RELEASE OF SALICYLIC ACID FROM OINTMENT AND CREAM BASES

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A large number of ointment and cream formulations, with emulsion, absorption and oleaginous bases have been prepared incorporating salicylic acid as the active component. The release of salicylic acid fromthese bases has been estimated which lies in the following order: emulsion > absorption > oleaginous bases. The effect of different concentrations of some non-ionic surfactants on diffiusion of salicylic acid from hydrophilic ointments has also been studied.

INTRODUCTION

Much work has been done on the physiological properties of a drug, but the role of the physicochemical factors in its overall availability has not been fully understood.

The nature of percutaneous absorption and the factors affecting the release of drugs from dermatological vehicles used for various types of ointments have been studied (1). Percutaneous absorption and diffusion of various medicinal compounds from silicone and petrolatum ointment bases (2), skin protective ointments (3), commercial ointments (4), and oil-in-water and water-in-oil bases (5) have been evaluated.

The clinical effectiveness of a drug may vary when it is incorporated in different vehicles for ointments. The choice of an optimum vehicles for a particular medicament depends on the physical and chemical properties of the drug alone and in the vehicle as well as the nature of the skin condition being treated. Much information has been gained on this subject in the last few years but much more is needed in order to treat the various skin disorders. [6–9].

The purpose of the present study was to evaluate the various ointment and cream formulations with emulsion, absorption and oleaginous bases, with respect to their ability to release the drug, in a specified time. Salicylic acid was chosen as a model compound since this is used along with other medicaments such as coaltar, resorcinol, precipitated sulphur, mercuric chloride and ammoniated mercury in topical application forms for treatment of various skin diseases. Moreover, salicylic acid is relatively stableandalso compatible with the various formulation ingredients used in the ointments and creams discribed in the present study.

EXPERIMENTAL

Preparation of Diffusion Ointments and Creams. 3% finely powdered salicylic acid (1.2g) was levigated with 10 drops of glycerin to form a smooth paste and then thoroughly incorporated in small increments into the ointment and cream bases to yield 40g of the finished product. The bases used were of the emulsion, absorption and oleaginous type and the formulations were prepared according to the B.P., U.S.P., & B.P.C. methods [10-12]. Surfactants such as Atlas G-7596J (Polyoxy ethylene Sorbitan monolaurate), Tween 40 (Polyoxyethylene (20) Sorbitan Monopalmitate) and Tween 85 (Polyoxyethylene (20) Sorbitan trioleate) were incorporated in hydrophilic petrolatum ointment U.S.P.

Procedure. The diffusion cell consisted of a 28 g ointment jar and the pretreated cellophane membrane. The jar was filled with the salicylic acid ointment/cream packed tightly to avoid air pockets and scrape-levelled with a spatula. The pretreated membrane was spread evenly over the open end of the jar and was securely fastened. The ointments/creams placed in the cell were allowed to stand for 24 hr prior to the diffusion study. The cell was inverted and placed on a 4 x 6 cm triangular glass stand immersed in a beaker containing 125 ml of distilled water and 5 drops of freshly prepared 9% ferric chloride solution. The cell was placed in such a way that the membrane was extended approximately 1 cm below the surface of the solution to make allowance for the removal of 5 ml aliquot for analysis without exposing the membrane to the atmosphere. As soon as the cell was placed in the position described above, the stop watch was started to record time allowed for the diffusion of salicylic acid from the base through the semi-permeable membrane.

Assay of Salicylic Acid. The diffusion of salicylic acid from the ointment/cream into the aqueous solution resulted in a purple colour formation by the reaction of salicylic acid and the ferric ions. At 10 min intervals 5 ml portions were transferred to a 1 cm glass cell and the salicylic acid content was assayed spectrophotometrically by measuring absorbance at 525 nm.

RESULTS AND DISCUSSION

The relative release of salicylic acid from the various bases is given in Fig. 1-3 and the effect of some surfactants, on the release of salicylic acid is reported in Fig. 4. It is apparent from Figs. 1 and 2 that the emulsion bases give better release of salicylic acid as compared to that given by the absorption and oleaginous bases (Figure 3) showing that the drug – vehicle interaction retards the release of salicylic acid in the latter bases.

