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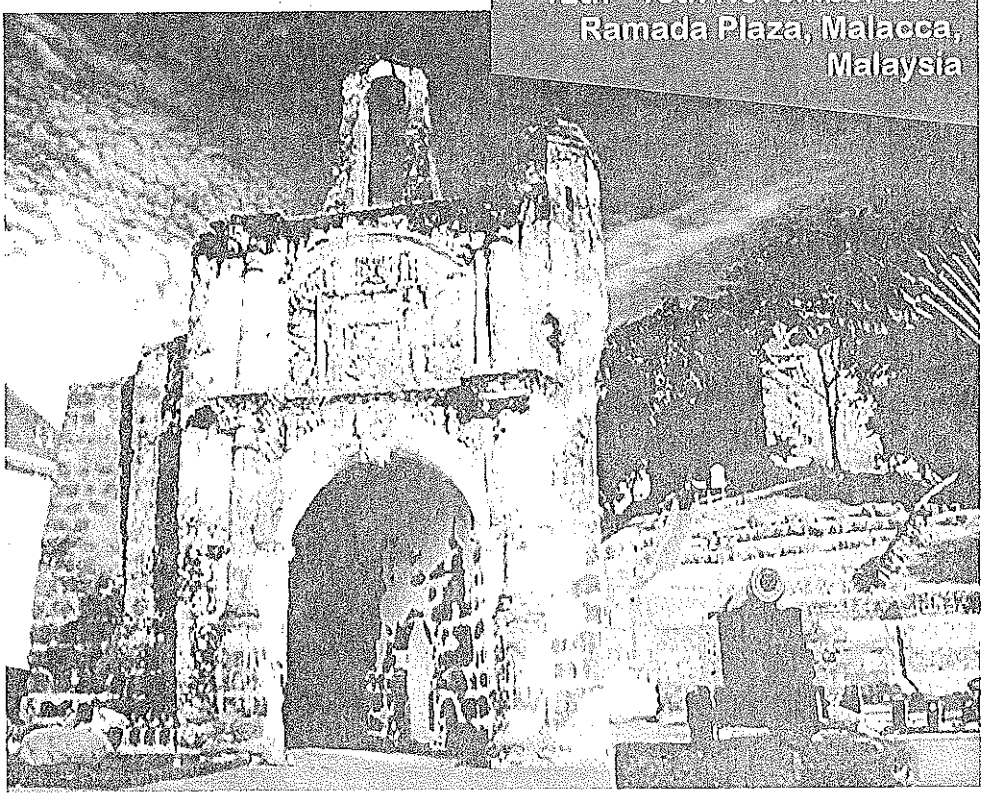

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PP42 EXPLORING POWDER BLEND UNIFORMITY OF A BINARY MIXTURE CONTAINING METFORMIN HCl AND HPMC BY DIFFERENTIAL SCANNING CALORIMETRY

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VBlender, also known as twin–shell mixer, is widely used in pharmaceutical industries for mixing powders, granules, and other solid materials. Its mixing mechanism involves continuous splitting, followed by intermixing of powder materials as the shell rotates on its horizontal axis. In pharmaceutical industries, mixing operation is considered a critical step in process scale upduring product development as well asroutine commercial manufacturing. In this research, HPMC and metformin HCl (95:5 w/w) at 50% and 60% occupancy of a V blender wasmixed to make a binary mixture and further analyzed for their mixing uniformity by a DSC method. The results of the DSC method were further confirmed by a UV method. Powder samples were withdrawn at 5 min, 10 min, 15 min, and 20 min intervals each from the top, middle, and bottom positions of the blender. Recovery of metformin HCl after 20 min of mixing by both the UV method (2.66±1.10% and 2.60±0.32% at 50% and 60% occupancy levels, respectively) and the DSC method (2.68±0.22% and 2.29±0.14% at 50% and 60% occupancy, respectively) were found comparable. Also, maximum RSD of enthalpy (21.55 at 10 min at 50% occupancy) for sample analysis by the DSC method was comparable to that of the UV method (25.201 at 15 min at 50% occupancy). As aconclusion, DSC method can be further explored as an alternative of UV spectroscopy or HPLC method to assess the mixing uniformity of powder samples in pharmaceutical industries.

