Drug Delivery and Translational Research
https://doi.org/10.1007/s13346-018-0489-5

ORIGINAL ARTICLE

Assessment of improved buccal permeation and bioavailability of felodipine microemulsion-based cross-linked polycarbophil gel

Mahendra Singh[1] · Jovita Kanoujia[1] · Poonam Parashar[1] · Malti Arya[1] · Chandra B. Tripathi[1] · V. R. Sinha[2] · Shailendra K. Saraf[3] · Shubhini A. Saraf[1]

Abstract

The oral bioavailability of felodipine (FEL) is very low, i.e., about 15%. This could be due to low water solubility and hepatic first-pass effect. The objective of the present study was to develop FEL microemulsion-based gel, to bypass the first pass effect, for buccal delivery. The optimized FEL microemulsion (OPT-MEF) was used to prepare buccoadhesive gels, with varying concentrations of hydroxypropyl methylcellulose (HPMC) E4M and polycarbophil (PCP), and evaluated. The cross-linking of the PCP gelling agent was done by adjusting the pH with a neutralizing agent, triethanolamine (TEA). The formulations, namely drug suspension, OPT-MEF, microemulsion-based buccal gel containing 1% *w/v* (MEF-E4M1), 2% *w/v* (MEF-E4M2), and 3% *w/v* (MEF-E4M3) of HPMC K4M and 1% *w/v* (MEF-PCP1), 2% *w/v* (MEF-PCP2), and 3% *w/v* (MEF-PCP3) of PCP were prepared and optimized on the basis of ex vivo permeation study, mucoadhesion force, and viscosity. The optimized buccal gel (MEF-PCP1) showed significantly higher ($p < 0.01$) permeation flux ($J = 0.44 \pm 0.16$ mg/cm^2/h), when compared with the drug suspension ($J = 0.17 \pm 0.14$ mg/cm^2/h). The permeation enhancement ratio of MEF-PCP1 was found to be 2.59 times higher than that of the aqueous suspension of the drug. The texture profile analysis of MEF-PCP1 was performed which showed spreadability (3.2 mJ), extrudability (151.8 mJ), hardness (13.8 g), and adhesiveness (41.0 g), and results indicated good spreadability and adhesiveness. The rheological study revealed the pseudoplastic flow behavior of MEF-PCP1 buccal gel. The C_{max} value 9.21 ± 2.88 μg/ml of MEF-PCP1 gel was found to be significantly higher ($P < 0.01$) compared to the same dose administered by oral route (C_{max} value 3.51 ± 1.74 μg/ml). The relative bioavailability (F_r) of the optimized MEF-PCP1 buccal gel was about 397.39% higher than that of oral route. In conclusion, consistent and effective buccal gel containing optimized FEL-loaded microemulsion, with improved buccal permeation and pharmacokinetic parameters was developed successfully to improve the bioavailability of FEL.

Keywords Felodipine · Buccal gel · Buccal delivery · Texture analysis · Permeation flux

Introduction

The safety of the drug, patient compliance, and effectiveness of a drug delivery system remains a vital concern for the researchers. The reason for modern advances in novel drug delivery systems is to enhance effectiveness and safety of drugs by formulating a dosage form which is suitable for administration and better in accomplishing patient compliance. Also, an improvement of the dissolution rates of water-insoluble drugs and avoidance of the first-pass effect of drugs remains the most difficult tasks for the formulation development scientists for industrial applicability, improved clinical efficacy, and successful marketing.

The peroral route is the preferred route of drug(s) administration, but it has numerous shortcomings such as the longer onset of action, hepatic first-pass metabolism, and enzymatic degradation of drugs within the gastrointestinal (GI) tract [1].

Reduction of dose-dependent side effects has been the focal endeavor for various studies [2].The buccal delivery system of drug(s) offers an alternative to peroral administration of

✉ Shubhini A. Saraf
shubhini.saraf@gmail.com

[1] Department of Pharmaceutical Sciences, Babasaheb Bhimrao Ambedkar University (A Central University), VidyaVihar, Raebareli Road, Lucknow, UP 226025, India

[2] University Institute of Pharmaceutical Sciences, Sector-14, Panjab University, Chandigarh, UT 160014, India

[3] Department of Pharmacy, B.B.D.N.I.I.T, Lucknow, India

Published online: 08 February 2018