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Formulation and evaluation of Mucoadhesive Buccal patches of Diclofenac sodium

G Divya [1*], B Roopa [2], P Sai Tarun [3], N Ashwitha [4], S Rahul [5], O Akshay [6]

[1] Assistant professor, Department of Pharmaceutics, Siddhartha Institute of Pharmacy, Korremula Rd, Narepally, Ghatkesar, Hyderabad, Telangana, India

[2-6] Deparment of Pharmaceutics, Siddhartha Institute of Pharmacy, Korremula Rd, Narepally, Ghatkesar, Hyderabad, Telangana, India

* Corresponding Author: **G Divya**

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Abstract

Mucoadhesive patches of Diclofenac sodium were prepared by solvent casting method. To develop mucoadhesive patches for buccal administration of Diclofenac sodium and evaluation. The Mucoadhesive buccal patches of Diclofenac sodium were formulated using HPMC (hydroxy propyl methyl cellulose) as polymer and Methanol as solvent. HPMC also helps in formation of Film. A full factorial design was used to design the experiments for each polymer combination. A total of six formulations were prepared.

All the patches were characterized by Physico-chemical evaluation. The prepared Patches were smooth, uniform in thickness, mass, drug content and showed no visible cracks or folds. Of these 15 formulations prepared 6 patches showed high folding endurance and these patches were selected for further evaluations such as thickness, surface pH, and uniformity weight and percentage moisture loss. These patches are best fitted to the Korsmeyer-Peppas model.

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Keywords: buccal delivery system, diclofenac sodium, polymers, solvent casting technique, mucoadhesive patches, in-vitro release studies

Introduction

Buccal Drug Delivery System (BDDS) has been studied as an advance drug delivery approach instead of using and following traditional drug administration routes [1]. Drug side-effects can be greatly reduced and drug delivery in a proper manner can be achieved at intended site through BDD [2]. The delivery of medicines by buccal mucosa (BM) has attracted great interest because of its convenient availability [3]. 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 [4]. Buccal film may be preferred over adhesive tablet in terms of flexibility and comfort. In addition they can circumvent the relatively short residence time of oral gels on the mucosa, which are easily washed away and removed by saliva. Moreover, the buccal films are able to protect the wound surface, thus reducing pain and treating oral diseases more effectively [5]. Diclofenac sodium is benzene acetic acid,-[(2, 6-dichlorophenyl) amino] monosodium salt. Diclofenac sodium is an analgesic and anti-inflammatory. Diclofenac sodium is a cyclo-oxygenase inhibitor; analgesic, anti-inflammatory agent [6].

Materials

Diclofenac was obtained from Hetero labs, HYD. HPMC procured from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

Methodology

Formulation studies [7]

Preparation of buccal patches of Diclofenac Sodium using methanol and its combinations:

The buccal mucoadhesive patches of Diclofenac Sodium were prepared by solvent casting technique using water as solvent. Different polymer combinations were tried out (HPMC) full factorial design was used to design the experiments for each polymer combination. Aqueous polymer solutions of different concentrations were mixed in different ratios as mentioned in table below.

Table 1: Composition of various patch formulations with methanol and its combinations

Formulation	HPMC(gm)	Methanol(ml)	Diclofenac sodium(mg)
A1	1.5	25	0.8
A2	1.5	5	0.8
A3	1.0	15	0.8
A4	4.0	60	0.8

The above polymer solutions were mixed with 3ml of Glycerol with continuous stirring for a period of 30 min to get a homogenous clear solution. To this mixture a drug solution and methanol was added this solution was then poured into a clean Petri dish. Patches were then allowed to dry at room temperature for 24hr [8]. Finally the patches were dried completely at room temperature. After careful examination, the dried patches were removed, checked for any imperfections or air bubbles and cut into 2cm diameter patches using a specially fabricated circular stainless steel cutter. The diameter of the patch was determined using Vernier calliper. The patches were laminated on one side with a water impermeable backing layer. The samples were packed in aluminium foil and stored in a glass container at room temperature [9].

