Development of Mucoadhesive Patches for Buccal Administration of Prochlorperazine: Evaluation of In Vitro Release and Mechanical Properties

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ABSTRACT: The aim of this investigation was to develop and evaluate mucoadhesive buccal patches of prochlorperazine (PCPZ). Permeation of PCPZ was calculated in vitro using porcine buccal membrane. Buccal formulations were developed by solvent-casting technique using hydroxy propylmethyl cellulose (HPMC) as mucoadhesive polymer. The patches were evaluated for in vitro release, moisture absorption and mechanical properties. The optimized formulation, based on in vitro release and moisture absorption studies, was subjected for bioadhesion studies using porcine buccal membrane. In vitro flux of PCPZ was calculated to be 2.14 ± 0.01 µg. h⁻¹.cm⁻² and buccal absorption was also demonstrated in vivo in human volunteers. In vitro drug release and moisture absorbed was governed by HPMC content. Increasing concentration of HPMC delayed the drug release. All formulations followed Zero order release kinetics whereas the release pattern was non-Fickian. The mechanical properties, tensile strength (10.28 ± 2.27 kg mm⁻² for formulation P3) and elongation at break reveal that the formulations were found to be strong but not brittle. The peak detachment force and work of adhesion for formulation P3 were 0.68 ± 0.15 N and 0.14 ± 0.08 mJ, respectively. The results indicate that suitable bioadhesive buccal patches of PCPZ with desired permeability and suitable mechanical properties could be prepared.

KEY WORDS: Buccal, Prochlorperazine, Bioadhesion, Mechanical properties.

Introduction

Buccal delivery of drugs provides an attractive alternate to the oral route of drug administration, particularly in overcoming deficiencies associated with the oral administration. It has excellent accessibility, an expanse of smooth muscle and relatively immobile mucosa, hence suitable for administration of retentive dosage forms. The direct entry of the drug into the systemic circulation avoids the first-pass hepatic metabolism leading to increase in bioavailability (Senel and Hincal, 2001; Choi et al., 2000). Various mucoadhesive formulations were suggested for buccal delivery that includes buccal patches (Anders and Merkle, 1989; Yamshi et al., 2007), adhesive tablets (Owens et al., 2005; Jafar et al., 2004) and adhesive gels (Ishida et al., 1983). Buccal patches over come some of the drawbacks of other dosage forms. They have unique characteristics including flexibility, relatively 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.

PCPZ is a piperazine derivative, used to treat dizziness due to labyrinthine disorder, postoperative vomiting and emesis related to chemotherapy. It is also used in treatment of psychosis and manic phase of bipolar disorder (Hao et al., 2002). Oral administration was the most common route of administration however, PCPZ undergoes extensive intestinal and first-pass hepatic metabolism. The oral route of administration of PCPZ is also impractical for patients who are vomiting or who have impaired gastric emptying. Both parenteral and suppository formulations have also been used, but these approaches have low patient acceptability. From both, physicochemical (low molecular weight 373.9 g/mol, low dose 15-30 mg, Log P 2.4) (Clarke, 1986) and pharmacokinetic (T ½ 4-8 h, absolute bioavailability about 5.7 %) (Finn et al., 2005) views PCPZ is considered to be suitable for buccal delivery. Buccal tablets are available for PCPZ, but buccal films are preferred over adhesive tablets in terms of flexibility and comfort (Peh and Wong, 1999).

In this investigation we developed PCPZ buccal patches with a dissolvable matrix using HPMC E 15, with an insoluble backing membrane. The developed patches were evaluated for in vitro release, in vitro permeation through porcine buccal membrane and mechanical properties. The in vitro release characteristics of the prepared systems were evaluated using Franz diffusion cells and the adhesion measurement was carried out using