ABSTRACT

Transdermal drug delivery system play is vital role because this route is free from invasive methods. Human skin is most considerable and targeted area/site for treatment of local skin diseases but skin acts as rate limiting barrier for entering or penetrating of drugs in body. Topical preparation is the best patient compliant manner of drug delivery in the body.

Proniosomal transdermal gel preparation has prolonged delivery and more importance because the proniosomes are more stable than existing liposomes and niosomes. Simultaneously, gel based formulations are better dermal absorption than other preparation such as already existing ointment and creams preparation. Consequently, dithranol proniosomes transdermal gel was formulated by means of surfactants and incorporated gel base polymers such as Carbopol 934.

Psoriasis is a provocative skin disease which is differentiated by hyperproliferation and abnormal differentiation of the stratified epidermis of skin. A lot of drugs are used for treatment of psoriasis in which dithranol is one of them old and gold.

The compatibility apparent from DSC studies in drug excipients were shown some interactions occur. The DTH thermographs by DSC were showed of endothermic peak at 170 °C which was equivalent to its melting point. The peak at 50°C of mixture of drug excipients has been reveals drug interact with excipients. This peak occurs due to phase transition temperature peak of surfactant demonstrated by peak at 50 °C. UV Spectroscopy analysis of DTH was prepared in dichloromethane and \( \lambda_{max} \) of solutions was found 257 nm. The \( R^2 \) values were for dichloromethane solution and with mixture of phosphate buffer and dichloromethane was found 0.998, 0.994 respectively. The solubility of drug was found that the drug is unsolvable in water and freely soluble in acetone, benzene, and dichloromethane and chloroform. Loss on drying was calculated which was found out to be 0.0241 % w/w. The partition coefficient of drug was found log P is 1.99 dithranol is a hydrophobic in nature.

Dithranol drug gets collected in mitochondria (cell power house), where it obstructs with the transfer of energy to the cell, possibly by releasing liberated radicals by oxidation of anthralin therefore delay DNA replication and disturbed cell division that happens in psoriasis plaques.
The most extensively established topical dosage form as ointment was used but a localized and staining effect of drug such as irritation and pigmentation of skin by short contact period of time and need frequent application of drug. The frequently shown side effects associated with DTH are skin rash, itching, peeling, redness, blistering, burning, stinging, swelling, or extra sign of skin irritation etc. In this research work we have overcome these problems and increased patient compliance by design of a substitute delivery arrangement in form of proniosomes.

Present research work related to preparation and formulation of proniosomal gel of dithranol was by using excipients such as Surfactant (span and tween), cholesterol, and lecithin, for entrapment of drug by technique of Coacervation phase separation. The studies were covered all related parameter of transdermal gel with correlated in vitro and in vivo data and also perform physical as well as chemical, means all physico-chemical performance i.e., drug content, DSC spectra spreadability, viscosity, and rheological consideration. Formulation optimization was subjected to $3^2$ full factorial designs by Design expert version 8.0.7 software. Additional, optimized preparations were estimated by rheological parameter and study of \textit{ex vivo} permeation. It was concluded that surfactant span 60 produced better results than other grade of Span with combination of cholesterol. Proniosomes incorporated in gel of carbopol and dithranol show spreadability, high-quality consistency, homogeneity as well as stability. Formulation batch DPNS6F8 was containing gel base Carbopol 934, Span 60 and cholesterol (act as permeation enhancer) showed 89.80 \% PDE and drug Flux 9.89 (µ/cm$^2$/h). Further evaluated of formulation with key parameter for pH, analysis of particle size, drug entrapment efficiency etc. The PDE and Flux for the 9 batches (DNPS6F1 to DNPS6F9) showed an extensive variation and 41.7 to 89 \% and 4.12 to 9.89; respectively. It was also seen that DNPS6F3, DNPS6F6, and DNPS6F9 more cholesterol level was minimum of drug encapsulation in the vesicles (41.7 \%, 62.4 \% and 62.8 \%) respectively. This is suggested that fact that concentration of cholesterol further than a definite concentration begins troublesome normal structure of layere of skin result to loss of drug entrapment. The all physical parameters of prepared gels were established to be inside the permissible restrictions. The \textit{ex-vivo} permeation (amount of dithranol permeated µg/cm$^2$) and deposition was shown the dithranol permeated from different PTG formulations of
dithranol and deposition amount in skin after one day has to be found 62.23 to 205.98 µg/cm² and 10.85 % - 18.37 respectively. The particle size of proniosomal transdermal gel formulations was found to be in the range from 1.759 to 5.438 µm confirming by particle size analyzer. These were rounded and uniform in organization if was seen in optical microscope. In-vitro drug diffusion, permeation flux and skin retention of drug, acute dermal toxicity, antipsoriatic activity, epidermal thickness, irritation test on Swiss albino mice along with stability studies was executed for optimized preparation (DNPS6F8). The drug in proniosomal gel was released from extended period of time contrast to conventional ointment Derobin and showed amplified in the deposition of drug in the dermis in contrast to conventional ointment. Not any apparent inflammation or edema or, erythema was shown on mice skin subsequent to two weeks of application of the optimized preparation. Antipsoriatic activity of proniosomal transdermal gel was revealed that prepared formulation was high competent than contrast with the Derobin ointment preparation. The stability test requirements for drug Stability studies as per ICH guidelines. Sealed glass ampoules (three each) were stored for this task at 5± 2°C in refrigerator, 25± 2°C, and 40± 2°C for a period of at least 8 weeks in dark place. The above results signified that the gels of proniosomal dithranol could be designated for deeper action. Proniosomal transdermal gel had wider prospect for treatment of Psoriasis.

**Keywords:** Dithranol, Proniosomal transdermal gel, Span, Cholesterol, *Ex-vivo* study.