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FORMULATION AND EVALUATION OF PANTOPRAZOLE BUCCAL PATCHES

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Abstract

Buccal delivery of the desired drug using mucoadhesive polymers has been the subject of interest since the early 1980s. Advantages associated with buccal drug delivery have rendered this route of administration useful for a variety of drugs. The goal of the present investigation was to design and evaluate mucoadhesive buccal patches of pantoprazole which offers an attractive route of administration for systemic drug delivery. Pantoprazole (dose, 10-40mg) is proton pump inhibitor used in treatment of erosion and ulceration of the esophagus caused by gastro esophageal reflux disease. Its oral bioavailability is 77% metabolized in the liver by cyp-450 system. The patches were prepared and evaluated for their thickness uniformity, folding endurance, weight uniformity, content uniformity, and *In vitro* release studies were conducted for pantoprazole loaded patches in phosphate buffer (pH, 7.4) solution.

Keywords: Pantoprazole, Mucoadhesive, Buccal drug delivery.

Introduction

Extensive research efforts have recently been focused on placing a drug delivery system in a particular region of the body for maximizing biological drug availability and minimizing dose-dependent side effects. Buccal delivery of drugs provides an attractive alternate to other conventional methods of systemic drug administration, since buccal mucosa is relatively permeable with rich blood supply and acts as an excellent site for the absorption of drugs[1,2]. The administration of drugs via buccal route facilitates a direct entry of drug molecules into the systemic circulation, avoiding the first-pass metabolism and drug degradation in the harsh gastrointestinal environment, which are often associated with oral administration[3–5]. The buccal cavity is easily accessible for self medication, and hence it is safe and well accepted by patients, since buccal patches can be very easily administered and even removed from the application site, terminating the input of drug whenever desired. Moreover, buccal patches provide more flexibility than other drug deliveries. Pantoprazole (dose, 10-40mg) is proton pump inhibitor used in treatment of erosion and ulceration of the esophagus caused by gastro esophageal reflux disease. Its oral bioavailability is 77% metabolized in the liver by cyp-450 system[6-7]. During last few decades, mucoadhesive polymers received considerable attention as platforms for buccal delivery of drugs due to their ability to localize the dosage form in the specific regions to enhance drug bioavailability[8].

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Materials and methods

Materials

The following chemicals were obtained from different sources and used as received. Pantoprazole was a gift sample from Dr.reddy's labs hyd, India; HPMC, PVP, and propyleneglycol were obtained from commercial sources. All other chemicals and reagents used were of analytical grade; double-distilled water was used throughout.

Preparation of Pantoprazole containing Buccal Patches

The buccal patche composed of different proportions and combinations of HPMC, PVP containing pantoprazole were prepared using a 54-cm^2 petri dish by solvent casting technique. The polymer solutions were prepared separately and these polymer solutions were poured into drug solution slowly drop by drop and this both solutions were mixed. Propylene glycol was incorporated as a plasticizer at a concentration of 7% w/w of total formulation and this solution was poured into a Petridish and closed with a funnel in an inverted position and allowed to dry at room temp at 35°C±0.5°C.

Table No. 01: Formulation chart of pantoprozole buccal patches

S.no	Formula code	Pantoprozole (mg)	PVP (mg)	HPMC (mg)	PG (ml)
1	F1	20	30	10	7
2	F2	20	30	20	7
3	F3	20	30	30	7

Measurement of Weight Variation and Thickness

The thickness of the patches was assessed at six different points of the patch using a thickness gauze (Mitutoyo, Japan). For each formulation, three randomly selected patches were used[9]. Six films from each batch, as a whole were weighed individually, and the average weights were calculated.

Measurement of Folding Endurance

The folding endurance was determined manually for the prepared films by repeatedly folding the film at the same place until it broke. The number of times the film could be folded at the same place without breaking or cracking gave the value of folding endurance[10].

Determination of Drug Content

The drug contents in the buccal patches were determined by dissolving 1 cm^2 patch in 100 ml phosphate buffer saline (pH = 7.4) and shaken vigorously for 24 h at room temperature. These solutions were filtered through Whatman® filter paper (No. 42). After proper dilution, optical density was measured spectrophotometrically using a UV–VIS spectrophotometer (UV-1700 Double beam spectrophotometer, SHIMADZU Corporation, Japan) at 295 nm against a blank. The drug content was estimated from the calibration curve, which was constructed between 1 and 5 µg/ml concentration ranges. The method was validated for linearity, accuracy, and precision.

Determination of Moisture Content

The buccal patches were weighed accurately and kept in desiccators containing anhydrous calcium chloride. After 3 days, the patches were taken out and weighed[11]. The moisture content (%) was determined by calculating moisture loss (%) using the formula:

$$\text{Moisture content}\,(\%) = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Folding endurance

Folding endurance of the patches was determined[12] by repeatedly folding one patch at the same place till it broke manually, which was considered satisfactory to reveal good patch properties. The number of times of patch could be folded at the same place without breaking gave the value of the folding endurance. This test was done on five patches.

