Research Article

The Relationship between Water Number and Release of Ketoconazole from Different Ointment Bases

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ABSTRACT

The objective of this study was to investigate the relationship between water number value of selected ointments and release of Ketoconazole as a model drug. The ointments used were soft paraffin, wool fat, cetostearyl alcohol and soft paraffin. The release of Ketoconazole absorption was determined by using UV-Visible Spectrophotometer at 269 nm. It was observed from the results that the addition of a fatty alcohol as cetostearyl alcohol to soft paraffin has increased the water number from 11.5 to 57.5 ml. However, based on the release of Ketoconazole in the ointments following descending order of soft paraffin with cetostearyl alcohol> wool fat >soft paraffin. The results of this study could be used as a base for further studies particularly when the same ointments are used with such Ketoconazole drugs.

Keywords: Ketoconazole, Model drug, Ointments, Water number.

INTRODUCTION

Water number is defined as the maximum amount of water that can be added to 100g of such base at a given temperature.[1] *In-vitro* release of medicaments from semi-solid dosage form can be detected by using many techniques. *In-vitro testing* is used as quality assurance (QA) tool to ensure batch-to-batch uniformity.[2] There are many types of ointment bases that act as vehicles for the drugs and designated to facilitate drugs delivery into or through the skin.[3] According to the United States Pharmacopeia (USP), there are four classes of ointment bases: hydrocarbon bases, absorption bases (further classified into anhydrous form and emulsion form), water-removable bases and water-soluble bases. The choice of ointment bases are dependent on several factors, including the site of application, the required rate of drug release and the chemical stability of the drug.[4] There are properties that affect the choice of ointment base, which are stability, penetrability, solvent property, irritant effects and ease of application.[5] In this study different ointment bases were used after calculating their water numbers. Several research works have been dedicated recently using*in-vitro* release of medicaments technique.[6-15] In this study, Ketoconazole as a model drug was used with various ointment bases to investigate the effect of the water number of each ointment on the release of the model.

MATERIALS AND METHODS

Ketoconazole, vaseline, wool fat and cetostearyl alcohol were obtained from Pharmaceutical Laboratory, Faculty of Pharmacy, Universiti Teknologi MARA (UiTM) PuncakAlam. All chemicals were used as received. The standard solution for solubility measurement was prepared by dissolving Ketoconazole in ethyl alcohol solution. A standard linear graph is obtained from Ketoconazole standard sample in the concentration of 0.0488 x10^{-3}, 0.0977 x 10^{-3}, 0.195 x 10^{-3}, 0.391 x 10^{-3}, 0.781 x 10^{-3}, 1.56 x 10^{-3}, 3.13 x 10^{-3} % w/v. The solutions were prepared from the stock solution with using 25 ml volumetric flask. The Ketoconazole absorption was determined by using UV-Visible Spectrophotometer at 269 nm. In order to determine the water number of ointment bases, the ointment bases need to be prepared. Water number was determined when there were droplets of water remaining at the walls of container. The bases were continuously stirred as the water was added from burette. Distilled water was used in this process. All three types of topical formulations were tested by using Franz diffusion cell method to observe the in vitro release of medicament from the formulations. All formulations was weighed and applied to the membrane. The membrane used was cellulose acetate synthetic membrane with size of 25 mm in diameter and 0.45 µm pore size. Phosphate buffer with pH of 7 was used as the media. The temperature was maintained at 32°C to mimic the temperature at the skin surface. Ketoconazole as a model drug was used in this study to declare whether the water number of ointment base affects the in vitro release of medicaments. 1% w/w Ketoconazole was weighed and dissolved into ointment bases. The sample was taken every one hour for three hours. The prepared samples were then tested with UV spectrophotometer at 269 nm to detect the medicament release from the bases.

RESULTS AND DISCUSSION

Table 1 shows the water number of both oleaginous and absorption bases. From the results it is obvious that addition of a fatty alcohol as cetostearyl alcohol to soft paraffin has increased the water number from 11.5 to 57.5 ml. The tested bases can be arranged in the following descending order according to their water

number: wool fat >soft paraffin with cetostearyl alcohol> soft paraffin.

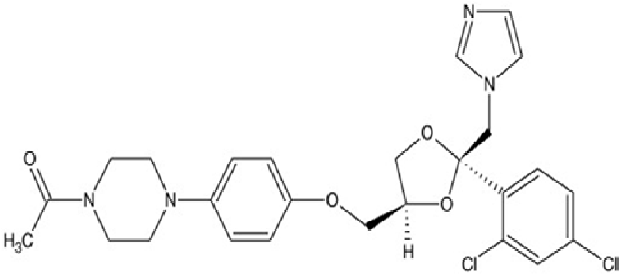

Figure 1: Molecular structure of Ketoconazole

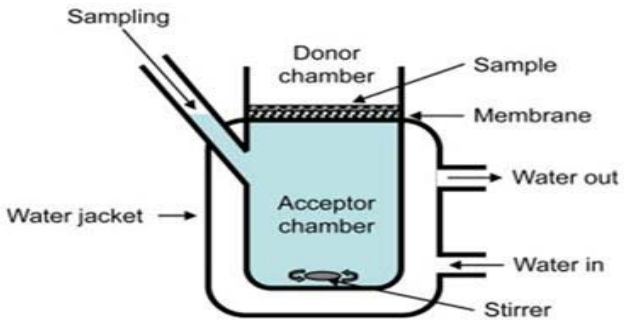

Figure 2: Scheme of a Franz diffusion cell for the study of release, diffusion and permeation processes through membranes for topical and transdermal formulations.[16]

Table 1: Water number of various ointment Bases at 25°C.

