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Research Article

OPTIMIZATION OF PLASTICIZER FOR DICLOFENAC SODIUM TRANSDERMAL FILM: PERMEATION ENHANCEMENT

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ABSTRACT

The present research work was performed to optimize a plasticizer for enhanced skin permeation of Diclofenac sodium through a transdermal film. Diclofenac sodium was used as a model drug to optimize a plasticizer for enhancing skin permeation. Ten different HPMC (3%w/v) based transdermal films using three different plasticizer in different concentration (20%w/w, 30%w/w, 40%w/w of polymer composition): Propylene glycol, Dibutyle phthalate, Diethyl phthalate were prepared & evaluated for ex-vivo drug release to optimize a plasticizer to increase skin permeation. The ex-vivo permeation of Diclofenac sodium through hairless rat skin was found to show maximum increase to 77.104% in 24 hours with Dibutyle phthalate (20% w/w of dry polymer) over propylene glycol (PG), Di-ethyl phthalate (DEP), Propyline glycol.

Key Word: HPMC, in vitro/Ex-vivo release study, Permeation, and Transdermal film.

INTRODUCTION

Transdermal delivery constitutes one of the most important routes for new drug delivery system (NDDS). Transdermal delivery of drugs offers several advantages over conventional delivery methods including oral and injection methods. Transdermal delivery, that traditionally uses a patch containing drug substances pressed onto the skin, is non-invasive, convenient and painless, and can avoid gastrointestinal toxicity (e.g. peptic ulcer disease) and the hepatic first pass metabolism[1].

Chemical penetration enhancers increase skin permeability by reversibly damaging or altering the physicochemical nature of the stratum corneum to reduce its diffusional Resistance[1-3]. One of the problems associated with many chemical penetration enhances it that they cause irritancy in the skin. This is not surprising in chemicals that disrupt organized lipid structures, cell membranes and components. The toxicity associated with many chemical penetration enhances has limited their usefulness for clinical application. In recent years there has been a move towards investigation of potential enhancers classified as GRAS (Generally Regarded as Safe) by the FDA, such as essential lils and terpenes, and polymeric enhancers[1-5].

MATERIALS AND METHODS

Diclofenac sodium was obtained from Kasliwal brothers, Indore and Hydroxyl propyl methyl cellulose was from Loba chemie Pvt. Ltd., Mumbai, India. All other chemicals used were of analytical grade.

Preparation of the Diclofenac sodium Transdermal film [5]

Matrix types Transdermal films were prepared using solvent evaporation technique in a glass ring. The bottom of the ring was covered by glycerin on which a backing membrane was casted by pouring 3% w/v solution. Keep HPMC solution followed by drying at room temperature for overnight. Dry matrix was prepared by dissolving requisite amount of drug and HPMC in methanol. To this solution plasticizer (20%, 30%, 40% w/w of polymer composition) was added and stirred. The uniform dispersion was casted on HPMC backing membrane and dried at room temperature for overnight. The dried films were removed and kept in a dessicator until used.

Solubility measurement

Solubility of drug substances is of extreme importance to the drug development process as intended therapeutic effect cannot be achieved until a drug is not properly soluble in a fluid medium. Solubility of Diclofenac sodium was found in different solvent like distill water, ethanol, chloroform, carbon tetra chloride.

Evaluation of Transdermal film[5-15]

The physical parameter such as thickness, weight variation, folding endurance, flatness and In virto diffusion study was determined.

Thickness

Patch thickness was measured using digital micrometer screw gauge at three different places and the mean value was calculated.

Weight variation

Weight variation was studied by individually weighing 10 randomly selected patches. Such determination was performed for each formulation.

Folding endurance

Folding endurance of film was determined by repeatedly folding a small strip of film (2 cm× 2cm) at the same place till it broke. The number of time the film could be folded at the same place without breaking was the folding endurance value.

Flatness

Three longitudinal strips were prepared/cut from each film: one from the center, one from the left side and one from the right side. The length of each strip was measured and the variation in length because of non-uniformity in flatness was measured by determining percent constriction, with 0% constriction equivalent to 100%flatness.