In Vitro Release Study

The commercially available dialysis membrane (obtained from Sigma Chemicals) was employed for the study[13], and the in vitro drug release study was carried out using a Franz diffusion cell. The effective diffusion area was 1.8 cm2. The receptor compartment (40 ml) was filled with phosphate buffer saline (PBS), pH 7.4 The patches were applied under occlusion on the dialysis membrane fitted between the donor and receptor compartments of the diffusion cell. The drug release was performed at 37 ± 0.5°C, at a stirring speed of 50 rpm using a magnetic stirrer. Five milliliters of the sample from receptor medium was withdrawn at regular intervals and replaced

immediately with an equal volume of phosphate buffer saline, pH 7.4. The amount of pantoprazole released into the receptor medium was quantified by using UV–visible spectrophotometer at 295 nm against a blank.

Results and discussion

The main goal of the present investigation efforts was to develop and evaluate new buccal patches comprising a drug-containing mucoadhesive polymeric layer using polymers like PVP and HPMC, in various combinations and proportions. The physicochemical evaluation (Table II) indicates that the weight variation of these formulated buccal patches varied between 2.64 ± 0.06 (F 1) and 2.94 ± 0.07 g (F 3). The thickness of these patches varied between 0.309 ± 0.03 and 0.322 ± 0.02 mm, the thinnest being formulation F 1 and the thickest being formulation F 3. Folding endurance was measured manually. The highest folding endurance was observed in the case of F 3 (295) and the lowest in the case of F 1 (210). The range of folding endurance study ensured flexibility of these formulated buccal patches. The drug content (%) in all formulations varied between the range91.80±0.10 % and 96.29±0.05%. This indicates that the drug dispersed uniformly throughout the polymeric film. The moisture content (%) study was done for 3 days. The percentage of moisture content (%) is varied between 1.33±0.01% (F 1) and1.69±0.02 % (F 3). In most cases, the moisture uptake content was found to increase with increasing concentration of polymers that are more hydrophilic in nature. The low moisture content in the formulation is highly appreciable to protect from microbial contaminations and bulkiness of the patches. Again, low moisture content in formulations helps them to remain stable from being a completely dried and brittle film.

Table No. 02: Physicochemical evaluation of pantoprazole buccal patches

S.no	Formulation code	Weight variation(gms)	Thickness (mm)	Folding endurance	Drug content %	Moisture content %
1	F1	2.64±0.06	0.309±0.03	210	91.80±0.10	1.33±0.01
2	F2	2.71±0.07	0.315±0.04	230	93.12±0.07	1.42±0.01
3	F3	2.94±0.07	0.322±0.02	295	96.29±0.05	1.69±0.02

The in vitro drug release pattern of pantoprazole from formulated buccal patches is shown in Fig. 1 All of these buccal patches slowly released the drug. The drug release from buccal patches varied with respect to the polymer composition and nature. An increase in drug release from the buccal patches was found with increasing concentration of polymers that are more hydrophilic in nature. Among all formulations, the maximum in vitro drug release (96.11%) over a period of 5h was and in the case of formulation no. F 3 the minimum in vitro drug release (91.38%) was found in the case of formulation no. F 1.The in vitro drug release was more for the pantoprazole buccal patches which were composed with high proportion of HPMC.

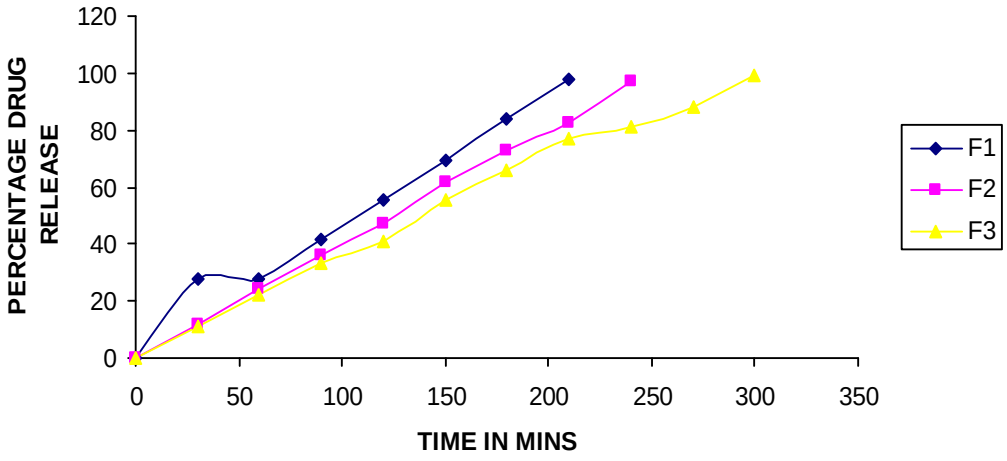

Fig. No. 01: In vitro release studies of F1, F2 & F3

Conclusion

Buccal patches of pantoprazole using polymers like HPMC and PVP in various proportions and combinations showed satisfactory physic mechanical and mucoadhesive characteristics. The proportional amounts of various hydrophilic polymers in various formulations have influence on drug release from these formulated pantoprazole buccal patches. From the present investigation, it can be concluded that such buccal patches of pantoprazole may provide buccal delivery for prolonged periods in the management of gastro esophageal reflux disease, which can be a good way to bypass the extensive hepatic first-pass metabolism.

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