ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Influence of *Sapindus mukorossi* on the permeability of ethylcellulose free films for transdermal use

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ABSTRACT

The influence of *Sapindus mukorossi* Gaertn, a member of *Sapindaceae* family (Popularly known as Soap nut) on the permeability of ethylcellulose free films was studied with a view to develop suitable rate controlling membranes for transdermal use. Dibutyl phthalate was incorporated at a concentration of 40% w/w of dry polymer as plasticizer. The dry free films were evaluated for various mechanical properties whereas the permeability characteristics of free films were studied using propranalol hydrochloride and diltiazem hydrochloride as model drugs. Both water vapour transmission and drug diffusion rate followed zero order kinetics. The spray dried powder of *Sapindus mukorossi* pericarps extract showed a significant influence on the mechanical as well as permeability characteristics. This may be due to difference in the affinity of *Sapindus mukorossi* with the film former. From this study it was concluded that the plasticized free films of ethylcellulose prepared with eco-friendly *Sapindus mukorossi* can be used as rate controlling membranes to develop transdermal drug delivery systems.

Keywords: *Sapindus mukorossi*, Soapnut, Ethylcellulose, Transdermal drug delivery system, Permeability, Rate controlling.

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ISSN: 0975-8585

INTRODUCTION

Soap nuts, such as those of *Sapindus mukorossi* (*Sapindaceae* family) are among the list of herbs and minerals in Ayurveda. They are a popular ingredient in Ayurvedic shampoos and cleansers. They are used in Ayurvedic medicine as a treatment for eczema, psoriasis, and for removing freckles. Soap nuts contain saponins, a natural surfactant and have been used as detergent[1]. The surfactant efficiency of soapnuts is comparable to that of sodium dodecylbenzenesulfonate, dioctyl sodium sulfosuccinate and sodium octanesulfonate [2]. Today, soapberries are being considered for commercial use in cosmetics and detergents, among many other products. While the *Sapindus* saponins cause less irritation, they are less potent bactericidal agents than modern chemical alternatives [3]. The development of transdermal drug delivery system (TDDS) using polymeric materials has become popular for various reasons. Among the various types of TDDS developed, one type utilizes a thin polymeric film as rate controlling membrane, which delivers the drug from the drug reservoir to the systemic circulation for an extended period of time. The permeability of drugs through the polymeric free films is dependent on characteristics of the polymer[4,5], casting solvent[6,7], permeability enhancer[8,9] and plasticizer[10,11] used.

The present investigation was carried out to study the influence of Soapnut (spray dried extract of the pericarp of the fruit of *Sapindus mukorossi*, family *Sapindaceae*) on the permeability of plasticized free films of ethylcellulose. Further the permeability characteristics of free films were studied using propranalol hydrochloride and diltiazem hydrochloride as model drugs.

MATERIALS AND METHODS

Ethylcellulose (with an ethoxyl content 46.5-53.0 by wt. and a viscosity of 14 CPS in 5% w/w 80:20 toluene: ethanol solution at 25^{o}C, SD Fine Chem, Mumbai). Dibutyl phthalate (Ranbaxy), ethyl alcohol (SD Fine Chem), toluene (Qualigens, HPLC grade), mercury (E-merck) were obtained commercially and used as received. Soapnut powder (a gratis sample from Dharani Forestry and Orchards Ltd., Kanigiri, Andhra Pradesh, India), propranalol hydrochloride and diltiazem hydrochloride (a gift sample from M/s NATCO Fine Pharmaceuticals, Hyderabad, India) were used.

Preparation of free films

Free films of ethylcellulose were prepared by mercury substrate method [12]. Dibutyl phthalate was used as plasticizer at a concentration of 40% w/w of dry polymer. A 2% w/v of polymer solution was prepared using different concentrations of the soapnut powder (0, 0.25, 0.5, 0.75, 1% w/w). A 6ml of polymer solution was poured on mercury surface contained in a petridish. The solvent was allowed to evaporate at a controlled rate by placing an inverted funnel over the petridish. The dry films were removed from the mercury surface and stored in a desiccator until use.

The thickness of free films was measured at five different places using micrometer (Mitutoyo, Japan) and the average value was calculated. The tensile strength and percent elongation of free films were determined according to A.S.T.M. procedure using INSTRON 1026 (Type 2512-119, model M.A 30-1014, U.K).

Determination of water vapour transmission (WVT)

The rate of WVT through the free films was determined as described by Utsumi et al [13]. For this a circular piece of film of known thickness was fixed with an adhesive (Feviquick®) over the brim of the glass vial containing three grams of fused calcium chloride powder as desiccant. The charged vial was weighed and kept in a desiccator maintained at 52 or 84% relative humidity (RH). The vial was taken out from the desiccator and weighed at regular time intervals for a period of 72 hrs. The experiment was carried in triplicate and the average values were calculated. The WVT rate through the free films was calculated from the plots of moisture gained vs time.

