Introduction

The stratum corneum is the prencipal barrier for cutaneous penetration and allows only slow absorption for the majority of the drugs. The use of appropriate vehicles allows drug absorption to be increased by changing either the permeability of the stratum corneum or the thermodynamic activity of the drug (1). In this respect, the best vehicle for topical controlled release would be the one which contributes to a reversible decrease in the stratum corneum resistance and allows the controlled diffusion of molecules into the vehicle itself.

Bioadhesive formulations have already shown their advantages. Bioadhesive formulations exhibit suitable rhelogical and mechanical properties, ease of application, good spreadability, approproate hardness (2).
Ketoprofen [2-(3-benzoylphenyl)propionic acid] (KP) is an analgesic and non-steroidal anti-inflammatory (NSAI) drug (3), widely prescribed for patients affected by dermatitis and rheumatic diseases (4). The mechanism of action of KP is mainly associated to the inhibition of the body's ability to synthesise prostaglandins (3). KP has poor solubility in water and acidic conditions and has short half-life, low bioavailability (5,6).

Solid dispersions (SDs) of many poorly water soluble drugs with hydrophilic carrier matrix have been formulated for improving drug dissolution rate. Moreover, SDs may improve the bioavailability of poorly soluble drugs by increasing the drug dissolution rate (7,8). Poloxamer 188 (P188) is selected to prepare SDs because of its low melting point (about 56-57oC), surfactant properties and safety (8).

The aim of the our study was to prepare bioadhesive polyethylene glycol (PEG) gel included KP–P188 solid dispersion and to compare the release profile of formulation with commercial gel product from cellulose acetate membrane as barrier.

Materials and Methods

Materials

Ketoprofen was a gift from Eczacibasi (Eczacıbaşı İlaç S.T.A.Ş. Turkey). P188 was a gift from Basf. PEG 400 and PEG 4000 were a gift from Santa-Pharma Drug Company. Carbopol 934 K90 were obtained from Merck. Polyvinilprolidon (PVP) were obtained from BDH Chemicals.

Preparation of Formulation

Firstly, solid dispersion included KP–P188 were prepared by melting method. KP and P188 were mixed at 1-3 weight ratio and obtained mixture was melted on water bath with stirring. After 10 -15 minutes, the mixture was cooled at fridge for 24 h. The solidified solid dispersion were then ground by using a mortar and pestle, sieved and stored in a vial at room temperature for further use. For the preparation of bioadhesive gel PEG 400 and PEG 4000 mixed at 70oC and cooled to room temperature. Carbopol 934 K90 and Polyvinilprolidon were added to this mixture. Finally, bioadhesive gel and solid dispersion were mixed.

In Vitro Release Studies

In vitro release experiments from cellulose acetate membrane were performed in pH 6.8±0.1 phospate buffer as a receptor medium during 8 h and estimated spectrophotometrically at 261 nm. The receptor phase maintained at 37oC±0.5 was continuously stirred with a small magnetic bar ensure homogeneity. Commercial gel product was investigated at the same procedure. The amount of KP permeated from bioadhesive PEG gel included KP–P188 solid dispersion and from commercial gel product at different time intervals was done by spectrophotometrically (n=3).

Results and Discussion

The in vitro release of KP through cellulose acetate membrane was studied for 8h. The release patterns were found non linear. The release profile of KP from bioadhesive PEG gel included K–P188 solid dispersion (F) and commercial gel product (CG) in pH 6.8 were shown in Figure 1.

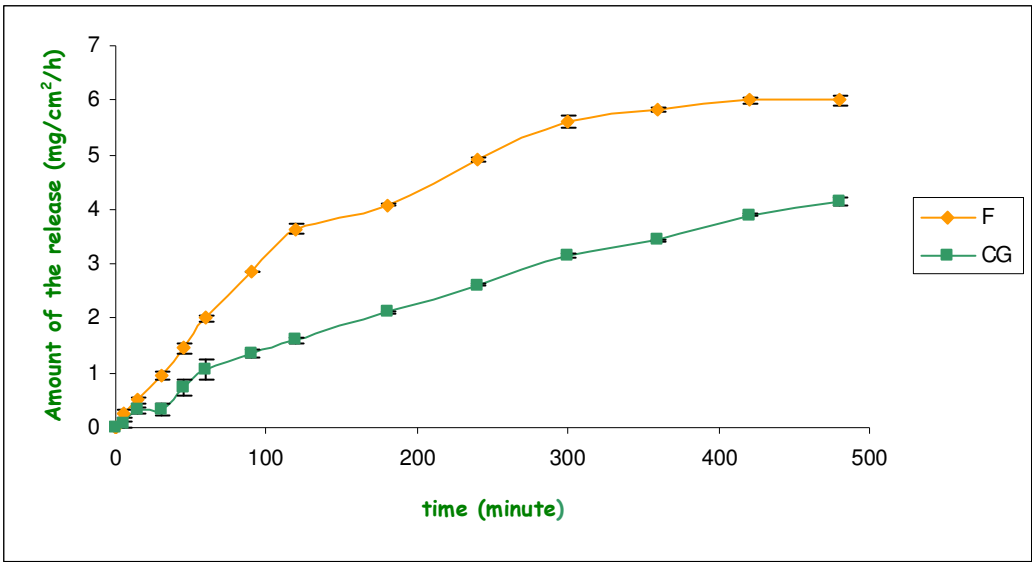

Figure 1. Cumulative amount of KP from the F and CG at the end of the 8h

	Formulation	Commercial Gel Product
Jss (mg/cm^2/h)	0.017	0.010
D*10^{-5}(cm^2/h)	4.223	12.076
r2	0.931	0.973
(n) lag time	0.667	0.233

Table 1. Results of kinetical parameters of the F and CG

At the end of the 8 h, significantly difference in drug release was obtained between bioadhesive PEG gel included K–P188 solid dispersion and commercial gel product. By the way an increase was observed in the steady - state flux of KP from the bioadhesive PEG gel included K–P188 solid dispersion than from the commercial gel product.

Conclusion

Bioadhesive PEG gel included K–P188 solid dispersion and commercial gel product as vehicles for topical delivery of KP was studied. Bioadhesive PEG gel included KP–P188 solid dispersion was shown to increase the dermal delivery of KP over the commercial gel product. Due to increasing KP solubility. Bioadhesive PEG gel included KP– P188 solid dispersion could be suggested as an effective carrier for KP.

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