P-066 **Hexosomes: a tool for transdermal delivery of poorly water soluble drug**

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INTRODUCTION

Intact skin has long been thought off as an interesting but very restricting port of entry into the body. Transdermal route though having number of advantages over other routes, still remains practically impermeable to various compounds (Bouwstra 2003). Paclitaxel being very effective drug is widely used in the treatment of variety of carcinomas. The most common problem with this drug is its solubility and dose related toxicities. The available vehicle is highly irritating causes variety of sensitivity reactions.

Liposomes were introduced in early 80s, to overcome the barrier nature of skin and control drug delivery has gained a lot of interest (Mezei 1980, Touitou 1994) but still there is a need of some better carrier. Here, is the application of monoglyceride based drug delivery systems (Hexosomes, Cubosomes), which have got excellent solubilizing properties and controlled release properties. We utilized hexosomes as drug delivery vehicle for paclitaxel because it offers systemic administration of drugs at very lower dose utilizing transdermal route.

MATERIALS AND METHODS

Monoolein, Pluronic F-127, ethanol and deionized water has been utilized in the preparation of hexosomes. Hexosomes, loaded with Paclitaxel were prepared by the method reported by Swarnakar *et al.* (Swarnakar 2007) and characterized for particle size and distribution, particle anisotropy, morphology and internal structure using dynamic light scattering method, cross polarizer microscopy, negative staining transmission electron microscopy (TEM) and small angle x-ray scattering (SAXS) respectively.

Prepared formulation was studied for its transdermal potential across rat skin using modified Franz diffusion cell. The cumulative amount of drug permeated per unit area was plotted as a function of time while the steady-state permeation rate (Jss) and lag time (LT, h) were calculated from the slope and X-intercept of the linear portion, respectively. To understand the probable mechanism of hexosomes penetration across intact skin, FTIR technique has been employed (Panchagnula, 2005).

RESULTS AND DISCUSSION

The entrapment efficiency of the system was 98 % and the mean paticle diameter was 152 nm. The developed system was characterized using cross polarizer microscopy revealed its anisotropic nature (Fig. 1). Further, hexagonal morphology of prepared formulation was clearly visible in TEM photomicrographs (Fig. 2). The SAXS analysis of drug loaded (Fig. 3) hexosomes revealed H_{II} phase which was characterized by three strong X-ray diffraction peaks with spacing ratios of $\sqrt{1}$: $\sqrt{3}$: $\sqrt{4}$.

Heavily drug loaded system delivered appreciable quantity of drug, thereby increasing the amount of free drug available for diffusion into deeper layer of skin. Thus gel-hexosomal formulation showed increased flux (4.7 ± 0.1 µg/ cm^2/ h) and decreased lag time (1.6 h) as compared to paclitaxel loaded gel (0.9 ± 0.1 µg/ cm^2/ h, lag time 2.3 h) and plain paclitaxel suspension (1.1 ± 0.1 µg/ cm^2/ h, 2.4 h)). The observed flux was 5 fold higher than that of drug loaded gel and nearly 4 fold higher than plain drug suspension (Fig. 4).

