

## DEVELOPMENT OF NEW TOPICAL FORMULATIONS CONTAINING 1% ATORVASTATIN FOR THE TREATMENT OF PRESSURE ULCERS

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**Purpose:** Pressure ulcers are a common problem between elderly patients in many clinical settings, especially for those in intensive care unit (ICU) and with chronic comorbidities as diabetes, vascular and neurological disease. Wound healing is a complex organized process involving soluble mediators, resident cells, corpusculated blood components and extracellular matrix (ECM). Extrinsic and intrinsic factors may impair healing, like prolonged immobility, ischemia due to it, malnutrition, infection, immunosuppression, dryness of skin, pain insensitivity etc. Current treatments include a multidisciplinary pathway ranging from surgery to medical management, depending also on the wound type based on an international accepted evaluation scale. Recently it has been demonstrated that topical application of 1% atorvastatin ointment for 14 days can lead to complete healing: this could be due to statins' pleiotropic effects which comprises increase in VEGF expression, antiinflammatory, immunomodulatory and antibacterial activity(1). For such reasons the aim of this work was the development of new topical formulations containing 1% atorvastatin.

**Methods:** Atorvastatin calcium (Teva Pharm. Ind. Ltd.) was characterized by DSC (Mettler Toledo) to check its thermal behaviour, to define its melting point and to confirm its crystalline physical state (polimorphous VIII). Furthermore it was investigated API's solubility in different skin compatible solvents to find the excipient, or mixture, which could best solubilize it. Based on solubility data, the drug was then dispersed in 4 new formulations: O/W cream, PEG ointment, Emulgel and Hydrogel. These preparations were finally tested for their rheological (Rotovisco RV20) and *in vitro* release performances (USP Apparatus 2), all compared with reference ointment.

**Results:** Atorvastatin calcium it has been found to be best soluble in PEG 400, Transcutol HP (Gattefossé) and in propylene glycol; all formulations developed were better than reference ointment in terms of rheology (patient compliance) and in terms of *in vitro* release. In particular PEG ointment and Emulgel showed the best drug availability, meanwhile Emulgel had the best dynamic viscosity properties.

**Conclusions:** Formulations developed showed promising results and should be taken into account in future RCT in the treatment of pressure ulcers, especially PEG ointment for its exudate absorption skill and Hydrogel/Emulgel for autolytic debridement and moistening effects.

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(1) Farsaei S, Khalili H, Farboud ES, Karimzadeh I, Beigmohammadi MT. Efficacy of Topical Atorvastatin for the Treatment of Pressure Ulcers: A Randomized Clinical Trial.

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