasticity of patch [8].

Table 1 Theophylline buccal patch composition

Components	F1	F2	F3	F4	F5
Theophylline	200 mg	200 mg	200 mg	200 mg	200 mg
HPMC	700 mg	-	200 mg	370 mg	450 mg
HEC	-	700 mg	450 mg	370 mg	200 mg
PVA	120 mg	120 mg	120 mg	120 mg	120 mg
ETHANOL	5 ml	5 ml	5 ml	5ml	5 ml
Propylene glycol	0.6 ml	0.6 ml	0.6 ml	0.6 ml	0.6 ml
Dist. water	20 ml	20 ml	20 ml	20 ml	20 ml

2.2. Physical parameter

2.2.1. Patch thickness

It is estimated by selecting randomly 5 separate location with a screw gauge. The std. deviation and mean are calculated[9].

2.2.2. Folding Endurance

It was measured by selecting a patch having dia. 20 milimeter and folded it until it may break. Folding endurance is calculated by folding the patch (no. of fold) until it may break[10].

2.2.3. PH of surface

Agar plate is used to determine it ,3 film of every formulation placed on agar plate for swelling for two hours and after it ph is measured with the help of pH paper. 3 reading mean is taken[11].

2.2.4. Water uptake study

It indicates polymer capacities of relative moisture absorption and idea of absorbtion of moisture. In this test 5% w/v of agar hot water after that transfer then in petri-dish and allow to solidify. Drug free six patch selected and wt. and placed it in vaccum over night for study to eliminate moisture, laminated on side of impermeable layer and incubate at 37°C for an hr. Percentage moisture absorption is measured by this formula[12].

$$\% \text{ Moisture absorption } = \frac{\text{F. I} - \text{I. W}}{\text{I. W}} \times 100$$

F.I : final wt

I.W: Initial wt.

2.3. Performance parameter

2.3.1. Uniformity of medicament content

It is determine by grasp 3 film of every preparation on different 100 ml volumetric flask and than phosphate buffer 100 ml having pH 6.8 is added with stirring for 24 hrs than filtered and observed at 276 nm in ultra violet spectroscopy. Final reading is taken by average of these three films [13].

2.3.2. Measurement of bioadhesive strength

S tube consist of a device which regulate flow and a thread of nylon to make glass plate and pan to suspended. A stage of acrylate is attached to glass beaker's centre and beaker is filled with phosphate buffer (pH 6.8) to maintain in vivo salivation condition. Phosphate buffer temperature was maintained by the temp. controller having magnetic stirrer. A 3 cm long porcine gastric membrane piece is tide up by thread to acrylate stage. A adhesive is used to attach film on glass plate center [14].

2.3.3. Mechanical strength

It were measured by the use of a advanced force gauze attached to motorized test which attached to a cell. Patch having diameter 60 × 10 mm without defect were taken and placed in middle of two clamps which having distance 3cm to each other. These clamps are designed to prevent the risk of patch crushing during the test. Upper clamp move at a pace of 2mm/sec and also pulled streps until the patch is broke and lower clamp act as a stationary force and patch elongation on the point at which the patch were broke is noted[15-17]. Break value at elongation and tensile strength were measured by the formula is

$$\text{Tensile strength (kg. mm} - 2) = \frac{\text{Force at break (kg)}}{\text{Initial cross} - \text{sectional area of sample (mm2)}}$$

$$\text{Elongation at break (\%. mm} - 2) = \frac{\text{Raise in length (mm)}}{\text{Actual length Cross sectional area(mm2)}} \times 100$$

2.3.4. In-vitro Release Study by Dissolution

Table 2 Evaluation parameters

Formulation Code	Physical Parameters			
	Thickness (mm)	**Folding Endurance**	**Mechanical Strength (kg/mm²)**	**H_2O Uptake study**
F1	0.22±0.004	306±4.05	6.27±0.085	2.14±0.63
F2	0.23±0.011	305±5.68	7.05±0.052	2.05±0.61
F3	0.25±0.003	315±3.21	13.54±0.089	2.95±0.115
F4	0.25±0.0021	317±2.50	12.14±0.041	1.94±0.153
F5	0.26 ±0.004	303±2.00	10.71±0.126	2.00±0.083

Medicament liberation from the b.p is reviewed and calculated with the help of US pharmacopoeia XXIII rotating paddle technique, using 500 mililiter phosphate buffer as dissolving medium at 37.5 ° C and round at speed of fifty r.p.m. Patches of 1cm2 were cut out and sandwiched between dialysis membranes. To keep the assembly from floating, a fragment of glass slide is use for support.The patched dialysis membrane tubing was sealed on both ends with closure clips before being placed in the vessel bottom with pH 6.8 p.b. At a predetermined time interval, 5ml samples were removed and displace along new buffer media. Sample are filter by Whatmann filter paper then examined at 277nm with a UV spectrophotometer. The tests were conducted three times, with the average values computed and presented[18-21].

In P.BpH 6.8, the *in vitro* disso. was investigated. The *in-vitro* disso. test are done 3 times, findings in the table represent the average of three replicates. Tables 7 to 11 show the Invitro data for patches F1 to F5.

