P-020 **Biocompatible Nanostructured lipid carriers (NLCs) for effective protection of skin against ultra violet radiation**

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INTRODUCTION

Sun rays can produce harmful effects in the skin, at short-term exposure, like erythema, langerhans cells depletion and at wide-term exposure, leads to photo ageing or even skin cancer. Due to the depletion in the ozone layer, research regarding protection of human body from sun rays has become a major concern. Sun-protecting substances or sunscreens are capable of protecting human skin from harmful effects of solar radiation such as aging and skin cancers. Therefore, effectiveness implies that UV filters adhere to skin like protective film. They should have a high affinity for the stratum corneum. Therefore sun-protecting preparations need to be controlled release with increased adhesiveness to surfaces with ultra fine properties. A new generation lipid nanoparticles, the NLCs produced by controlled mixing of solid lipids with spatially incompatible liquid lipids leading to special nanostructures with improved drug incorporation and release properties and also act as physical barrier for the UV rays due to their particulate characteristics (Muller et al., 2007). A major advantage of lipid nanoparticles with solid matrix is their high physical stability in these systems (Muller et al., 2002).

EXPERIMENTAL METHOD

NLCs were prepared by ethanol injection method reported by Stevens et al. (2004) for SLNs. Briefly, molar ratio of TS (Tristearin, solid lipid), OA (Oleic acid, liquid lipid) and PC (Soya lecithin) in 5:1:4. Lipids and drug (oxybenzone) were dissolved in ethanol at 50ºc and added drop wise in aqueous surfactant of 1% tween 80 solution at 50ºc with a continuous stirring (4000 rpm) for 45 min. Lipid dispersion was sonicated for 3 min to obtain oxybenzone loaded nanostructured lipid carriers. NLCs were characterized for particle size, shape, zeta potential, poly dispersity index, entrapment efficiency and *in vitro* drug release. *In-vitro* sunscreen efficacy test was performed for drug loaded NLCs and cream base using aqueous solution of sodium nitroprusside. *In-vivo* sun protecting factor (SPF) was measured for different formulation using albino rats (Wistar strain) 8 to 10 week of age. The SPF was determined for each individual by the following formula:

$$SPF = MED_{\text{Protected Skin}}/MED_{\text{Unprotected Skin}}$$

The fluorescence microscopy was performed to confirm the deposition/ retention pattern of lipid nanoparticles. Rhodamine 6G was used as florescent marker and was encapsulated into NLCs. These formulations were applied topically to albino rats.

RESULTS AND DISCUSSION

Physically stable NLCs with a narrow size distribution were produced by solvent injection method and successfully incorporated into the water removable cream base. The tristearin, oleic acid and soya lecithin optimized ratio exhibited a particle size of 197±5.1 nm, poly dispersity index 0.259±0.11, zeta potential -38.6±1.6 mV and maximum entrapment efficiency of 92.5±4.94%. Moreover, findings of the microscopic (scanning electron microscopy) study also suggest a slightly oval nature of NLCs (Fig. 1).

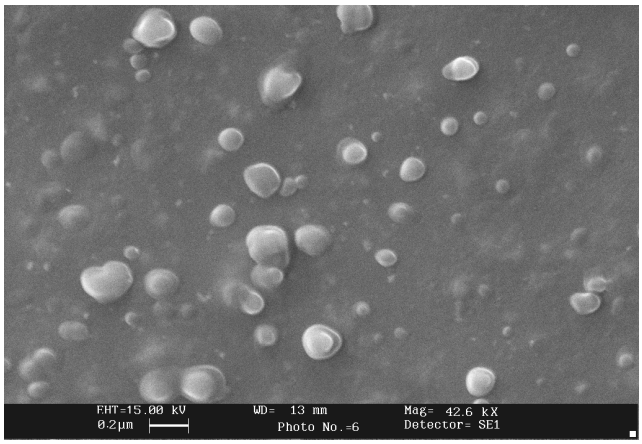

Fig.1. SEM of NLCs

In- vitro drug release study shows that the oxybenzone loaded NLCs exhibited the initial burst release and sustained release subsequently (Fig. 2).

