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Der Pharmacia Lettre, 2012, 4 (4):1115-1118
(<http://scholarsresearchlibrary.com/archive.html>)



ISSN 0975-5071
USA CODEN: DPLEB4

Study on permeation enhancement of sparfloxacin from certain selected ointment bases

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ABSTRACT

Sparfloxacin ointments were prepared by fusion method. Simple, paraffin and emulsifying ointment base with two different permeation enhancers PEG 400 and Tween 80 were used for the study. In vitro drug release was studied through rat skin by using Franz-type diffusion cell. Antibacterial activity was carried out by filter paper disc method to find out the drug release of the ointment preparations. It was found that the zone of inhibition was higher for the drug with PEG 400 as base than other ointment preparations. It was concluded based on the results that the formulation having permeation enhancers in the formulation increases drug release.

Keyword: anti-bacterial activity, ointment, sparfloxacin, tween 80, polyethylene glycol, permeation study.

INTRODUCTION

The skin, as a drug delivery system has advantages as ease of access, larger surface area, noninvasive nature of treatment, vast exposure to circulatory and lymphatic system. Drug must be transported through different skin layers [1]. The drug should penetrate the stratum corneum barrier in the skin. It is expected to be a good drug delivery system through skin if the drug has the ability to penetrate the stratum corneum barrier in the skin. Barrier penetration enhancers are used to reduce the diffusion barrier which disrupts the membrane structural layer [2,3].

Ointment contains fluid hydrocarbons meshed with higher melting solid hydrocarbons. Mineral oil and petrolatum are the major components of most ointments. Alternatively, a plastic matrix was obtained by mixing polyethylene glycol or mixtures of polyethylene glycols incorporated into the mineral oil. The addition of polyethylene glycol to ointment will increase its consistency.

Skin penetration enhancers (PE) are used to remove the barrier resistance of the stratum corneum reversibly. PE allows drugs to penetrate to the viable tissues and thus enter the systemic circulation [4]. The rate of permeation of the drug molecule through topical route is increased by using chemical agents or physical method [5,6]. There is several permeation enhancement mechanism of ointment [7].

Sparfloxacin is one of the antibacterial agents. It is effective against a wide range of gram-positive and gram-negative infection; clinical trials will determine its ultimate role in the treatment of infectious diseases [8].

An attempt has been made in the present study to incorporate sparfloxacin in various ointment bases and to study the effect of permeation enhancer on the release of drug from different bases.

MATERIALS AND METHODS

Sparfloxacin was obtained as a gift sample from Micro Labs Ltd, Hosur. emulsifying wax, white wax, soft paraffin, polyethylene glycol (PEG 400), tween 80, wool fat, cetostearyl alcohol, hard paraffin, white bees wax (S.D.fine-Chem Ltd, Mumbai) were used in the present study.

Method of preparation of ointments:

The sparfloxacin ointment was prepared by using the different ointment bases like simple ointment base (SOB), emulsifying ointment base (EOB) and paraffin ointment base (POB). Compositions of each ointment base were specified in **Table 1**.

All the ingredients were melted in a china dish on a water bath. Sparfloxacin was added in the molten state. Then it was allowed to cool with continuous stirring to form a semi solid mass.

Permeation Enhancers:

PEG 400 and Tween 80 permeation enhancers were used separately in our studies at a concentration of 0.5% w/w. Higher concentration were not used since such concentration have been reported to decrease the drug release from topical formulations [9,10]. In all the ointment bases, permeation enhancers were added in the molten condition.

In-vitro permeation study:

Hairless albino rat skin was selected for the study. After removing fat, the rat skin was mounted on a vertical diffusion cell (Franz-type) with dermis part facing the receptor compartment. The donor compartment was placed with prepared sparfloxacin ointment. The receptor compartment was completely filled with phosphate buffer solution (pH 7.4) as the diffusion fluid. The temperature was maintained at $37 \pm 0.5^\circ\text{C}$ and the receptor compartment was constantly stirred at 300 rpm. Samples were withdrawn at predetermined time intervals and replaced immediately with an equal volume of diffusion fluid. Drug release contents were measured using Shimadzu UV double beam spectrophotometer at 304 nm [11]. Each release determination was carried in triplicate. The results were shown in **Figure 1**.