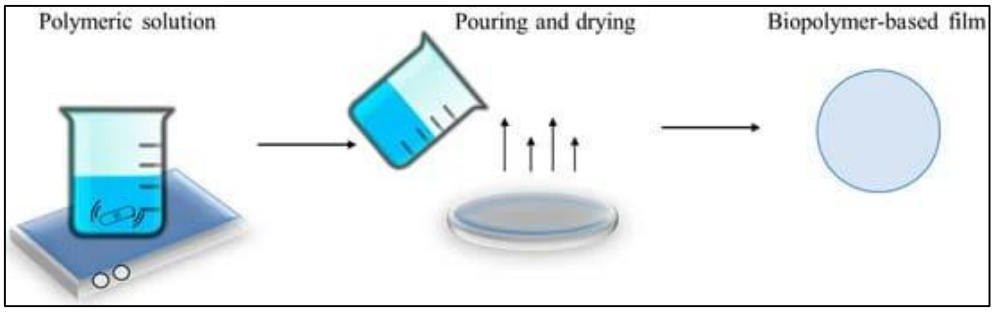

Fig 1: Preparation of buccal patch

Characterization of Buccal formulation

Physical appearance

All the formulated Diclofenac Sodium films were observed for color, clarity, flexibility, and smoothness [10].

Folding endurance

Buccal patches folding endurance was estimated by frequently double over at the same place till it broke. The number of times the film could be folded at the same place without breaking is the folding endurance. This was restate on all the films for three times and the mean values plus standard deviation was calculated [11].

Thickness of the film

The thickness of each film was measured by using screw gauze. Buccal patches thickness was estimated at various sites on each patch and the average thickness of the buccal patch was capture as the thickness of the patch [12].

Weight uniformity

The formulated buccal patches are to be dried at 600C for 6 hours before trial. A identify the area of 4.52 cm2 of film is to be cut in different parts of the patch and weigh in digital balance. The average weight and standard deviation values are to be calculated from the individual weights [13].

Drug content

The formulated buccal patch were assayed for drug content in each case. Patches from each formulation were assayed for content of drug. Each formulation was casted in triplicate and one patch from each was taken and assayed for content of drug.

The Buccal films (4.52 cm2) were added to conical flask containing 100 ml of phosphate buffer pH 7.4 contain 0.5% SLS. This was then stirred with magnetic bead at 400 rpm for 2 hrs. The contents were filtered and the filtrate was analysed spectrophotometrically. Similarly a blank was prepared from buccal films without drug [14].

Moisture absorption studies

The buccal patches were weighed exactly and placed in a desiccators containing aluminium chloride to maintain 79.50% RH. After 3 days, the films were taken out and weighed. The percentage of moisture uptake was calculated using the following formula [15].

Percentage moisture uptake= (Final weight- Initial weight)/(Initial weight) ×100

Moisture loss studies

Three patches were weighed separately and kept in a desiccator contains calcium chloride at 370C for 24 hours. Then the last weight was noted when there was no further change in the weight of the patch. The percentage of moisture loss was calculated using the following formula [16].

Percentage moisture loss= (Initial weight-Final weight)/

(Final weight) ×100

Swelling study

three buccal patch were weighed individually (W1) and placed separately in 3% agar gel plates and incubated at 37 ± 1°C. After every 15min time interval until 1 h, the patches were removed from the Petri dish and excess surface water was removed carefully with blotting paper. The swollen patch was then reweighed (W2) and the swelling index (SI) were calculated using the formula given in equation [17].

[Swelling Index = [(W2-W1) ÷ W1] × 100,]

Where W1 = initial weight of the patchW2 = final weight of the patch

Stability studies

Optimized medicated buccal films were subjected to short term stability testing. The Buccal films were sealed in aluminium foils and kept in a humidity chamber maintained at 40 ± 2 0C and 75 ± 5% RH for 3 months as per ICH guidelines [18].

Results and Discussion

Compatibility studies of drug and polymers

All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between Diclofenac Sodium and polymer. It also confirmed that the stability of drug during microencapsulation process.