Keywords: mixing uniformity, DSC, UV, V blender, binary-mixture.

PP43 TRANSDERMAL PERMEATION MECHANISM OF SODIUM DEOXYCHOLATE AIDED NANO-TRANSFERSOMES BY DIFFERENTIAL SCANNING CALORIMETRY (DSC)

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Transfersomes are lipid based nano-vesicles made of phospholipid and surfactant. Their drug permeation mechanism through the skin has been attributed to the moisture seeking tendency (xerophobia) of the lipid vesicles followed by destabilization of lipid bi-layer in the stratum corneum (SC) by surfactant. However, structural changes of SC due to surfactant need further elucidation to know the specific role of the surfactant in doing so. The objective of this study was to evaluate drug permeation mechanism of Raloxifene loaded nano-transfersomes containing sodium deoxycholate as a surfactant. Phospholipon® 90G was used as a lipid composition in the nano-formulation. Three different types of skin i.e. mice, guineapig and rabbit were used in this study. The SC was microtomed from the rest of the skin layers with chemical treatment, thoroughly washed, and kept for drying in a vacuum desiccator. The SC samples were then subjected to an ex-vivo permeation study of the transfersomal formulation for a period of 8 hrs. A control sample was prepared in a similar way, without any formulation treatment. A sample of the SC section was cut, sealed in aluminum hermetic pans and scanned using DSC at a scanning rate of 5°C per min over the range of 25°C–125°C. The characteristic bi-layer lipid and keratin transition peaks found in the control SC samples were: 75°C, 78°C, and 95°C for mice; 820C, 900C, and 990C for guineapig; and 840C, 920C, 990C for rabbit. However, upon treatment with sodium deoxycholate aided Raloxifene nano-transfersomes, most of the peaks were shifted towards lower melting points and some of them were disappeared. This finding confirmed disruption of lipid bi-layer and denaturation of keratin in the SC layer of the investigated skin samples by nano-transfersomes with sodium deoxycholate. The results of the present study clearly highlighted the role of sodium deoxycholate in transdermal permeation of drug loaded nano-transfersomes formulation.

Keywords: Transfersomes, differential scanning calorimetery, Raloxifene, sodium deoxycholate.

TRANSDERMAL PERMEATION MECHANISM OF SODIUM DEOXYCHOLATE AIDED NANO-TRANSFERSOMES BY DIFFERENTAIL SACNNING CALORIMETRY (DSC)

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BACKGROUND

Transfersomes are lipid based nano-vesicles made of phospholipid and surfactant. They have been reported as ultra-deformable and elastic nano-carriers which are superior to the conventional liposomes in terms of delivery of drugs through the stratum corneum (SC) (1). They can overcome the barrier properties of the SC to achieve high drug permeability and deliver drugs in systemic circulation for the required therapeutic actions. Their drug permeation mechanism through the skin has been attributed to the moisture seeking tendency (xerophobia) of the lipid vesicles followed by destabilization of lipid bi-layer in the SC by surfactant (2). However, the specific role of a surfactant in permeation enhancement of transdermal nano-carriers like transfersomes and the structural changes of the SC are not fully elucidated.

OBJECTIVES

The objective of this study was to evaluate drug permeation mechanism of Raloxifene loaded nano-transfersomes containing sodium deoxycholate as a surfactant and phospholipon 90G as bilayer vesicles composition.

METHODS

Preparation of drug loaded transfersomal vesicles with phospholipon 90G and sodium deoxycholate by conventional thin-layer rotary evaporation method (2).

Three different animals skin i.e. mice, guinea-pig, and rabbit were used for this study. The SC was detached from the rest of the skin layers with a chemical treatment, thoroughly washed, and kept for drying in a vacuum desiccator. The SC samples were subjected to an *ex-vivo* permeation study of the transfersomal formulation for 8 hours. The control samples of each skin type were prepared in a similar way, without any formulation treatment. All the samples were weighed (20±1 mg), cut, sealed in aluminium hermetic pans and scanned using DSC (Mettler Toledo DSC 1) at a scanning rate of 5°C per minute over the range of 25°C–125°C. The transition and melting peaks were observed for the all the samples by STARe software.