Antibacterial activity:

The antibacterial activity of the compounds thus prepared has been evaluated by filter paper disc technique [12]. *Escherichia coli* (*E. coli*) and *Staphylococcus aureus* (*S. aureus*) have been used as test organisms. 500 mg of ointment containing 5000 μg of sparfloxacin (1% w/w) was used for the formulation. Filter paper disc was applied with and without permeation enhancer for the study. Sterile Mueller Hinton agar medium was poured into sterile petri dishes with uniform diameters and allowed to solidify. Then 0.5 ml of the inoculums were transferred over the solidified agar medium and allowed to settle. Small filter paper discs containing the above ointment preparations were planted over the inoculate aseptically and incubated at 37°C for 18 h and the zone of inhibition of bacterial growth was measured [13]. The results were presented in **Table 2**. **Figure 2-3** represents the different zone of inhibition of the prepared formulations against *E. coli* and *S. aureus*.

RESULTS AND DISCUSSION

The 1% w/w sparfloxacin ointments were prepared by using simple ointment, emulsifying ointment and paraffin ointment bases. Fusion method was used for the preparation of ointment by using permeation enhancers like PEG 400, tween 80 (0.5% w/w) and without permeation enhancers. The use of tween 80 (0.5% w/w) as the permeation enhancer had an enhancing effect on the permeation of sparfloxacin because tween was one of the surfactant. It interacts onto the stratum corneum thereby disorganizing its structure. Sparfloxacin permeated from PEG 400 (0.5% w/w) containing ointment bases increases than other formulations because it can solubilize or remove lipids or water soluble constituents in or on the surface of the stratum corneum and improve partitioning coefficient. *In vitro* permeation study was carried out by using vertical diffusion cell. It was observed that PEG 400 showed good permeation ability than tween 80. It could be due to the better solubilizing ability with lipids than tween 80.

Drug release from various ointment preparations was analyzed by antibacterial activity. It was carried out using Mueller Hinton agar medium against *E. coli* and *S. aureus*. The formulation having highest zone of inhibition was considered the best release ointment preparation. It was observed that the zone of inhibition was higher for PEG 400 than other formulations. This indicates that the PEG 400 containing formulation was the best formulation.

Table 1. COMPOSITION USED IN THE STUDY TO PREPARE OINTMENT

Ingredients in gm	SOB	EOB	POB
White bees wax	–	–	20
Wool fat	50	–	–
Hard paraffin	50	–	30
Cetostearyl alcohol	50	–	50
White soft paraffin	850	500	900
Emulsifying wax	–	300	–
Liquid paraffin	–	200	–

Table 2: RELEASE OF SPARFLOXACIN FROM VARIOUS OINTMENT PREPARATIONS WITH AND WITHOUT PERMEATION ENHANCERS

Sparfloxacin (1%w/w) ointment preparation	Zone of Inhibition (mm) against <i>E. coli</i>			Zone of Inhibition (mm) against <i>S. aureus</i>		
	without permeation enhancer	with PEG 400	with Tween 80	without permeation enhancer	with PEG 400	with Tween 80
SOB	16	23	21	21.5	24	23
POB	17	28	22	19.5	23.5	21
EOB	19	27	23	22.5	24	23

Figure 1: IN-VITRO PERMEATION STUDY OF SPARFLOXACIN IN DIFFERENT OINTMENT BASE WITH AND WITHOUT PERMEATION ENHANCERS

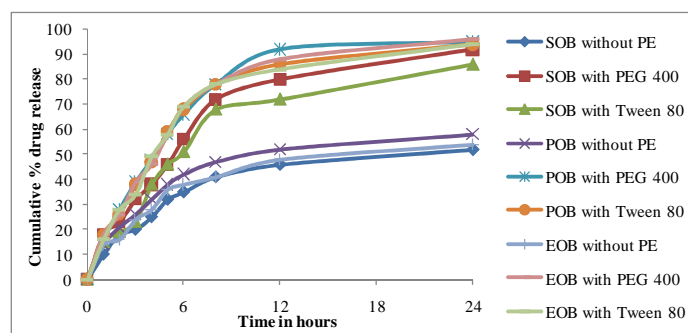


Figure 2: SPARFLOXACIN IN EOB WITHOUT PERMEATION ENHANCER
E. coli *S. aureus*

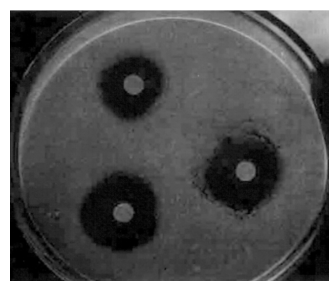


Figure 3: SPARFLOXACIN IN POB WITH 0.5%W/W OF PEG 400



CONCLUSION

Sparfloxacin ointments were prepared by fusion method using SOB, POB, and EOB with two permeation enhancers PEG 400 and tween 80. Ointments were also prepared without the addition of permeation enhancers, which helped in comparing the formulation. Formulation with PEG showed better *In vitro* drug release and permeation enhancer effect than tween 80.

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