RESEARCH PAPER

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Drug Release from Terbutaline Sulphate Transdermal films across Human Cadaver Skin

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Transdermal films of Terbutaline Sulphate were formulated as mololithic matrices using cellulose polymers like Hydroxy propylmethyl cellulose (HPMC), Sodium Carboxy methyl cellulose (Sod. CMC), Cellulose acetate and Ethyl Cellulose. *In vitro* diffusion studies were carried out across isolated stratum corneum of fresh human cadaver skin, using keshary-Chien type diffusion cell. Skin irritancy test was carried out on human voulnteers. The formulations were subjected to stability studies at different temperatures. The films were found to be stable at all temperature conditions. The human volunteers did not show any signs of erythema and oedema. The formulations showed an appreciable release after eight hours.

TERBUTALINE sulphate is one of the widely used drugs in the prophylaxis and treatment of asthma. The drug has a short half life and undergoes extensive first pass metabolism on oral administration[1]. These factors necessitated formulation of a controlled release transdermal drug delivery system for terbutaline sulphate.

In this, study, the transdermal films were formulated using various cellulose derivatives as monolithic matrices and were evaluated for drug release pattern across the stratum corneum isolated from fresh human cadaver skin.

EXPERIMENTAL

Terbutaline sulphate USP (Astra-IDL, Bangalore), HPMC, 15 cps at 1% w/v solution and Sodium CMC, 16 cps at 1% w/v solution (Rolex Laboratory, Bombay), Cellulose acetate, 3 cps at 2% w/v solution in acetone, Ethyl cellulose, 22 cps at 5% w/v solution in alcohol : toluene (1:4) and PEG-400 (Loba Chemicals) were obtained.

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Preparation of Films[2,3]

A 2% w/v solution of the polymer was prepared in suitable solvents using a mechanical stirrer. Terbutaline sulphate (0.25% w/v) and PEG-400 (30% w/w of polymer concentration) were dispersed in the solution. Five ml of the casting solution was poured within the round aluminium foil cup (prepared by telescoping between two round plastic lids) of area 12 sq. cm and dried at 40-50° in air circulation drier for 12 h. The films were cut into 10 sq. cm area and were taken for evaluation.

Isolation of Stratum Corneum[4]

A skin specimen was excised from the chest portion of a fresh (male) cadaver of age 52 years. The skin was soaked in hot water (60°) for 1 min. The epidermis was peeled away from the dermis. The isolated epidermis was rinsed with hexane to remove surface lipids and washed with sufficient distilled water. The epidermis was kept on a filter paper soaked in a solution of 0.1% trypsin in saline to digest all the bottom layers. The stratum corneum (10 microns) was then lifted on to a cellophane sheet,

Table - 1
The drug release rate from transdermal films across stratum corneum

Each Film contains 10 mg/sq.cm of Drug

Polymer film matrix	Rate of drug release mg/hr.
HPMC	0.24 ± 0.08
Sod. CMC	0.19 ± 0.06
Cellulose Acetate	0.10 ± 0.04
Ethyl Cellulose	0.09 ± 10.03

n = 4

washed with distilled water and dried at room temperature.

In vitro Diffusion Studies

Keshary-Chein type diffusion cell was used to study *in vitro* permeation of drug. Five ml of the receptor medium (Normal saline, 100 ml) was withdrawn at hourly intervals for 8 h and analysed spectrophotometrically at 340nm[5].

Skin Irritancy Test

The films containing the drug were placed on the back of the human volunteers, secured it firmly in place with adhesive plaster. Aqueous solution of 0.8% formalin was applied as a standard irritant. The volunteers were observed for 5 days for any sign of oedema and erythema.

Stability Studies[6]

The films were stored at various temperatures such as R.T., 37° ± 1°, 45° ± 1° and R.T. + 65% R.H. for a period of 6 weeks and the % drug content was determined in samples withdrawn at weekly intervals.

RESULTS AND DISCUSSION

The transdermal films showed a zero order drug release pattern. The rate of drug release from various polymer matrices is shown in Table 1. The films made of hydrophilic polymers showed a greater rate of release than that of hydrophobic polymers.

The formulations exihibited good stability at all storage conditions after 6 weeks. However, the hydrophilic polymers had become slightly soft due to moisture absorption when stored at higher R.H.

The human volunteers subjected to skin irritancy test showed no sign of erythema or oedema during the observation period of 5 days.

The results obtained in the study revealed that a good transdermal film containing Terbutaline sulphate can be formulated using cellulose polymers. Such monolithic transdermal formulations are advantageous in providing effective treatment for bronchitis with enhanced patient compliance.

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