The diffusion of salicylic acid from the various ointment and cream bases can be considered as a measure of the release of the drug from these bases. A comparison of the rates of release indicates that it lies in the following order: Emulsion base > absorption base > oleaginous

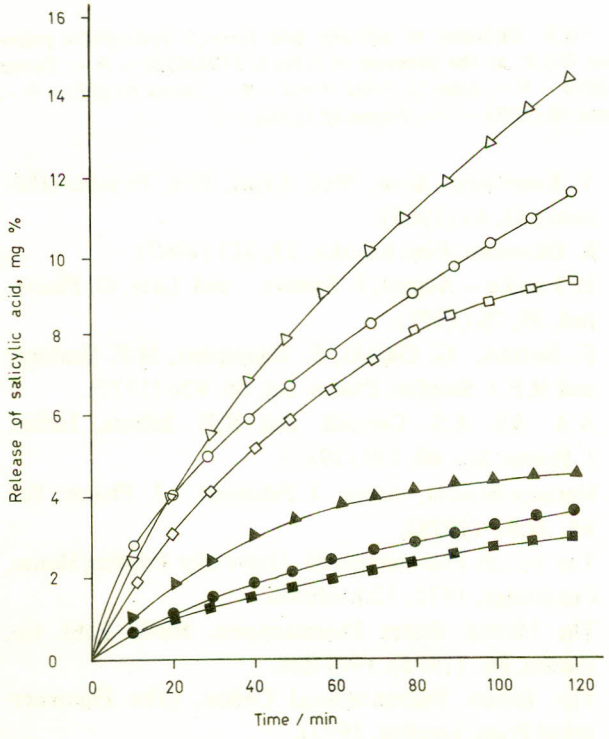

Fig.1. Diffusion of salicylic acid through emulsion bases, Aqueous cream. Oil-in-water B.P. – △ –, Semisolid base – ○ –, Petrolatum emulsion base – □ –, Emulsifying ointment – ▲ –, Ointment of benzoic acid compound – ● –, Cold cream water-in-oil U.S.P – ■ –.

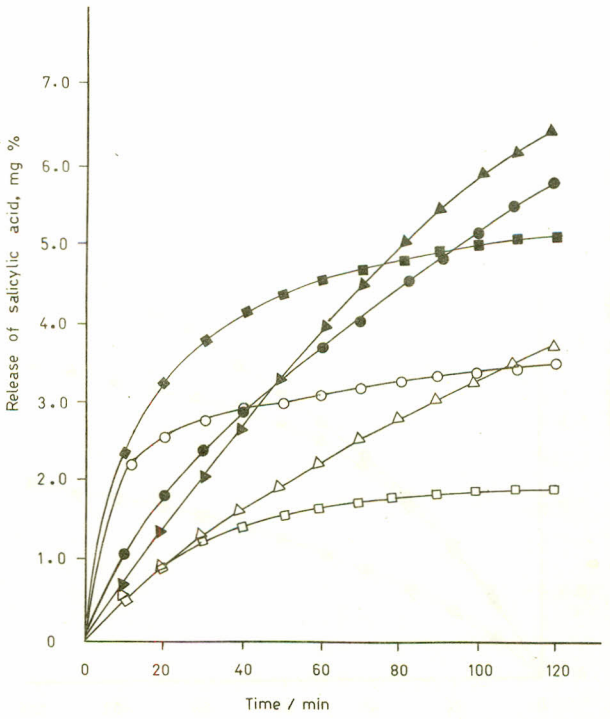

Fig.2. Diffusion of salicylic acid through emulsion bases, Oil-in-water cream of cetrimide ointment B.P.C – ▲ –, Water miscible base – ● –, Oil-in-water base – ■ –, Cetrimide emulsifying ointment B.P.C. – △ –, Beeler's base – ○ –, Hydrophilic ointment U.S.P. – □ –.

base. It may be observed that in the emulsion bases, the aqueous cream has the highest release (15.30%) while the cold cream has the lowest release (2.92). This may be explained on the basis of the oil to water ratio in these preparations. In the aqueous cream this ratio (3:7) is lower than of the cold cream (7.5:2.5) and hence the release of a water soluble drug such as salicylic acid would be higher from the aqueous cream. The cream of cetrimide BPC has the oil to water ratio of 5:5, thus showing an intermediary release of salicylic acid (6.42). The cetrimide emulsifying ointment BPC contains an oily base with the result that the rate of release is reduced to 3.80, but the presence of cetostearyl alcohol gives higher release as compared with the absorption (2.76 and 1.91) and oleaginous (1.22) bases. The other emulsion bases behave in a similar manner. From the data it can be concluded that in the emulsion bases the oil to water ratio determines the extent of release of salicylic acid. As the amount of water in the base is decreased, the rate of release is also decreased. Alteration in oil to water ratio in a particular base may lead to a desirable rate of release for a particular drug.

