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Research Article

PREDNISOLONE MUCOADHESIVE BUCCAL DISC: FORMULATION AND CHARACTERIZATION

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ABSTRACT

Present research investigation involves the formulation of mucoadhesive discs. Mucoadhesive disc have been prepared by using the polymers alone and in different combinations. One of the most prominent and preferred route of drug administration is oral among all other routes. Various dosages forms for local and systemic action includes ointments, lozenges, gels, buccal tablets, mouth paints, pastes and suspension. Buccal administration of drugs prevents hepatic metabolism and gastro-intestinal degradation. Among all other mucosal membranes buccal mucosa provides inevitable advantage of ease administration. Direct compression method is employed to formulate the mucoadhesive disc. This research article involve the formulation of mucoadhesive buccal discs containing 10 mg Prednisolone. Formulations are developed using polymers like SCMC, HPMC K100M, CARBOPOL-934 and CHITOSAN . The prepared patches were evaluated for their weight, surface pH, thickness, drug content uniformity, *in vitro* residence time, permeation studies, folding endurance and *in vitro* release. The formulation with HPMC shows the best sustained result, whereas the formulation having the polymer SCMC and Chitosan shows the best ex-vivo mucoadhesion time.

Keywords: Mucoadhesion disc, Prednisolone, Direct compression, Characterization, Permeation studies.

INTRODUCTION

Several formulations have been developed earlier using mucoadhesive polymers like ointments [1], patches [2], films [3], tablets [4], strips [5], gels [6] containing several classes of drugs including anti- dental caries drugs, antimicrobials, antibiotics, anti-fungal, topical corticosteroids and local anesthetics [7]. Release from the conventional oral dosage form is uncertain and shows a burst release in initial administration phase but gradually declines to a therapeutic levels [8]. An oral mucoadhesive dosage form containing active moiety is useful in delivering in appropriate amount at specified rate. Many diseases like bacterial infections, fungal infections, aphthous ulcers, dental stomatitis and periodontal disease are still being treated by the local delivery of drugs to the tissues of oral cavity [9].

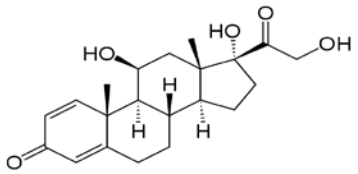

Fig. 1: Structure of Prednisolone

Prednisolone is a corticosteroid drug with predominant glucocorticoid and low mineralocorticoid activity, making it useful for the treatment of a wide range of inflammatory and auto-immune conditions. Prednisolone is the active metabolite of prednisone which is also used as a drug. Buccal drug delivery system provides many advantages for instance prevention of drug degradation from hepatic-metabolism and gastro-enteric environment, ease of administration and removal of drug and patient compliance.

This study was performed to demonstrate the properties of mucoadhesive disc composed of polymers like SCMC, CHITOSAN, HPMC K100M, PVA.

MATERIALS AND METHODS

Prednisolone sodium phosphate mucoadhesive disc are prepared using the polymers or mixture composition of different polymers like Hydroxypropylmethylcellulose (HPMC K100M) was obtained as gift sample from Rui Tai cellulose derivatives Shanghai Province China, carboxymethylcellulose sodium salt (SCMC) high viscosity was obtained from Central Drug House (P) Ltd. N.D., Poly vinyl alcohol cold (PVA cold) pure was obtained from Neelu Medicare Pvt. Ltd., Chitosan (from crab shell) was obtained from Sigma Life sciences Biochemika 48165-100G Sigma Aldrich, UP, Prednisolone was procured from Rajiv Pharma Pvt. Ltd. Solan. All the other chemicals used were of analytical grades.

Preparation of Mucoadhesive Disc by Direct Compression:

Mucoadhesive disc of Prednisolone sodium phosphate were prepared by direct compression using the hydraulic press (press used for preparing K Br pellets). The dried and finely grinded mixture of drug and polymer/polymers was poured in the die used for preparing the pellets and was compressed at 15 tons for 3 minutes. Before filling the die it was thoroughly cleaned with methanol and dried. The disc was taken out with care so that they do not break.