Table 3 Performance parameters evaluation of Theophylline

Formulation code	Performance parameters (Bio adhesive)		
	B.A.S (gms)	Force of adhesion	B.S (kg/mm²)
F1	143.5±2.65	1.41±0.02	456.04±5.48
F2	148.30±2.14	1.45±0.03	438.11±4.12
F3	189.68±0.98	1.83±0.06	588.07±5.36
F4	175.23±0.89	1.65±0.03	553.48±1.76
F5	165.37±1.41	1.75±0.02	483.72±3.44

Table 4 Performance parameters evaluation of Theophylline

Formulation code	Performance parameters (Bio adhesive)		
	Medicament content (mgs)	Surface PH	In vitro residence time (min (kg/mm2)
F1	3.72±0.24	6.5±0.48	330±5
F2	3.68±0.78	6.3±0.42	360±10
F3	3.75±0.014	6.7±0.49	480±10
F4	3.65±0.21	6.4±0.56	410±10
F5	3.70±0.38	6.3±0.51	460±5

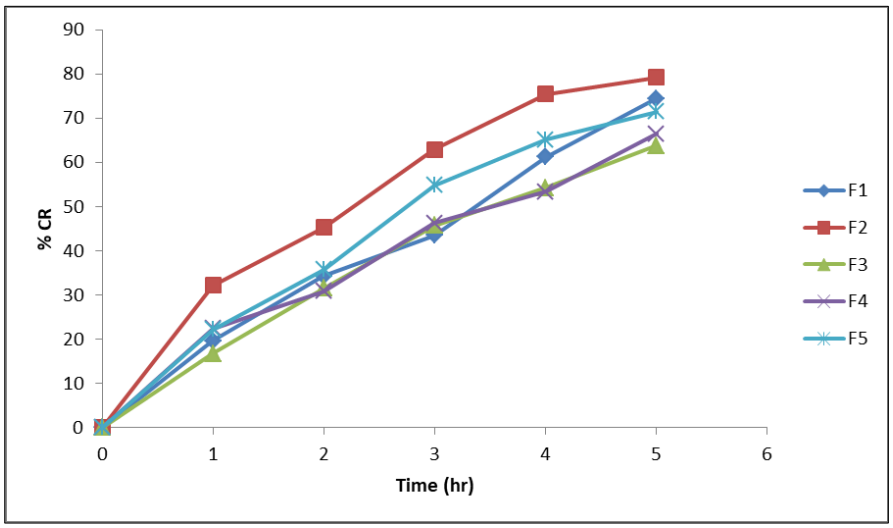

Figure 1 Release profile of formulations

3. Discussion

Mucoadhesive B.P are produced along various polymer like HEC, HPMCand PVA in different ratio with the help of Solvent casting technique. The patche are assign for numerous tests like folding endurance, thickness, variation in wt., uniformity of medicament content, surface p^H, kinetic study, Mechanical strength, bioadhesive strength and in-vitro release study.

Buccal patch produced from each formulation having thickness in range btw0.22 – 0.26mm.

Each formulation folding endurance was establish in range btw 303 – 317. It shows that the patch flexibility is good. For evaluation three patch of every formulation is taken and mean value is noted. Value was come within range 6.27 – 13.54 kg/mm^2. This indicates good mechanical strength of patch. Table no-5 show water uptake study of theophylline containing buccal patches. Patch swelling was altering with respect to ratio of polymer. The value came under the range 1.94 – 2.95. Formulation F3 has maximum that is 2.95. It shows polymer swelling nature.

The consistency of drug content of each batch shown in table – 6.2. Test were accomplished with the replicate of three each. Drug content mean establish within range 3.65 – 3.75 (diameter of each patch is 10mm) the produce formulation of buccal patch. It represents constant drug dispersal in matrix of polymer.

Device for buccal mucosa should maintain contact to mucous layer which cover the epithelial tissue. This is very useful parameter for the utilization of dosage form, so in- vitro detection is carried out by use of gastric mucosa of porcine. It tells us about bioadhesive strength indirect quantification in gms. F3 formulation shows greatest adhesion of force and bioadhesive strength and the result is189.68 - 1.83 resp. Time of in- vitro test is recorded and the result may vary due to the change in polymer and highesttimeis 490mins for F3.

It is in btw 6.3 - 6.7 for all drug formulations andwithin the salivary pH range 6.2 to 7.4. Surface p^H of patches have no difference. It denotes good patient acceptability. Study of dissolution was done with phosphare buffer having pH 6.8, done in three times and replicate value mean are seen in result table. Data extracted through patch F1 – F5 are in table number 7 -15. The highest data is obtained by F3, it is upto 10 hrs. The uniform release of drug is due to true blending of ingredients and polymers hence the medicament shows steady state release**.** To learn kinetic of drug liberation data is plotted in different kinetics models'mechanism of release of drug is observed by curve fitting. All formulations show n value 1.700 – 1.806, release of drug obey anomalous diffusion which denotes pairing of erosion mechanism and diffusion and also define that the measurement is done more than one time. Zero order kinetic is best explain and it show highest linearity which is $r^2 = 0.983$ and it also denotes that the drug release rate is independent to concentration.

