RESEARCH PAPER

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Comparative Release Studies of Transdermal films of Terbutaline Sulphate across various diffusion barriers

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Transdermal films of Terbutaline Sulphate were prepared using polymers such as HPMC and Sodium CMC. The drug release was studied across various diffusion barriers that include cellophane membrane, rat abdominal skin and stratum corneum of fresh human cadaver skin. The permeation rate from various diffusion barriers were compared. The HPMC films showed a greater rate of release compared to that of Sodium CMC across all the barriers used.

TRANSDERMAL drug delivery systems use intact skin as a dependable route for systemic drug absorption. The transdermal permeation of a drug involves partitioning into and transport through the cutaneous layers, namely the stratum corneum, the viable epidermis and the upper dermis. **In vitro** experiments have shown that stratum corneum is the principal barrier[1,2].

In the present study, an attempt has been made to compare and correlate the rate of permeation of Terbutaline sulphate from polymer matrix films across different diffusion barriers such as cellophane membrane, rat abdominal skin and the stratum corneum of fresh human cadaver skin.

EXPERIMENTAL

Terbutaline sulphate USP (Astra-IDL, Bangalore) Hydroxy propyl methyl cellulose (HPMC) and Sodium carboxy methyl cellulose (Sodium CMC) (Rolex Laboratory, Bombay), PEG-400 (Loba Chemicals), Cellophane membrane (South India Viscose Ltd.,) were obtained.

Preparation of films[3]

The casting solution was prepared by dissolving the polymer in distilled water to form a 2% w/v Solution. The plasticiser (30% W/W of polymer concentration) and the drug Terbutaline Sulphate (0.25% W/V) were dispersed in the polymer solution using a mechanical agitator.

The films were prepared by casting 5 ml of the solution within a round aluminium foil cup of area 12 Sq. cm. and dried at 40- 50° in an air circulation drier. The films were cut into 10 sq.cm area and taken for evaluation. The physicochemical features of the films are presented in **Table 1**.

In Vitro Diffusion

Cellophane membrane (70 Microns), full thickness rat abdominal skin[4] and stratum corneum layer (10 microns) of a human cadaver of age 48 years were used as diffusion barriers. The stratum corneum was isolated from the skin layer.[5] Keshary chein[6] type diffusion cell was used to study the **in vitro** permeation of drug. Five ml of the receptor medium (Normal saline) was withdrawn at hourly intervals for 8 h. and analysed spectrophotometerically at 450 nm.[7] The permeation rate of drug from HPMC and Sodium CMC polymer matrices are given in the table. 1.

Stability Studies

The films were stored at various temperatures such as R.T., 37° ± 1°, 45° ± 1° and RT + 65% RH

Table 1 : Physicochemical features of polymer films and permeation rate of drug across various diffusion barriers

Polymer	Thickness of Film (microns)	Drug Content %	Permeation rate (mg/hr)		
			Cellophane	Rat skin	Stratum Corneum
HPMC	115 ± 0.9	97.28 ± 1.01	1.00 ± 0.26	0.67 ± 0.07	0.24 ± 0.02
Sodium CMC	103 ± 0.3	98.11 ± 0.55	0.7 ± 0.09	0.45 ± 0.11	0.18 ± 0.05

n = 4

Table 2 : Comparative drug permeability rate across various diffusion barriers

Polymer film matrix	Stratum Corneum vs cellophane	Stratum corneum vs rat skin
HPMC	1:4.16 (1.03)	1:2.79 (1.46)
Sodium CMC	1:3.88 (0.93)	1:2.50 (1.22)

(n = 4) (% coefficient of standard deviation)

for a period of 6 weeks and the drug content was determined spectrophotometrically in samples drawn at weekly intervals. The intactness of the drug in the polymer matrix was confirmed by T.L.C.

RESULTS AND DISCUSSION

The polymers selected for the formulation of transdermal films are indegenously abundant and inexpensive compared to the other synthetic polymers used for the purpose. The films were found to be uniform and opaque. The thickness of the films did not vary by more than 1%. The drug content was also found to be uniform with a maximum variation of about 1%.

The films exhibited good stability at all storage conditions after 6 weeks. However, they had become slightly softer due to moisture absorption at 65% R.H. The HPMC films showed a greater rate of release compared to that of Sodium CMC across all the diffusion barriers used.

The drug release rates across various barriers can be correlated as shown in **Table 2**. The percent co-efficient of standard deviation shows that the ratio values are homogeneous.

Such several comparative studies help in relating and computing the drug permeation rate with the barrier properties into suitable mathematical expressions, which is the major objective of the type of research.

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