RESULT

The thermograms of untreated SC of all three animals were compared with the treated SC samples. Melting peaks found in the control SC samples were: 75°C, 78°C, and 95°C for mice; 82°C, 90°C, and 99°C for guinea-pig; and 84°C, 92°C, 99°C for rabbit (**Fig.1, Fig.2 & Fig.3**, respectively). The first two peaks of each sample were due to the melting of lipids and the third peak was due to the denaturation of the α-protein (3). However, upon treatment with sodium deoxycholate aided Raloxifene nano-transfersomes, most of the peaks were shifted towards the lower melting points and some of them were disappeared. In case of guinea-pig SC, when treated with transfersomes, the melting was observed for two peaks only and they were shifted to 64°C and 94.5°C. For mice SC, the gross melting peak was observed at 75.5°C. In case of rabbit SC, only one gross peak was observed at 93°C. In all three cases, the peaks were shifted towards the lower melting point which indicate that the extraction of the lipid takes place due to the disruption of intercellular lipid lamellar structure when nano-transfersomes are applied to the SC and enhances the skin permeation (4).

Fig.1

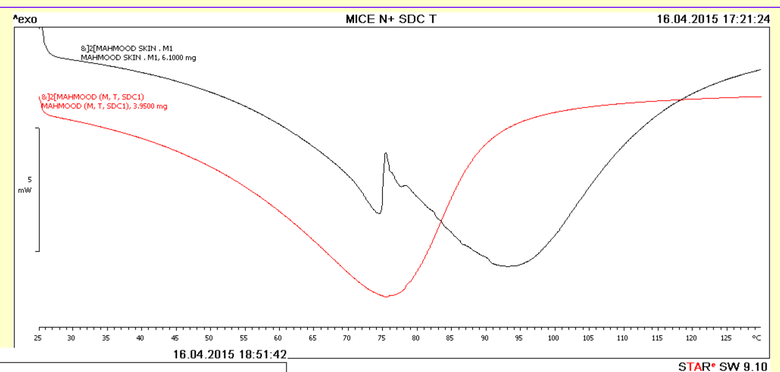


Fig.2

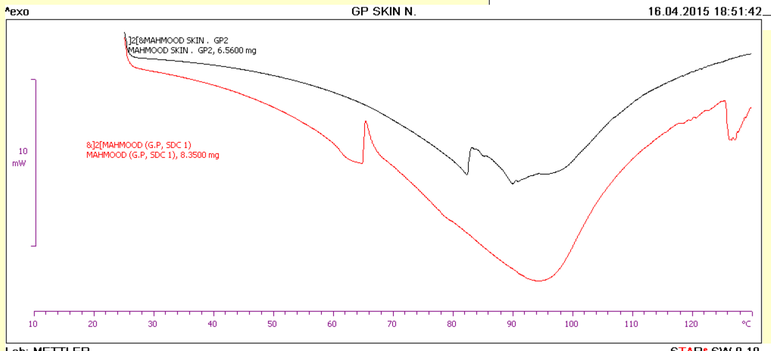
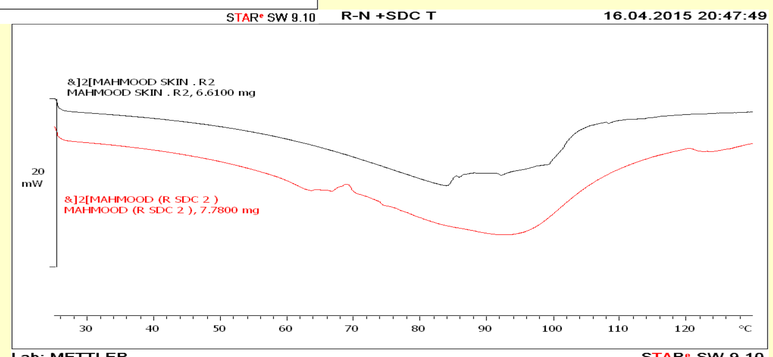


Fig.3



CONCLUSION

These findings confirmed disruption of lipid bi-layer and denaturation of keratin in the SC layer of the investigated skin samples by nano-transfersomes with sodium deoxycholate. It also established the role of sodium deoxycholate in transdermal permeation of drug loaded nano-transfersomes formulation.

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