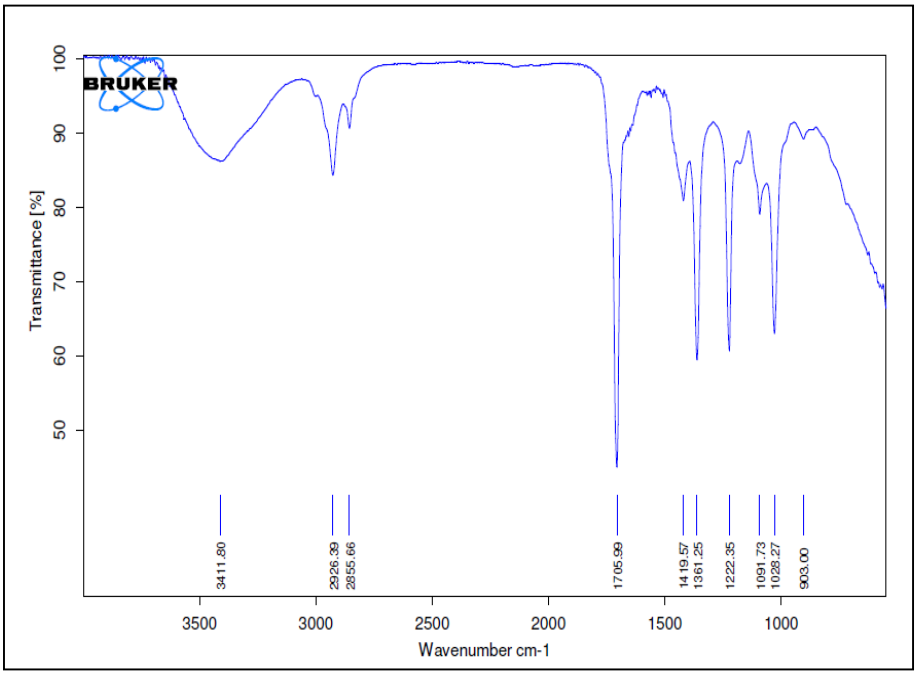

Fig 2: FTIR Studies of Diclofenac Sodium

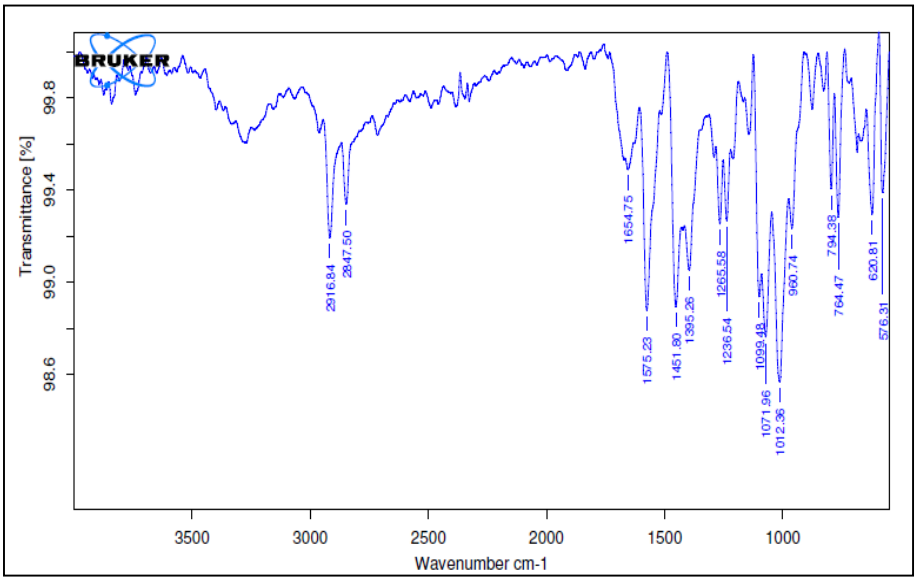

Fig 3: FTIR Studies of Physical mixture of drug and excipients

Table 2: Physicochemical evaluation data of Diclofenac Sodium Buccal Patches

A. code	A1	A2	A3	A4
Thickness (mm)	0.38	0.28	0.24	0.21
Weight variation (mg)	47.60	49.16	45.62	44.29
Drug content	91.96	92.26	93.46	95.38
Folding endurance	71	75	80	98
% Moisture Loss	7.61	8.15	8.90	9.0
% Moisture Absorption	10.26	10.47	10.62	10.23
Swelling index	14.98	15.45	15.86	15.45

Physical appearance and surface texture of buccal patches

These parameters were checked simply with visual inspection of patches and by feel or touch. The observation reveals that the patches are having smooth surface and they are elegant in appearance.

Weight uniformity of buccal patches

The weight of the patches was determined using digital balance and the average weight of all patches.

Thickness of buccal patches

The thickness of the patches was measured using screw gauge and the average thickness of all patches.