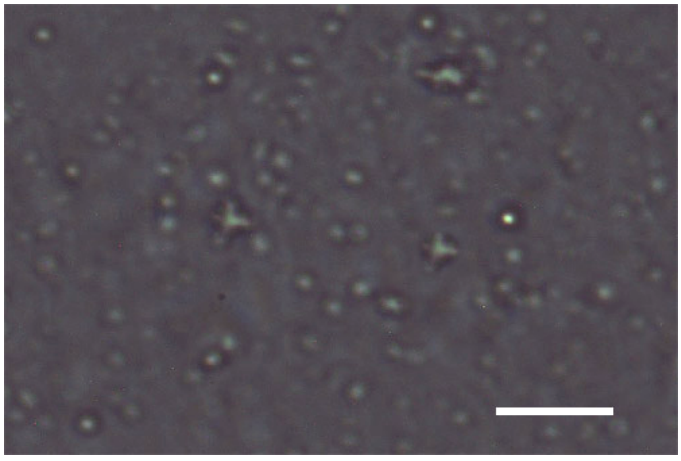

Figure 1: CPLM of Hexosomes

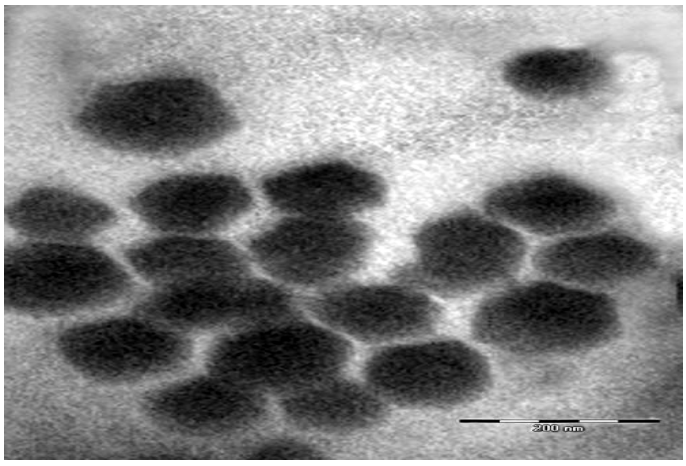

Figure 2: TEM of Hexosomes

During FTIR studies, dried skin when extracted with ethanol shows a reduction of C-H stretching frequency suggesting that C-H bands correspond to long chain lipids present in the skin (Fig. 5B). After incubation of skin with hexosomal dispersion, stretching vibrations were broadened but no significant shift was observed. It was shown that areas were decreased with 4 h treatment with Hexosomal dispersion (Fig. 5C) when compared to intact tissue (Fig. 5A). So, FTIR analysis suggests that hexosomes exerts its penetration enhancer effect by extracting the lipids present in the skin.

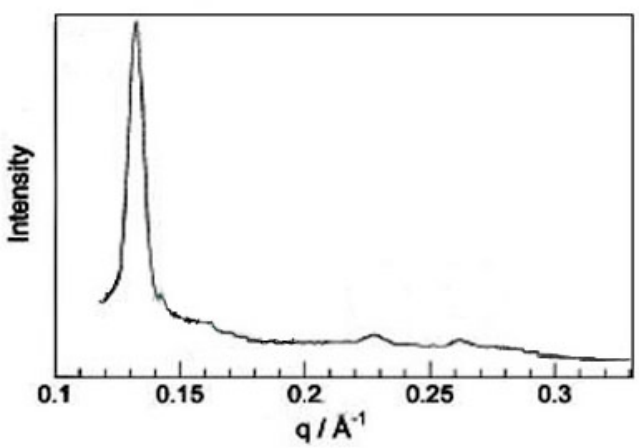

Figure 3: SAXS of Hexosomes

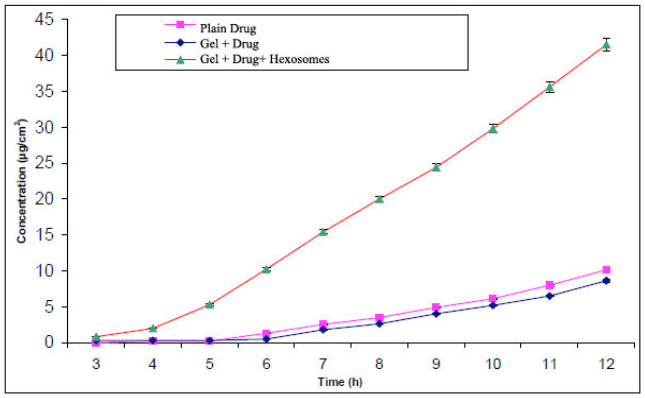

Figure 4: Drug release profile

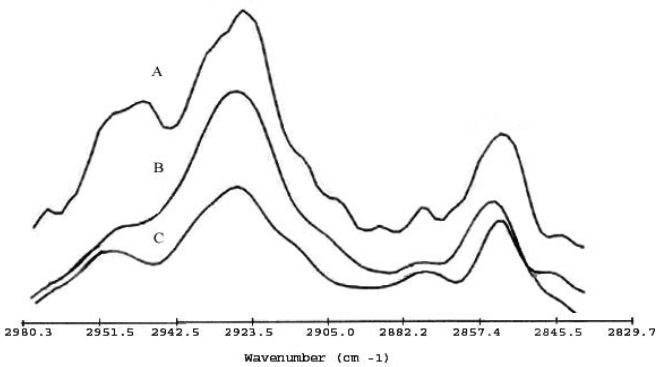

Figure 5: FTIR of skin

CONCLUSION

The present study suggests the potential of hexosomes as innovative drug delivery systems for transdermal administration paclitaxel. The extent of skin penetration and extraction of lipids of skin as suggested herein may be employed as alternative approach beyond systemic administration. Further, *in-vivo* studies are necessary to elicit the exact utility of these systems in drug delivery.

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