Table 1: Formulation composition consisting of single polymer

S. No.	Drug (mg)	SCMC (mg)	Chitosan (mg)	HPMC (mg)	Carbopol-934 (mg)
F1	10	40	-	-	-
F2	10	-	40	-	-
F3	10	-	-	40	-
F4	10	-	-	-	40

Table 2: Formulation composition consisting of polymer mixture

S. No.	Drug (mg)	SCMC (mg)	Chitosan (mg)	HPMC (mg)	Carbopol-934 (mg)
E1	10	20	20	-	-
E2	10	20	-	20	-
E3	10	20	-	-	20
E4	10	-	20	20	-
E5	10	-	20	-	20
E6	10	-	-	20	20

Evaluation

Thickness and Drug Content uniformity

Three discs are selected randomly from every formulations and were evaluated for the weight, thickness and drug content uniformity mean were calculated.

Swelling study

Disc containing the API were allowed to swell in watch glass containing excess of water at 37^{0}C. The difference in the initial and the final weight are calculated at predetermined intervals (30, 60, 90 min). Excess of water is swiped of using cotton swab. The percentage swelling, %S was calculated by the equation A [10]. The swelling behaviour of the disc which shows best in vitro release is shown in table 3 and table 4

Equation A

$$\%s = \frac{Xt - Xo}{Xo} * 100$$

Where, %S denotes the swelling percentage, Xo is the original weight or diameter at time t = 0, and Xt is the weight or diameter at time t = t.

