A STUDY OF MICROEMULSION SYSTEMS FOR TRANSDERMAL DELIVERY OF NAPROXEN: EX-VIVO

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ABSTRACT

The aim of this study is to formulate new microemulsion systems for transdermal delivery of naproxen and compare the potential of them and commercial formulation for effectively penetration of naproxen.

INTRODUCTION

Microemulsion is defined as a dispersion consisting of oil, surfactant, cosurfactant and aqueous phase, which is a single optically isotropic and thermodynamically stable liquid solution (1). Oral therapy of NSAIDs is very effective, but the clinical use is often limited because of their potential to cause adverse effects such as irritation and ulceration of the gastro-intestinal mucosa. Administration of these agents via the dermal route can bypass these disadvantages of the oral route and may maintain relatively consistent plasma levels for long term therapy from a single dose (2). Therefore in this study suggested that, microemulsion systems are prepared for transdermal delivery of naproxen.

MATERIALS AND METHODS

Naproxen (Deva Holding, Istanbul, Turkey), Isopropyl myristate (Talkoteks chemical LTD, Turkey), Span 80 (Merck, Hohenbrunn, Germany), Labrafil-M (Gattefosse, Cedex, France), Labrasol (Gattefosse, Cedex, France), Ethanol (J.T.Baker, Deventer, Holland), Cremophor-EL (Sigma, Steimheim, Germany), Methanol (Merck, Hohenbrunn, Germany), Acetonitrile (Sigma, Aldrich, Germany). All chemicals were used as analytical grade.

Preparation of w/o microemulsion formulations

Microemulsions were prepared using isopropyl myristate (IPM) as oil phase, Span 80, Labrafil-M, Labrasol, Cremophor-EL as surfactants, ethanol as co-surfactant and distilled water or 0.5N sodium hydroxide solution as aqueous phase. All transdermal formulations were loaded with 10% naproxen (Table 1).

HPLC analysis of naproxen

HPLC system consisted of a UV spectrometric detector and C18 column (HP Angilent 1100 series). The mobil phase contained methanol/acetonitrile/purified water (20/28/52 v/v/v) and 0.4mL triethylamine (adjusted to pH 3.2 using orthophosphoric acid). The flow rate was adjusted to 1.5 mL/min. The UV detection wavelength was at 270 nm (3).

Ex-Vivo permeation studies

Diffusion cell was used in the permeability studies of naproxen. The apparatus consisted of clamped preconditioned male rat abdominal skin onto glass diffusion cell between donor and receptor compartments. Phosphate buffer pH 7.4 (10 mL) (600 rpm, 37°C) was used in the receptor compartment. The donor compartment contained 500 mg microemulsion formulations or commercial formulation (C). The samples were withdrawn at predetermined time intervals then, immediately analyzed HPLC system consisting of a UV spectrometric detector and C18 column (270 nm), directly. Three replicates of each experiment were performed.

RESULTS AND DISCUSSION

Microemulsions areas obtained using various surfactants: co-surfactant ratios and then the pseudo-ternary phase diagrams for different microemulsions were ploted (4). Optimum formulations were selected according to the gravity centers of these diagrams.The percutaneous permeation parameters of the tested formulations were calculated (Table 2). The permeation profiles of naproxen through rat skins from different formulations were plotted (Figure 1). The percutaneous permeation parameters of the tested formulations were calculated with the Fick equation from the slope of linear portion of these plots. Statistical comparison of the flux throughout 24 h showed that, all of the microemulsions provided fluxes higher than the commercial formulation (C < M1 < M2 < M3 < M4) (P<0.05).

Table 1: Compositions of the microemulsion formulations

Formulation (%)	M1	M2	M3	M4
IPM	2.943	2.766	3.109	2.622
Labrafil-M	0.443	-	0.520	-
Labrasol	-	0.123	-	0.138
Span 80	-	0.618	-	0.691
Cremophor EL	0.221	-	0.260	-
Ethanol	5.981	5.939	5.467	5.81
Distilled water	0.411	0.552	-	-
0.5N NaOH solution	-	-	0.643	0.738
HLB	6.833	5.916	6.833	5.916

Table 2: Permeation rate from different microemulsion formulations and commercial formulation.

Formulation	Permeation rate (mg/cm²min)	Lag time (h)	r²
M1	0.611±0.011	0.874±0.076	0.970 ±0.002
M2	0.700 ±0.163	0.684±0.176	0.977 ±0.002
M3	0.908±0.129	0.586±0.186	0.985 ±0.014
M4	1.279 ±0.007	0.699±0.047	0.988 ±0.563
C1	0.158±0.006	0.056 ±0.013	0.992 ±0.001

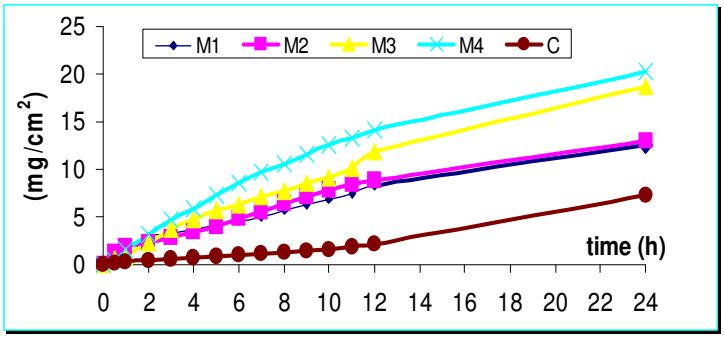

Figure 1: Permeation profiles of naproxen through male rat abdominal skin from different microemulsion formulations and commercial formulation.

CONCLUSION

According to the ex vivo permeation studies, microemulsion formulations containing naproxen could be promising formulations as an alternative anti-inflammatory dosage form for effective therapy.

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