ISSN: 0975-8585

Drug diffusion studies

Diffusion of drugs such as propranalol hydrochloride and diltiazem hydrochloride through the free films was studied using diffusion cell was designed as described by Fites et al [14]. The solubility of selected drugs in distilled water was determined. A free film of known thickness was sandwiched between the donor and receptor compartments. The drug solutions were poured into the donor compartment. The receptor fluid consisting of distilled water was agitated using magnetic stirrer while maintaining a temperature of $37\pm1^{O}C$. Samples (5 ml) were collected from the receptor compartment at predetermined time intervals and replaced with an equal volume of distilled water. The samples were analysed for drug content after suitable dilutions using double beam UV-visible spectrophotomer (Schimadzu, Japan) at λ_{max} 290 and 240 nm for propranalol hydrochloride and diltiazem hydrochloride respectively. The diffusion rate and permeability coefficient were calculated from plots of cumulative amount of drug diffused vs time.

RESULTS AND DISCUSSION

All the prepared free films are uniform and flexible. The spray dried extract of pericarp of the fruit of *Sapindus mukorossi* (soapnut) used for forming ethylcellulose free films showed a significant influence on the mechanical and permeability characteristics as summarized in Table 1. The low standard deviation values in thickness measurements ensured the uniformity of the films prepared by mercury substrate method. The thickness of the films was found to be between 30.4 and 38.9 μm. The incorporation of dibutyl phthalate (40%w/w of dry polymer) resulted flexible films. The tensile strengths decreased slightly as the concentration of the soapnut powder increased. The tensile strength of the free films varied considerably between 34.7 and 37.1 $kg.cm^2$ but the percentage elongation changes (51.8 to 53.7%) are negligible as compared to the films without soapnut powder whose elongation was found to be 51.2%. This shows that concentration of soapnut powder influenced the mechanical properties of the prepared films.

The solubility of propranolol hydrochloride and diltiazem hydrochloride in distilled was found to be 150mg/ml and 480mg/ml respectively. Water vapour transmission and drug diffusion through the films followed zero order kinetics, and decreased with increase in film thickness (Table 1). The WVT rate of the films was found to be between 1.135×10^{-4} to 1.71×10^{-4} $gm.cm/cm^2$. 24hr. The rate of WVT was found to be in the order of 1.0 > 0.75 > 0.5 > 0.25 > 0% w/w for films prepared with various concentrations of soapnut powder. The difference in mechanical and permeability characteristics of ethylcellulose free films may be due to the difference in the concentration of the soapnut powder.

Table- 1: Mechanical properties and water vapour transmission rates of ethylcellulose free films in the presence of *Sapindus mukorossi*

Concentration of Soapnut (%w/w)	Thickness (μm)	Tensile strength ($kg.cm^2$)	Percentage elongation	Water vapour transmission rate ($gm.cm/cm^2$. 24hr)
0	30.4±1.2	38.2±1.6	51.2±3.8	1.135×10^{-4}
0.25	32.8±1.4	37.1±1.4	51.8±2.6	1.317×10^{-4}
0.5	34.5±0.8	36.2±1.2	52.4±2.4	1.449×10^{-4}
0.75	36.3±1.6	35.4±1.8	53.1±1.9	1.561×10^{-4}
1.0	38.9±1.3	34.7±1.4	53.7±2.4	1.714×10^{-4}

The rate of diffusion of propranolol hydrochloride was found to be from 6.08×10^{-4} to 9.60×10^{-4} mg/hr.cm for the films containing different concentrations of soapnut powder from 0-1%w/w indicating that the drug diffusion increased proportionately with the concentration of the soapnut powder. A similar result was observed for diltiazem hydrochloride whose diffusion rate was found between 5.17×10^{-4} and 8.94×10^{-4} mg/hr.cm. The drug diffusion rate through the films was in the order of 1.0 > 0.75 > 0.5 > 0.25 > 0% w/w of

soapnut powder for both drugs which shows that both the WVT rate and drug diffusion rate were in the same order as shown in Table 2.

Table- 2: Permeability coefficient of propranalol hydrochloride and diltiazem hydrochloride through ethylcellulose films

Concentration of soapnut powder (% w/w)	Average permeability coefficient mg/hr.cm	
	Propranalol hydrochloride	Diltiazem hydrochloride
0	6.08 x 10-4	5.17 x 10-4
0.25	7.34 x 10-4	6.03 x 10-4
0.5	8.02 x 10-4	7.27 x 10-4
0.75	8.86 x 10-4	7.96 x 10-4
1	9.60 x 10-4	8.94 x 10-4

The permeability of both the drugs was increased with increase in the concentration of soapnut powder indicating that the concentration of soapnut powder influences the permeability of the free films than those made from without soapnut. From this study it may be concluded that the films prepared from solution in *Sapindus mukorossi* powder which released the drugs at steady rate for an extended period of time, can be used as a rate controlling membrane for the development of transdermal drug delivery systems.

ACKNOWLEDGEMENTS

Authors are thankful to Faculty of Pharmacy, 7th April University, Al-Zawia, Libya for the lab facilities provided and M/S NATCO Pharmaceutical Ltd, Hyderabad, India for the provided gift samples for the present research approach.

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