

## Resveratrol-Phospholipid Complex for Sustained Delivery of Resveratrol via the Skin for the Treatment of Inflammatory Diseases

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**Abstract :** The poor oral bioavailability of resveratrol (RSV) due to presystemic metabolism can be avoided via dermal route of administration. The hydrophilic-lipophilic nature of resveratrol-phospholipid complex (RSVPs) favors the delivery of resveratrol via the skin. The RSVPs embedded polymeric patch with moderate adhesiveness was developed for dermal application for sustained anti-inflammatory effect. The prepared patches were evaluated for various physicochemical properties, surface morphology by SEM, TEM, and compatibility of patch components by FT-IR and DSC studies. The dermal flux of the optimized patch formulation was found to be at  $4.28 \pm 0.48$  mg/cm<sup>2</sup>/24 h. The analysis of skin extract after permeation study revealed the presence of resveratrol, which confirmed the localization of RSVPs in the skin. The stability of RSVPs in the polymeric patch and the physiologic environment was confirmed by FE-SEM studies on the patches after drug release and skin permeation studies. The RSVPs particles released from the polymer matrix maintaining the structural integrity and permeate the keratinized horny layer of skin. The optimized patch formulation showed sustained anti-inflammatory effect (84.10% inhibition of inflammation at 24 h) in carrageenan-induced rat paw edema model compared to marketed diclofenac sodium gel (39.58% inhibition of inflammation at 24 h). The CLSM study confirmed the localization of RSVPs for a longer period, thus enabling drug targeting to the dermis for sustained anti-inflammatory effect. Histological studies with phase contrast trinocular microscope suggested no alteration of skin integrity and no evidence of the presence of inflammatory cells after exposure to the permeants. The patch was found to be safe for skin application as evaluated by Draize method for skin irritation scoring in a rabbit model. These results suggest the therapeutic efficacy of the developed patch in both acute and chronic inflammatory diseases.

**Keywords :** resveratrol-phospholipid complex, skin delivery, sustained anti-inflammatory effect, inflammatory diseases, dermal patch

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