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<b>Abstract title</b>	FORMULATION AND OPTIMIZATION OF RALOXIFENE LOADED NANOTRANSFERSOMES BY RESPONSE SURFACE METHODOLOGY FOR TRANSDERMAL DRUG DELIVERY
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<b>Topic</b>	Formulation Design and Pharmaceutical Technology
<b>Abstract text</b>	

Raloxifene HCl loaded transfersomes were fabricated, optimized, and characterized as carrier for transdermal delivery to overcome the poor bioavailability issue with the drug. Response surface methodology (RSM) was applied for optimization of the formulation with Box-Behnken experimental design. Phospholipid PC90G (A), sodium deoxycholate (SDC) (B) and sonication time (C), each at three levels, were selected as independent variables while entrapment efficiency (EE%) ( $Y_1$ ), vesicle size ( $Y_2$ ), and transdermal flux ( $Y_3$ ) were the response variables. The optimized formulation was further characterized for vesicular size distribution, shape, surface morphology, and zeta-potential. Response variables data were analyzed by Design expert® software and the best model for all three response variables was found to be quadratic. Formulation No13 with composition of 300mg PC90G (A), 35mg SDC (B) and 15min sonication time (C) was predicted as the optimized formulation. The optimized formulation resulted a particle size of  $134 \pm 9.0$  nm with  $91 \pm 4.9\%$  EE%,  $6.5 \pm 1.1 \mu\text{g}/\text{cm}^2/\text{h}$  transdermal flux, and  $-2.61 \pm 0.5$  mV zeta potential. Transmission electron microscopy, scanning electron microscopy, and dynamic light scattering study defined transfersomes as spherical, unilamellar structures with a homogenous distribution and low polydispersity index ( $0.080 \pm 0.021$ ). Transfersomal formulation proved significantly superior in terms of amount of drug permeated and deposited in the skin, with an enhancement ratio of  $6.25 \pm 1.5$  and  $9.25 \pm 2.4$  when compared with conventional liposomes and ethanolic phosphate buffer solution of the drug respectively. Confocal scanning laser microscopy proved an enhanced permeation of coumarin-6 loaded transfersomes to the deeper layers of the skin ( $160 \mu\text{m}$ ) as compared to the rigid liposomes ( $60 \mu\text{m}$ ). These *in-vitro* findings proved that raloxifene HCl loaded transfersomal formulation could be a superior alternative to oral delivery of the drug.

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