Folding endurance of buccal patches

The folding endurance gives the idea of flexible nature of patches. The folding endurance was measured manually, patches were folded repeatedly till it broke, and it was considered as the end point. The folding endurance was found optimum and the patches exhibited good physical and mechanical properties and the average folding endurance of all patches.

Drug content uniformity of buccal patches

Diclofenac Sodium buccal patches prepared with various polymers were subjected to the valuation for uniform dispersion of drug throughout the patch. In each case three patches were used and the average drug content was calculated.

% Moisture loss

The moisture content in the buccal patches ranged from 8.57 to 8.78%. The moisture content in the formulations was found to be increased by increase in the concentration of polymers.

% Moisture absorption

The moisture absorption in the buccal patches ranged from 9.29 to 10.25%.

Swelling index

The swelling index in the buccal patches ranged from 14.85 to 15.98 %.

Drug release studies

Table 3: *In vitro* release data of film A_1 to A_4

Time (hrs.)	A_1	A_2	A_3	A_4
0	0	0	0	0
1	24.53	25.53	26.88	25.98
2	45.501	46.95	49.81	44.32
3	63.66	65.54	68.57	69.53
4	72.89	74.23	75.98	71.43
5	85.23	81.82	88.88	87.77
6	91.12	91.35	93.54	94.05

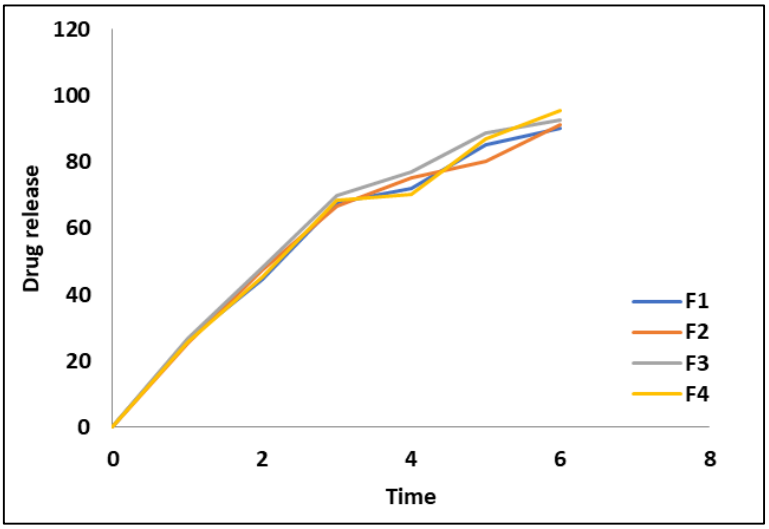

Fig 4: *In vitro* drug release of (A1- A4) formulation

Stability studies

Optimized formulations A4 was selected for accelerated stability studies as per ICH guidelines. The patches were observed for colour, appearance and flexibility for a period of three months. The folding endurance, weight, drug content, % cumulative drug release of the formulation was found to be decreasing. This decrease may be attributed to the harsh environment (40^0C) maintained during the studies.

Table 4: Stability studies of optimized formulations

Formulation Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
A-4	25^0C/60%RH	94.05	93.86	92.38	91.79	Not less than
A-4	30^0C/75% RH	94.05	93.58	92.87	91.45	Not less than
A-4	40^0C/75% RH	94.05	93.05	92.58	91.74	Not less than

Conclusion

FTIR studies revealed that there is no incompatibility or interaction between Diclofenac Sodium and excipients. Formulated buccal films gives satisfactory film characteristics like physical appearance, surface texture, weight uniformity, thickness uniformity, folding endurance, surface pH, percentage swelling index, percentage moisture uptake, drug content uniformity, in-vitro drug release. The low values for standard deviation for average weight, thickness, surface pH, percentage swelling index, percentage moisture uptake, in vitro drug release and drug content indicated uniformity within the batches. Based on in vitro drug release, formulation A4 exhibited a drug release of 94.05 % in 6 hours. The drug release could be retarded more than 6 hr with controlled release behaviour. The prepared buccal patches were found to stable after performing stability testing for three month. Short term stability studies of optimized formulation as per ICH guidelines indicated that there is no significant change in physical appearance, drug content determination and in vitro drug release. So finally, it can be concluded that mucoadhesive buccal films of Diclofenac Sodium could provide sustained buccal delivery for prolonged period. A further clinical investigation has to be conducted to establish the safety and efficacy of the developed formulation.

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