## Preliminary Studies on Poloxamer-Based Hydrogels with Oregano Essential Oil as Potential Topical Treatment of Cutaneous Papillomas

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Abstract: Oregano essential oil is obtained from different parts of the plant Origanum vulgare (fam. Lamiaceae) and carvacrol and thymol are primary components, widely recognized for their antimicrobial activity, as well as their antiviral and antifungal properties. Poloxamers are triblock copolymers (Pluronic®), formed of three non-ionic blocks with a hydrophobic polyoxypropylene central chain flanked by two polyoxyethylene hydrophilic chains. They are known for their biocompatibility, sensitivity to temperature changes (sol-to-gel transition of aqueous solution with temperature increase), but also for their amphiphilic and surface active nature determining the formation of micelles, useful for solubilization of different hydrophobic compounds such as the terpenes and terpenoids contained in essential oils. Thus, these polymers, listed in European and US Pharmacopoeia and approved by FDA, are widely used as solubilizers and gelling agents for various pharmaceutical preparations, including topical hydrogels. The aim of this study was to investigate the posibility of solubilizing oregano essential oil (OEO) in polymeric micelles using polyoxypropylene (PPO)-polyoxyethylene (PEO)-polyoxypropylene (PPO) triblock polymers to obtain semisolid systems suitable for topical application. A formulation screening was performed, using Pluronic® F-127 in concentration of 20%, Pluronic® L-31, Pluronic® L-61 and Pluronic® L-62 in concentration of 0.5%, 0.8% respectively 1% to obtain the polymeric micelles-based systems. Then, to each selected system, with or without 10% absolute ethanol, 5% or 8% OEO was added. The obtained transparent poloxamer-based hydrogels containing solubilized OEO were further evaluated for pH, rheological characteristics (flow behaviour, viscosity, consistency and spreadability), using consacrated techniques like potentiometric titration, stationary shear flow test, penetrometric method and parallel plate method. Also, in vitro release and permeation of carvacrol from the hydrogels was carried out, using vertical diffusion cells and synthetic hydrophilic membrane and porcine skin respectively. The pH values and rheological features of all tested formulations were in accordance with official requirements for semisolid cutaneous preparations. But, the formulation containing 0.8% Pluronic® L-31, 10% absolute ethanol, 8% OEO and water and the formulation with 1% Pluronic® L-31, 5% OEO and water, produced the highest cumulative amounts of carvacrol released/permeated through the membrane. The present study demonstrated that oregano essential oil can be successfully solubilized in the investigated poloxamer-based hydrogels. These systems can be further investigated as potential topical therapy for cutaneous papillomas. Funding: This research was funded by Project PN-III-P1-1.1-TE2019-0130, Contract number TE47, Romania.

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