4. Conclusion

The current analysis, an effort has made to advance DDS in mucoadhesive buccal cavity patches form for the liberation of theophylline in synergetic way, to uphold continuous medicative quantity of drugs for long time period. Design of buccal mucoadhesive patches of theophylline were advance to an acceptable extent in the term of release of drug, bioadhesive strength, uniformity of content, surface p^H, water uptake percentage, mechanical strength and thickness.

If all patches of buccal display suitable results, finest results were achieve with enhanced formulations F3 holding HEC and HPMC in the ratio 1:3. In-vitro study of dissolution of enhanced formulation manifest that cum. drug liberation percentage of theophylline arising out the patches showed because of study of erosion mechanism and diffusion. The Non –fickian released pattern were establish.

The overhead study come to an end that the surety of manufacturing of mucoadhesive DDS for theophylline can be much effective and allowable likewise convectional drug delivery of theophylline and also possess adequate profile of controlled release that can give an enlarge therapeutic efficacy.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest statement.

References

[1] Sang-Chul Shin, Jin-Pil Bum, Jun-Shik Choi. Enhanced bioavailability by buccal administration of triamcinolone acetonide from the bioadhesive gels in rabbits, Int. J. Pharmaceutics. 2009; 209: 37- 43.

[2] Shoba Rani R. Hiremath; Industrial Pharmacy, Orient Longman private limited, First edition. 2008; 73-77.

[3] Giradkar KP. Design development and *in vitro* evaluation of bioadhesive dosage form for buccal route, International journal of pharma research & development. 2010; 2.

[4] Bhartee Pathak, Kapil Kumar. Buccal drug delivery system: a tool for the effective delivery of pharmaceuticals. Universal Journal of Pharmaceutical Research. 2017; 2(3): 19-24.

[5] Calum R, Park, Dale L, Munday. Development and evaluation of a biphasic buccal adhesive tablet for nicotine replacement therapy. Int. J. Pharm. 2002; 237: 215-26.

[6] Subhash V, MadhuriChannawar, Anil V, Unmesh, Kailash R. Chitosan based sustained release mucoadhesive buccal patches Containing verapamil HCl, Int. J. Pharm. Pharm. Sci., 2009; 1(1): 216-29.

[7] Güneşm, Karavana Sy, Algin Yapar E. Buccal drug delivery system: an overview about dosage forms and recent studies. Universal Journal of Pharmaceutical Research. 2019; 4(6): 69-74.

[8] Rao NGR, Shravani B, Reddy MS. Overview on buccal drug delivery systems. J Pharm Sci Res. 2013; 5: 80-8.

[9] Nayaka SK, Manjunath K, Pawan C. Formulation and evaluation of mucoadhesive buccal films of dothiepin HCL. Int J Pharm Pharm Res. 2020; 18: 535-48.

[10] Okorochukwu Nnamdi, Ihuaku Emmanuel C. Development and characterization of mucoadhesive patches for buccal delivery of pregabalin. Universal Journal of Pharmaceutical Research. 2017; 2(3): 6-9.

[11] Miller NS, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery.Adv Drug Deliv. 2002; 57: 1666-91.

[12] Moataz MF, Mohamed JS. Creation and assessment of buccal mucoadhesive sustained release oral films. Int J Pharm Pharm Res. 2019; 16: 30-41.

[13] Singh S, Virmani T, Virmani R, Kumar P, Mahlawat G. Fast dissolving drug delivery systems: formulation, preparation techniques and evaluation. Universal Journal of Pharmaceutical Research. 2018; 3(4): 56-64.

[14] Benedict A, Mathew MM, Sathyan J, Thomas J. Buccal film: An emerging technology for oral drug delivery. Int J Pharm Pharm Res. 2017; 9: 204-13.

[15] Omer AM. The efficiency of inefficiency: medicine distribution in Sudan. Universal Journal of Pharmaceutical Research. 2018; 3(2): 47-57.

[16] Roychowdhury S, Gupta R, Saha S. A review on buccal mucoadhesive drug delivery systems. Indo Glob J Pharm Sci. 2011; 1: 223-33.

[17] Fatima AA, Chukwuka UK. Development and in-vitro evaluation of matrix-type transdermal patches of losartan potassium. Universal Journal of Pharmaceutical Research. 2017; 2(2): 16-20.

[18] Miller NS, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery, Advanced Drug Delivery Reviews. 2005; 57: 1666–91.

[19] Patel KV, Patel ND, Dodiya HD, Shelat PK. Buccal bioadhesive drug delivery system: An Overview.Int J Pharm Bio Arch. 2011;2(2): 600-9.

[20] Francis DJE. Development and evaluation of matrix type transdermal patches of pioglitazone hydrochloride. Universal Journal of Pharmaceutical Research. 2016; 1(1): 17-20.

[21] Amir H. Systemic drug delivery via the buccal mucosal route, Pharmaceutical technology. 2001; 1- 5.