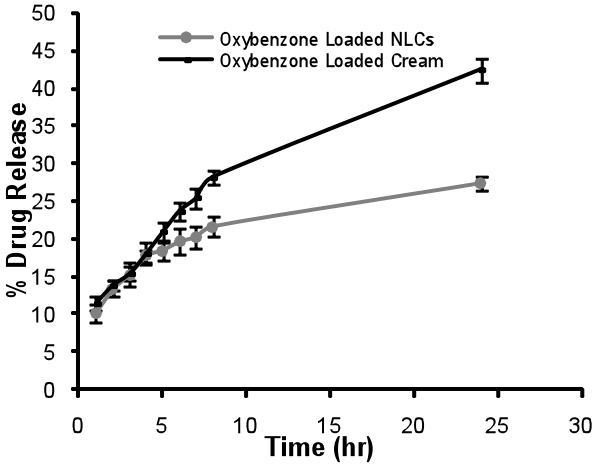

Fig. 2 *In Vitro* Drug Release

The liquid lipid enriched shell possessed soft and considerable higher solubility for oxybenzone, in which the drug was easily loaded to higher amount, and the drug could be easily released as well by the drug diffusion or the matrix erosion manners. *In-vitro* sunscreen efficacy test shows that oxybenzone loaded NLCs give higher protection than NLC, and oxybenzone loaded cream base in a following manner (Cnd>Cn>Cd>Cc). *In-vivo* sun protecting factor (SPF) shows oxybenzone loaded NLCs (Cnd) gives higher protection (Cnd>Cn>Cd>Cc) (Fig. 3).

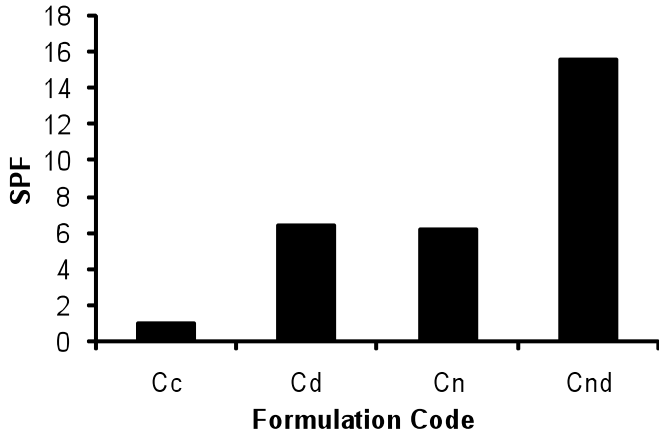

Fig. 3 *In Vivo* Sun Protection Factor

In-vitro sunscreen efficacy and *in-vivo* SPF test shows that NLCs formulation gives higher efficacy for UV blocking which potentiate the effect of oxybenzone. The photomicrograph shows the distribution of marker in the different layers (Fig. 4). As compared to conventional water removable cream base, NLC appear to reduce dye penetration into rat skin.

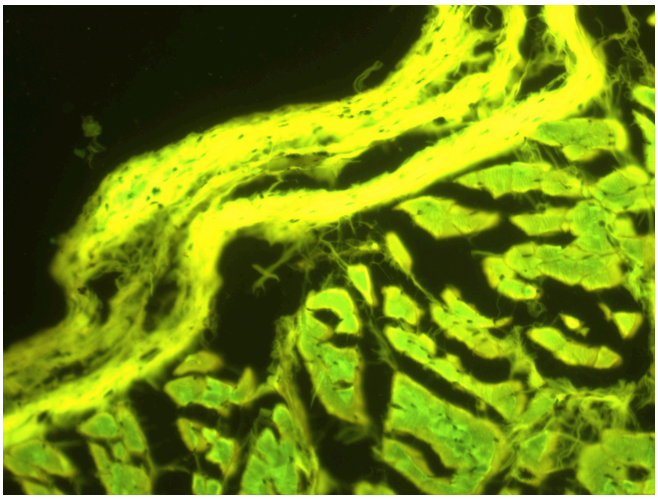

Fig. 4 Fluorescence microscopy after topical application of NLCs

Table: 1. Optimization of NLCs for lipid ratio

Formulation	TS:OA:PC	Average Particle Size (nm)	Zeta Potential (mV)	Poly Dispersity Index	% Entrapment Efficiency
NLC-A	5.5:0.5:4	176±2.3	-38.3±3.1	0.324±0.25	85.3±3.73
NLC-B*	**5:1:4**	**197±5.1**	**-38.6±1.6**	**0.259±0.11**	**92.5±4.94**
NLC-C	4.5:1.5:4	524±3.4	-36.8±2.8	0.273±0.32	95.2±3.67
NLC-D	4:2:4	100±2.8	-31.6±3.5	0.460±0.41	78.4±2.39

Mean ± SD n± 3

CONCLUSION

The advantage of this method is the instantaneous and reproducible formation of small nanoparticles exhibiting high percentage entrapment efficiency. The encapsulation of sunscreen agent in NLCs also provided the advantages of overcoming skin irritancy problem. After entrapment of oxybenzone in NLCs, it could be easily incorporated in to cream base. The topical application of cream formulation containing oxybenzone loaded NLCs may be more efficient in protecting against UV induced erythema probably due to the uniform thin film formation over the skin which itself act as a physical barrier toward the UV radiations. In conclusion, the results of this study emphasize the potential of NLCs as a new topical drug delivery system for enhancing the sunscreening efficacy of oxybenzone.

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