PHYSICOCHEMICAL PROPERTIES AND EVALUATION OF MICROEMULSION SYSTEMS FOR TOPICAL DELIVERY OF NAPROXEN

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ABSTRACT

The aim of this study is to develop novel naproxen microemulsion formulations for topical application and to investigate the physicochemical properties of them and to evaluate the in vitro permeation rate of naproxen from these formulations.

INTRODUCTION

Microemulsions are clear, stable, isotropic mixtures of oil, water and surfactant, frequently in combination with a cosurfactant (1). Microemulsions can be used to deliver drugs to the patients via several routes, but the topical application of microemulsions has gained increasing interest (2). Naproxen, is a non-steroidal anti-inflammatory drug (NSAID) compound whith analgesic and antipyretic effects, used for treatment of rheumatoid arthritis, osteoarthritis and traumatic contusions. However, it has been associated with gastrointestinal side effects. It is possible to minimize these problems by developing drug carriers in order to allow the topical administration of drug (3). Therefore, in this study, micoemulsion systems were prepared for topical application.

MATERIALS AND METHODS

Naproxen (Deva Holding, Turkey), Isopropyl myristate (Talkoteks chemical LTD, Turkey), Span 80 (Merck, Germany), Labrafil-M (Gattefosse, France), Labrasol (Gattefosse, France), Ethanol (J.T.Baker, Holland), Cremophor-EL (Sigma, Germany), Cellulose membrane (Sigma, USA). All chemicals were used as analytical grade.

Preparation of w/o microemulsion formulations

Naproxen was dissolved into the mixtures of oil (isopropyl miristate), surfactants (Span 80, Labrafil M, Labrasol, Cremophor EL) and co-surfactant (ethanol) and then the formulation was carried out by titrating slowly with distilled water or 0.5N sodium hydroxide solutions (Table 1).

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

Characterization of microemulsions

The physicochemical properties of microemulsions were measured such as electrical conductivity, droplet size, viscosity, pH, density and phase inversion temperature (PIT).

In vitro permeation studies

In permeability study, diffusion cell was used. The apparatus consisted of clamped preconditioned cellulose membrane onto glass diffusion cell donor and receptor compartments. The aliquots were withdrawn at predetermined time intervals then, immediately analyzed spectrophotometrically.

RESULTS AND DISCUSSION

Microemulsion formulations were prepared and the physicochemical parameters of developed microemulsions were observed. The physicochemical parameters of the microemulsions were listed in Table 2.

The cumulative amounts of naproxen through cellulose membrane from the microemulsions prepared with different surfactants were evaluated and it was also found that the naproxen permeation rate values from the microemulsion formulations significantly higher than commercial formulation (C) from cellulose membrane. The rank order for in vitro release of naproxen from the five formulations was found to be: M4>M3>M2>M1>C (Figure1 and Table 3).

Table 2: Characterization of the microemulsion formulations

Formulation / Characterization	M1	M2	M3	M4
pH	5.79±0.01	4.97 ±0.025	6.45 ±0.05	6.39 ±0.025
Viscosity (cP)	13.33 ±0.577	15 ±1	14.33 ±1.527	15.33 ±0.577
Droplet size (nm)	1.590 ±0.114	1.701 ±0.060	3.253 ±0.064	1.405 ±0.040
Electrical conductivity (µs)	23 ±0.05	18.7 ±0.02	147.9 ±1	141.5 ±0.1
Density (g/mL)	0.920 ±0.010	0.917 ±0.030	0.924 ±0.012	0.922 ±0.025
Refractive index (nm)	1.405 ±0.002	1.429 ±0.006	1.385 ±0.02	1.468 ±0.02
PIT (°C)	44 ± 0.001	40 ± 0.020	38 ±0.002	41 ±0.006

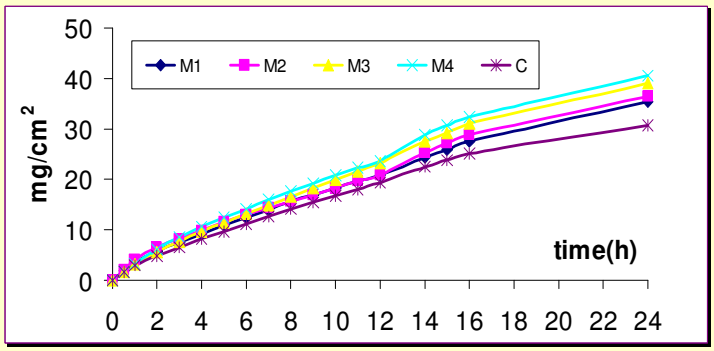

Figure 1: Permeation profiles of naproxen through cellulose membrane from different microemulsion formulations and commercial formulation.

Table 3: Permeation rate from different microemulsion formulations and commercial formulation.

Formulation	Permeation rate (mg/cm^2min)	Lag time (h)	r^2
M1	1.611±0.069	2.292±0.260	0.992±0.003
M2	1.856±0.024	1.754±0.103	0.970±0.004
M3	1.831±0.080	1.758±0.199	0.995±0.001
M4	1.869±0.021	2.254±0.065	0.987±0.595
C	1.508±0.044	1.779±0.164	0.994±0.001

CONCLUSION

The results of in vitro release study, physicochemical property tests and permeation study showed that all four microemulsion formulations studied may be appropriate vehicles for topical application. Moreover the physicochemical properties of the microemulsions are suitable for topical application.

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