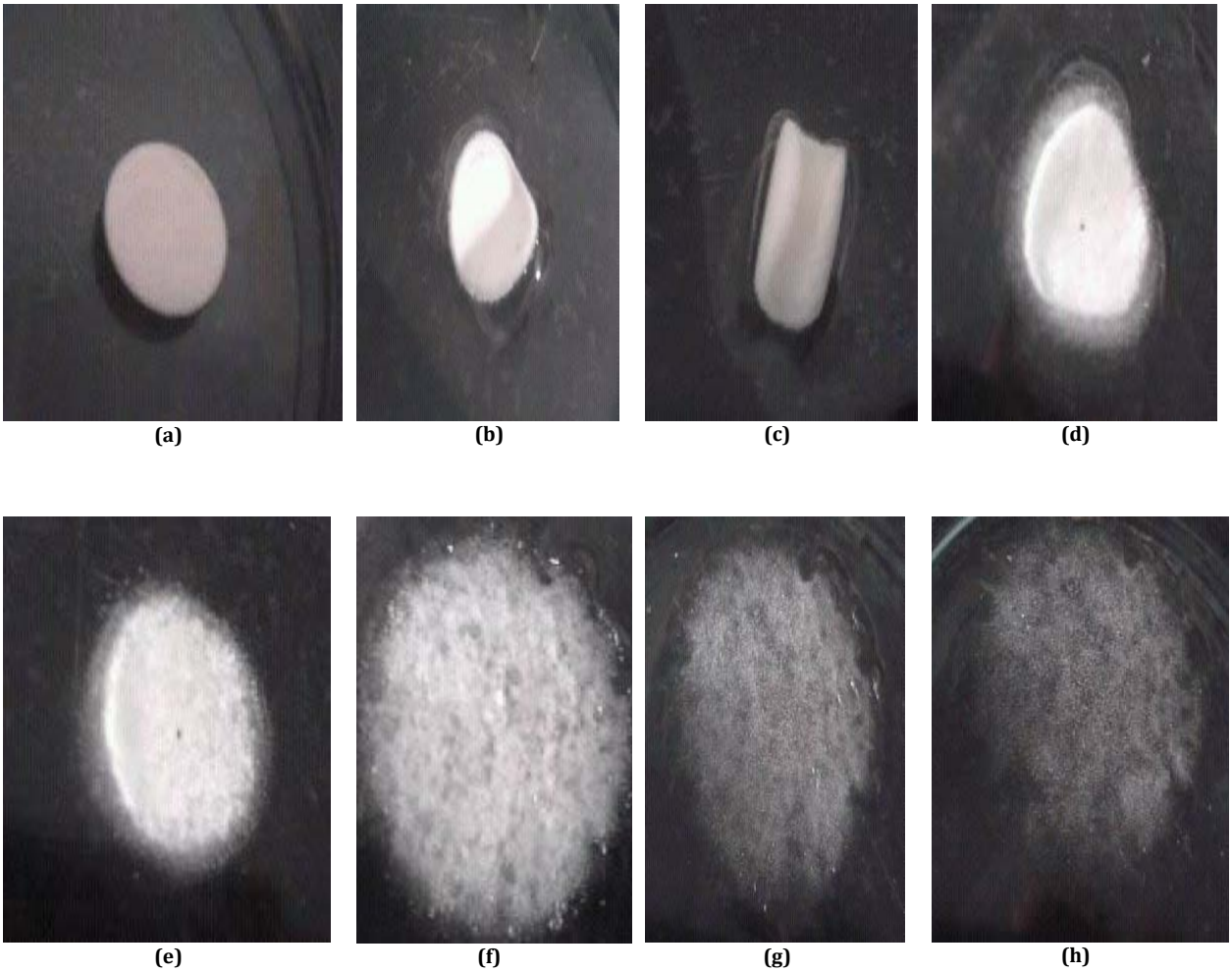

Fig. 2: Swelling behaviour (pattern at an interval of 1 hour) of medicated disc E 6.

Surface pH

The surface pH was calculated after placing the selected disc in watch glass containing 10 ml of distilled water. Disc were left over for 1 hour for swelling And pH was determined by placing the tip of pH potentio meter (L1-06pH analyser) for 1 m on the distilled water [11].

Ex-vivo mucoadhesion time

The ex vivo mucoadhesion study was performed using chicken buccal mucosa. The chicken buccal mucosa was fixed on the beaker using double sided tape. Medicated was wetted with one drop of simulated saliva fluid and pasted on the mucosa by applying light force with finger for 20 s. 800 ml of simulated saliva fluid was used to fill and kept at 37^{o}C. 150 rpm rate was applied after 2 min to simulate the buccal cavity environment and film adhesion was monitored. The freshly excised chicken buccal mucosa was obtained from slaughter house. The time which the disc requires to get detached from the mucosa was noted as the mucoadhesion time [12].

In vitro release study

In vitro release study were carried using 500 ml of phosphate buffer pH 6.8 fluid as the dissolution medium at 50 rpm at 37-$^+$ 0.5 c in an 600ml capacity beaker which is placed inside an glass beaker having large enough base to be kept on a heating magnetic stirrer. The outer beaker is levelled with distilled water to the same level. A thermometer is placed in the outer beaker to keep a check on temperature. The medicated disc was glued on beaker using cynoacrylate adhesive. An aliquot of 3 ml was withdrawn at 10 min. intervals and replaced by fresh phosphate buffer pH 6.8 [11] and was determined by U.V. spectrophotometer (U.V.-1700,schimadzu) at 247 nm and concentration was calculated using the standard plot of Prednisolone in phosphate buffer (pH 6.8) at 247nm.

Membrane Permeation Studies

The medicated disc which shows best in vitro release are selected for the permeation studies. Chicken pouch mucosa was wrapped on the one open end of the test tube using rubber band to make it water tight containing the disc firmly attached to mucosa by pressing on the surface, an aliquot of 4ml phosphate buffer was transferred on from the other open side [12]. The test tube was placed in such a way that the mucosa just lies below the phosphate buffer solution contained in 6000ml beaker. A sample of 3 ml is withdrawn at predetermined interval and was determined spectrophotometrically at 247nm. The figure 3 represents the permeation study profile of the disc.

RESULT AND DISCUSSION

The weight and drug content does not differ within different formulations. pH of the prepared disc ranges from 5 to 7. Table 1 and Table 2 shows the physical characteristics of the prepared medicated mucoadhesive disc. The formulation F 1 shows least %swelling whereas the formulation E 2 showed with maximum % swelling upto 49%. The thickness of the discs ranges from 0.4 mm to 1 mm. The discs prepared by HPMC and Chitosan shows the maximum water absorption. The formulation F 4 shoes the least thickness among all the formulations and the formulation E 4 shows the maximum among all the formulation.

Table 3: Physical characteristics of formulations comprising single polymer

S. No.	Surface pH [n]	% Swelling [n]	Thickness (mm ± SD)	Mucoadhesion Time (h) (h ± SD)
F1	6.3 ± 0.05	27 ± 0.09	1 ± 0.007	2.7[a] ± 0.012
F2	5.7 ± 0.03	34.4 ±0.1	1.2 ± 0.0025	3.5 ± 0.15
F3	6 ± 0.012	48.3 ±0.17	0.99 ± 0.003	4.2 ± 0.02
F4	6.1 ± 0.017	45.3 ±0.16	0.97 ± 0.005	2.9[a] ± 0.027

(a) Indicates the time when the patch detaches from the wall and n is average of 3

