

## Importance of Stable, Efficient and Safer (Nano-) Emulsions for Topical Application: Case of a New Promising Cosmetic Formulation containing a Grape Extract against Premature Skin Aging

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Many innovative cosmetics are nowadays based on the concomitant use of ingenious materials (e.g. conventional or innovative emulsions, nanoparticles for deeper skin penetration) and plant extracts, encapsulated in them, exerting strong anti-oxidant properties enough to prevent premature skin aging and/or whitening properties, thereby capable of satisfying populations with physiological or pathological skin pigmentation [1-4]. However, the high cost related to the design and development of such products as well physical-chemical stability issues encountered in most of the considered "final products" represent few of the most important limitations for safer efficacy in translational medicine [5].

Emulsion of water-in-oil type (W/O type) is generally and increasingly used in cosmetics for dry skin treatment [6]. Emulsion (including macro-, micro- and nano-) is a dispersed colloid two-phase system of matter, stabilized by an emulsifying agent (e.g. dimethicone), which is constituted of small globules/droplets of liquid (e.g. paraffin oil) known as dispersed phase, and assumed to be statistically distributed in another immiscible (i.e. non-mixable or unblendable) solvent/liquid matrix of the continuous phase (e.g. water), called dispersion medium [7]. The emulsifying agent possesses hydrophilic and hydrophobic groups adsorbed at the interphase of water and oil, and reduces the interfacial tension. Different methods for formulating an emulsion are available and include dry gum, wet gum, phase inversion, or membrane emulsification strategies [8].

Recently, we pioneered a stable cream of water-in-oil (W/O) type emulsion for topical application which contained 'Muscat hamburg' seed extract, and could prevent premature skin aging and other skin conditions (e.g. hyperpigmentation, acne) [3-4]. M. hamburg is a blue-black table grape cultivar that belongs to *Vitis vinifera* (Family: Vitaceae), a grapevine crop species which comprises about 60 inter-fertile wild *Vitis* varieties distributed in Asia, North America and Europe, under subtropical, Mediterranean and continental-temperature climatic conditions [9].

Importantly, M. hamburg black grape extracts contain one of the greatest amount of polyphenolic compounds [10], including flavonoids and stilbenoids (e.g. resveratrol), are known to possess potent antioxidant activity, as confirmed by our DPPH assay (3). Natural phyto-antioxidants, including phytophenols and carotenoids, are well-known contributors in the inhibition or prevention of harmful effects of oxidative stress by acting as free radical scavengers or promoters of enzymatic-based anti-oxidation, subsequently delaying the skin ageing process and preventing other pathologies [1-2, 11-14].

In our experimental conditions, the W/O cream developed as a carrier for this active ingredient, was found to be overall stable for 21 days and is considered as satisfactory skin care product when applied frequently and regularly in individuals.

From our in-vitro studies extended to 12 weeks [3], we compared the effects of the active formulation containing 2% of M. hamburg black grape seed extract to the placebo ("base") (3). We showed (i) unchanged organoleptic properties in terms of appearance, color and odor ( $p > 0.05$ ); (ii) unchanged properties after centrifugation, phase separation, and in terms of electrical conductivity, liquefaction, or viscosity ( $p > 0.05$ ); (iii) a remaining acceptable dermal pH ( $p > 0.05$ ).

From our in-vivo studies involving the enrollment of a relatively large number ( $n=110$ ) of young and healthy male individuals enrolled in a course period of 8 weeks [4], we reported the effects of an occlusive patch test, a non-invasive procedure containing either the active formulation or the base simultaneously applied twice a day on both human cheeks separately (4). We consequently showed overall promising results, with (i) lower melanin production ( $p < 0.05$ ) (p); (ii) better elasticity ( $p < 0.05$ ); (iii) lower sebum production ( $p < 0.05$ ); (iv) no skin reactivity/hypersensitivity (e.g. allergy, erythema) ( $p > 0.05$ ); (v) unchanged skin moisture content ( $p > 0.05$ ).

Eventually, compared to other grapes, M. hamburg grape seed extract can be considered as a great candidate for its exploitation in the development of stable cream nanoemulsions destined to improve the skin appearance safely.

### Conflict of Interest

None

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