Ex- vivo diffusion study

Ex-vivo diffusion studies were performed by using a *Franz diffusion cell* with a receptor compartment capacity of 60 ml. The rat skin was mounted between the donor and receptor compartment of the diffusion cell *(Institutional Ethics Committee Reg. No. 9LB/ac/05/CPCS)*. The Transdermal film was mounted between the donor and receptor compartment of the diffusion cell. The Transdermal film was placed on the rat skin and on it donor compartment are put. The receptor compartment of the diffusion cell was filled with phosphate buffer pH 6.8. The whole assembly was fixed on a hot plate magnetic stirrer, and the solution in the receptor compartment was constantly and continuously stirred using magnetic beads and the temperature was maintained at 32±0.5°C. The sample were withdrawn at different time intervals and analyzed for drug content spectrophotometrically. The receptor phase was replenished with an equal volume of phosphate buffer at each sample withdrawal.

Table 1: Formulation of Diclofenac Sodium Transdermal Films

Formulation	Polymer (3%)	Plasticizer(PG%w/w)	Plasticizer(DEp%w/w)	Plasticizer(DBP%w/w)	Drug (mg/ml)
F1	HPMC	20	-	-	3
F2	HPMC	30	-	-	3
F3	HPMC	40	-	-	3
F4	HPMC	-	20	-	3
F5	HPMC	-	30	-	3
F6	HPMC	-	40	-	3
F7	HPMC	-	-	20	3
F8	HPMC	-	-	30	3
F9	HPMC	-	-	40	3

Table 2: Evaluation of Transdermal Films 0f Diclofenac Sodium

Code	Thickness (mm)	Flatness (mm)	Folding Endurance	% Drug Diffuse (in 24 hrs)
F1	0.15 ± 0.04	100.83 ± 0.02	154 ± 2.31	77.104
F2	0.14 ± 0.01	99.12 ± 0.05	167 ± 3.14	22.204
F3	0.17 ± 0.07	100.03 ± 0.04	188 ± 2.41	60.864
F4	0.17 ± 0.07	100.24 ± 0.01	142 ± 1.46	47.888
F5	0.15 ± 0.09	100.01 ± 0.02	175 ± 1.51	24.208
F6	0.19 ± 0.02	99.94 ± 0.05	182 ± 3.18	19.68
F7	0.12 ± 0.01	100.83 ± 0.03	195 ± 2.17	75.472
F8	0.13 ± 0.05	100.13 ± 0.02	177 ± 5.03	19.68
F9	0.14 ± 0.03	100.41 ± 0.03	203 ± 1.23	20.224

RESULT AND DISCUSSION

Low bioavailability of drug through skin is one of the major obstacles to the development of Transdermal drug delivery products. Several enhancers have been studied for permeation enhancer effect. Majority of them were found to produce undesirable effect on skin or body.

Diclofenac sodium was used as a model drug to optimize a plasticizer for enhancing skin permeation. Nine different HPMC (3%w/v) based transdermal films using three different plasticizer in different concentration (20%w/w, 30%w/w, 40%w/w of polymer composition) namely propylene glycol, dibutyle phthalate, diethyl phthalate were prepared & evaluated for ex-vivo drug release to optimize a plasticizer to increase skin permeation.

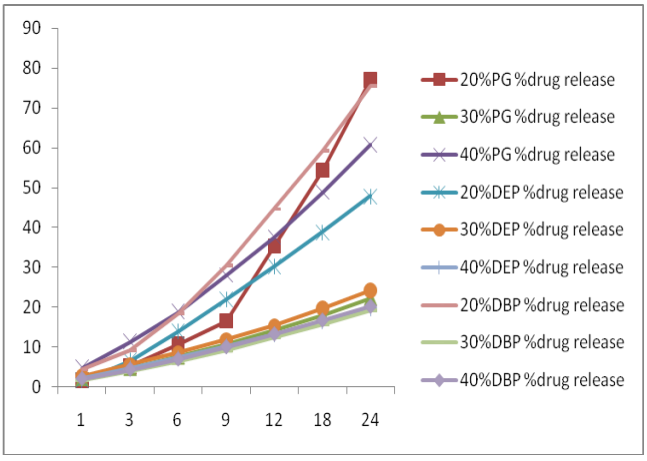

Fig: Comparative study of all plasticizers showing %drug release.

The ex-vivo permeation of Diclofenac sodium through hairless rat skin was found to show maximum increase to 77.104% in 24 hours with Dibutyle phthalate (20% w/w of dry polymer) over propylene glycol (PG), Di-ethyl phthalate (DEP), Propyline glycol.

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