Table 4: Physical characteristics of formulation comprising polymer mixture

S. No.	Surface pH [n]	% Swelling [n]	Thickness (mm ± SD)	Mucoadhesion Time (h) (h ± SD)
E1	5.7 ± 0.03	37.2 ±0.019	1.2 ± 0.006	3.7 ± 0.013
E2	6.9 ± 0.08	48.9 ±0.24	1 ± 0.002	4.4 ± 0.021
E3	6.3 ± 0.05	38.7 ± 0.018	1 ± 0.0016	3.7 ± 0.019
E4	5.8 ± 0.01	41.6 ± 0.014	1.2 ± 0.0012	3.2[a] ± 0.020
E5	6.4 ± 0.07	38.9 ± 0.012	0.9 ± 0.007	4.5 ± 0.024
E6	5.9 ± 0.06	42.6 ± 0.21	1.2 ± 0.009	4.4 ± 0.020

(a) indicates the time when the patch detaches from the wall and n is average of 3

Table 5: *In-vitro* drug release profile of medicated discs comprising single polymer

Time (hours)	F1 (%±SD)	F2 (%±SD)	F3 (%±SD)	F4 (%±SD)
	Percentage drug release			
1 (h)	18 ± 0.018	26 ± 0.019	36 ±0.01	22.3 ± 0.014
3 (h)	47 ± 0.025	48 ± 0.21	48 ± 0.015	54 ± 0.029
5 (h)	83 ± 0.19	87 ± 0.230	63 ± 0.19	86 ± 0.10

Table 6: *In-vitro* drug release profile of medicated discs comprising polymer mixture

Time (hours)	E1(%±SD)	E2(%±SD)	E3(%±SD)	E4(%±SD)	E5(%±SD)	E6(%±SD)
	Percentage drug release					
1 (h)	9 ± 0.016	17.8 ± 0.019	8.3 ± 0.019	12.7 ± 0.015	29.2 ± 0.019	15 ± 0.017
3 (h)	41.5 ± 0.029	32.4 ± 0.024	28.5 ± 0.026	47.3 ± 0.031	49.6 ± 0.032	47.3 ± 0.024
5 (h)	92 ± 0.034	93.2 ±0.12	73 ± 0.11	86.4 ± 0.15	89.8 ± 0.17	63.9 ±0.11

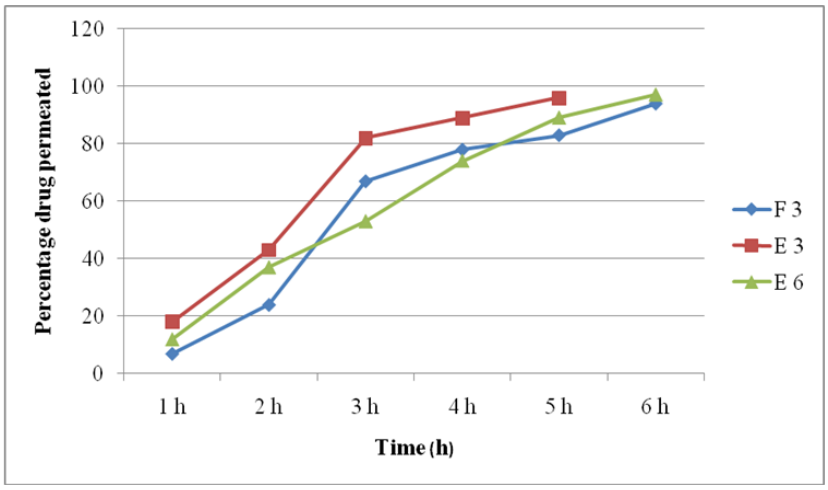

Fig. 3: Permeation study profile

The F 3, E 2, E 5 and E 6 show satisfactory mucoadhesion time. The formulation comprising SCMC only shows a burst release within 30 minutes. The formulation F 3 and E 6 shows good in vitro release profile, whereas the E 1 and E 2 shows almost complete drug release in 5 h duration of time. The formulation E 1 also shows a delayed release kind of action as only 9% of the total drug is release in the first hour duration.

The formulations F 3, E 3 and E 6 show satisfactory in vitro release so they are selected for the permeation studies. During the permeation studies the formulation E 3 shows complete drug permeation within 5 h duration. The formulation F 3and E 6 shows a permeation of drug for more than 6 hours.

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