Ointment Base	Water Number (ml)
Soft Paraffin	11.5±0.1
Soft Paraffin + 20% of Cetostearyl Alcohol	57.5±0.3
Wool Fat	202.5±0.2

In the physical sciences, a partition-coefficient (log P) or distribution-coefficient (log D) is the ratio of concentrations of a compound in a mixture of two immiscible phases at equilibrium. These coefficients are a measure of the difference in solubility of the compound in these two phases. It is defined as the ratio of the compound's concentration in a known volume of the base to its concentration in a known volume of water after the base and water have reached equilibrium point.[17] The release of Ketoconazole (1%) from the tested bases is demonstrated in Table 2. From these results it is clear that: Ketoconazole being a hydrophobic drug is completely miscible with both olaginous and absorption bases and the values of drug released are low. Addition of water to the base disturbs the miscibility of the drug in these bases, thus increasing the partition coefficient and enabling more drug to be released. The tested bases can be arranged in the following descending order according to the release of Ketoconazole in the following descending order: soft paraffin with cetostearyl alcohol> wool fat >soft paraffin.

Concentrations of Ketoconazole after Franz diffusion cells were conducted can be calculated by:

$$y = 0.0416x$$

Where, y = absorbance of Ketoconazole

x = concentrations of Ketoconazole

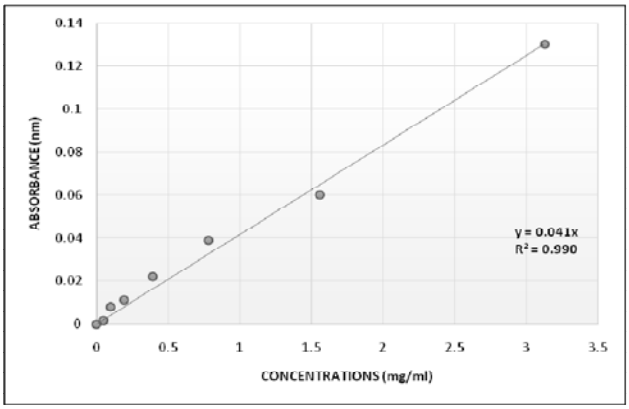

Figure 3: Calibration curve of ketoconazole

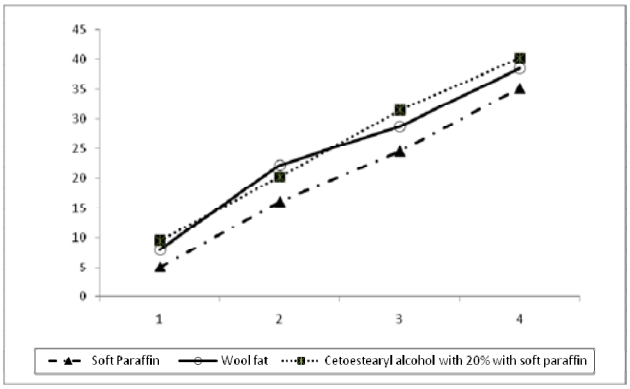

Figure 4: Cumulative Release of Ketoconazole from Different Ointment Bases Before addition of water as Measured by Franz Diffusion Cell.

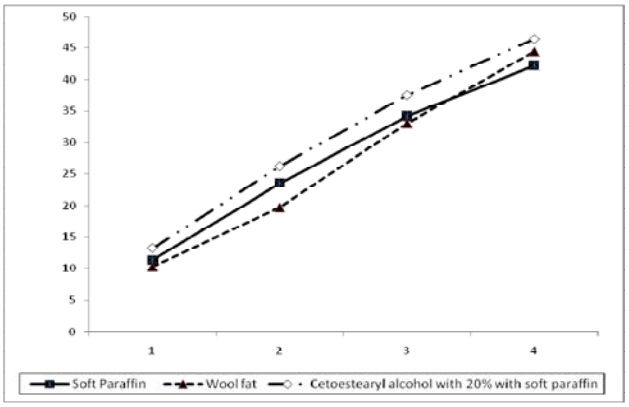

Figure 5: Cumulative Release of Ketoconazole from Different Ointment Bases after addition of water as Measured by Franz Diffusion Cell.

CONCLUSION

This research focuses in measuring the value of drug from selected ointments - drug loaded formulations. Ketoconazole was used in these formulations because it has limited water solubility and also it is not very stable

and could undergo chemical degradation, such as oxidation and hydrolysis. In terms of drug release and its relationship with the water number of the bases used, it was observed that soft paraffin with cetostearyl alcohol> wool fat >soft paraffin.

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