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**ePoster Viewing**

**Mechanisms of action, preclinical data & pharmacology of antibacterial agents**

**Development and sequential analysis of a new multi-agent, anti-acne formulation based on plant-derived antimicrobial and anti-inflammatory compounds**

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**Background:** The antibacterial and anti-inflammatory potential of plant-derived compounds have been reported in many studies. Emerging evidence indicates that plant-derived essential oils and/or their major compounds may represent a plausible alternative treatment for acne, a prevalent skin disorder in both adolescent and adult population. Therefore, the purpose of this study was developing and sequential analysis of the antimicrobial activity of a new multi-agent, synergic formulation, based on plant-derived antimicrobial compounds (i.e., eugenol, beta-pinene, eucalyptol, limonene) and anti-inflammatory agents (salicylic acid) for potential use in the topic treatment of acne and other skin infections. The synergism between the natural compounds and conventional preserving system, 2-phenoxyethanol : potassium sorbate was also assessed.

**Material/methods:** The antimicrobial qualitative screening was carried out against standardized microbial strains recommended by the European Pharmacopoeia (8th ed.) for the microbiological quality assessment of topical drug formulations, i.e.: *S. aureus* ATCC 6538, *P. aeruginosa* ATCC 27853 and *C. albicans* ATCC 10231. Quantitative analysis was performed by the serial microdilution technique. The fractional inhibitory concentrations (FIC) and index (FICI), were calculated based on the MIC results, using specific formula, for determining the possible synergism of action between the tested compounds. The flow cytometry assay was carried out in order to evaluate the possible mechanism of action of the tested compounds, as well as of their mixtures with the conventional preserving system 2-phenoxyethanol : potassium sorbate – mixture 1, or with salicylic acid – mixture 2. The tested concentrations for the flow cytometry assay were MIC and MIC/ 2. The antimicrobial combinations were included in a cream base formulation.

**Results:** The optimal antimicrobial combinations selected in this study were: eugenol:  $\beta$ -pinene: salicylic acid and eugenol:  $\beta$ -pinene: 2-phenoxyethanol: potassium sorbate. The tested mixtures revealed FICI values in the range of 0.5-0.75, demonstrating a partial antimicrobial synergism. The possible mechanisms of action revealed by flow cytometry were cellular coatings permeabilization and

inhibition of efflux pumps activity. The cream base formulation demonstrated thermodynamic stability and optimum microbiological characteristics.

**Conclusions:** The complex algorithm proposed in this study allowed the in vitro selection of natural active compounds for optimized combinations with antimicrobial activity, with applications in cosmetic and pharmaceutical industries.