The absorption and oleaginous bases used for the ointments are mainly oily and thus show relatively low rates of release. This may be expected from salicylic acid which would very slowly diffuse through these media. The nonio-

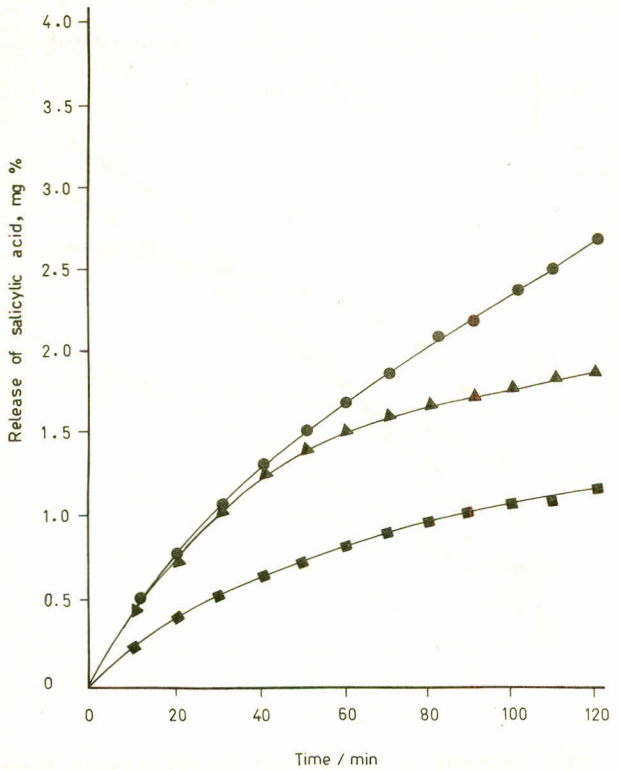

Fig.3. Diffusion of salicylic acid through absorpition and oleaginous bases, Petrolatum absorption base – ● –, Hydrophilic petrolatum U.S.P – ▲ –, White ointment U.S.P – ■ –.

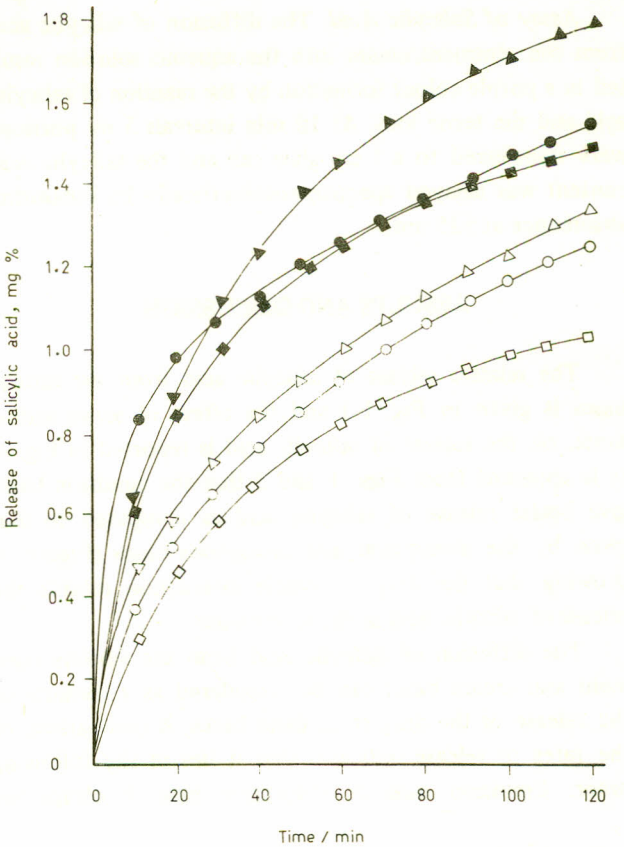

Fig.4. Diffusion of salicylic acid through hydrophilic petrolatum U.S.P. in the presence of Atlas G-7596J(5%) – ▲ –, Tween 85 (5%) – ● –, Atlas G-7596J (10%) – ■ –, Tween 40 (5%) – △ –, Tween 40 (10%) – ○ –, Tween 85 (10%) – □ –

nic surfactants in different concentrations considerably affect the rate of release of salicylic acid. The relatively higher release of salicylic acid from the hydrophilic petrolatum base USP in the presence of Atlas G 7596 J compared with the Tweens is in agreement with the earlier observations [13,14] For a given concentration of surfactant, there occurs a definite change in the oil to water ratio of the base leading to an alteration of the rate of diffusion. The lower rate of release at a higher concentratio of the surfactant (10 %) may also be, to some extent, due to the drug surfactant interation. (Fig. 4)

From the results it may be concluded that the release of salicylic acid from an ointment or cream base to an aqueous medium depends largely on factors such as partition coefficient, diffusion coefficient, drug-vehicle interaction and the nature and amount of the surfactant.

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