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## NEW TRENDS IN TOPICAL PRODUCT FORMULATION: THE "BIO-LOGICAL FORMULATIONS"

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Human *stratum corneum* lipids organisation mimics a skin care emulsion: its complex molecular structure is composed of an hydrophilic phase stabilized in a lipophilic continuous phase. Nowadays, topical products composition is very far away from the "natural skin composition": petroleum derivatives, cross linked acrylate polymers, ethylene oxide based surfactants, formaldehyde donors... are largely and frequently used and often responsible of irritations or allergies. In order to enhance the activity of topical products and improve their local tolerance, one of the current galenical challenges is the "Bio-Logical" formulation giving a new generation of skin care formulations.

Existing galenical forms for topical products are usually composed of one or two phases (three phases for multiphasic emulsions and dispersions). A classification according to the number of the non-miscible phases can be proposed (monophasic or multiphasic products), taking into account the external phase (water or oil).

A topical product is composed of galenical compounds (excipient components) as well as "active ingredients". Excipient components provide cosmetic qualities to the product (texture, comfort, skin after-feel), and can hide certain trade-off related to the use of some active ingredients (colour, odour, texture...). These ingredients are not active biologically, but are necessary for the product's stability (especially for emulsions), or used to modify viscosity, prevent microbiological contamination and/or a physico-chemical degradation (i.e. fatty chains oxidation). More generally, these ingredients are used to enhance the organoleptic qualities of the product. On the other hand, they can compromise local skin tolerance: such is the case with certain preservatives, fragrances, sunscreens and colour additives. **They have no biological activity/benefit for the skin: they are useful "in the packaging", useless for the skin.**

Active ingredients provide the product with a specific activity (moisturizing, sebum control, photo-protection, soothing...). They do not generally improve the texture and in most cases reduce product stability. The biological activities (if sufficient dosages are used) are Moisturizing (superficial epidermal layers), Healing (wound healing/anti-ageing), Antimicrobial (antiseptic), Soothing (anti-inflammatory/free-radical scavenging), Keratolytic/Keratoplastic, Sebum control or Photo-protection. Mostly, they modify the product texture, colour and odour, and can be incompatible with the other ingredients (excipient components). **Active ingredients are useful for the skin but not for the product's physico-chemical characteristics and stability!**

**There is therefore a duality, in a topical formulation's development, between ingredients with a galenical function and those with a biological one.**

**In order to enhance the activity of topical products and improve their local tolerance, one of the current galenical challenges is the "Bio-Logical" formulation.**

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## **Towards "Bio - Logical" formulations**

The "Bio-Logical" formulation concept consists in reducing (and if possible removing) galenical ingredients with no use for the skin (preservatives, surfactants, fragrances, colour additives), and replacing them with ingredients:

- with both functions: galenical and biological actions
- bio-compatible (respect of the skin organisation and structure)
- bio-mimetic (copy of skin components molecular structure)

Preservatives stop micro-organism proliferation in the product (bacteria, yeast, fungi) during the manufacturing process and throughout the product's life (including during use). Preservatives can be responsible for discomfort and cause irritations or allergies. Removing preservatives from topical products is a difficult challenge. It is however possible to reduce their concentration using components potentializing their activity, such as Polyols and sugars (osmotic effect), Ethanol (2 - 4%), Sodium Lactate, Salts: Copper and Zinc Sulfates, Amino Acids (glycin), C8, C11 up to C12 Fatty acid derivatives and Antimicrobial Peptides.

Fragrances are used either to mask bad odours or enhance pleasure when using the product, but they can create allergy problems. It is recommended to reduce their concentration or substitute them with non-allergenic ingredients (plant extracts), natural odour absorbers or neutralisers, or food industry flavours.

Sunscreens are chemicals UV light absorbers. Commonly used ingredients are benzophenone, camphor, triazone and cinnamate derivatives. They can generate phototoxic reactions or be photosensitizing. The tendency to over-use them in skin care products increases the risk of sensitisation and can generate discomfort (especially in the eye area). Therefore, the objective is to use them when necessary (in sun creams) and reduce their concentration (adding mineral screens like titanium and zinc dioxide) or use natural ingredients with sunscreen activity or encapsulated filters (to keep filters on the skin surface, enhancing the Skin Protecting Factor).

Surfactants are amphiphilic molecules (compatible with oil and aqueous phases), stabilising oil in water (O/W) and water in oil (W/O) emulsions. These molecules are composed of lipophilic (apolar) and hydrophilic (polar) parts. A favoured method is to use bio-compatible Sugar Esters, or better "bio-mimetic", surfactants such as Lecithins and Glycerol Esters, naturally present in the skin (*stratum corneum*).

Common fatty ingredients used for the formulation of topical products are synthetic oils (that may present traces of catalysts, solvents...), mineral oils (extracted from petroleum with potential impurities such as toluene, xylene, benzene...), Lanoline (extracted from sheep wool with potential traces of insecticides...). It is therefore recommended to use vegetable oils or derivatives with bio-mimetic structures: C8 to C24 fatty acids (preferentially C12-C18), Triglycerides or ester derivatives.

Chemical gelling agents are often used in various galenical forms: they have different properties (including emulsification), are stable at extreme pH values, give light textures and crystal gels. Commonly used polymers are Acrylic derivatives (Carbomers) and Polyurethane; unfortunately they can induce intolerance reactions (especially around the eyes and on sensitive skin). When possible, use of natural polymers such as Carouba, Guar and Xanthane gums or better bio-mimetic polymers such as Sodium Hyaluronate and ADN salts can improve topical products local tolerance.

Free-radical scavengers and anti-oxidants generally used in topical formulations are BHA (Butyl Hydroxy Anisol), BHT (Butyl Hydroxy Toluene), Propyl Gallate, Sodium Metabisulfite...; they can now be favourably substituted by bio-compatible vegetable extracts such as Rosemary, Tea, Sophora Japonica, bio-mimetic Tocopherols or Ascorbic acid derivatives.

Demineralised water, the main constituent of all topical products..., is a hypotonic medium. The use of isotonic formulations or cellular culture medium can also improve the local tolerance.

But "Bio-Logical" formulation remains a difficult experience: bio-compatible molecules, mainly used in the food industry, are difficult to use for topical product formulations (better for sauces and desserts...). Bio-mimetic equivalents to existing synthetic ingredients are rare (oils, thickeners, preservatives) or do not exist at the moment (sunscreens, fragrances). Isotonic solutions modify product texture and stability and cells culture medium modify odour and stability, and make very difficult the preservation from micro-organisms contamination.

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Some companies have already faced this galenical challenge: Etat Pur<sup>®</sup> containing 98% of bio-compatible and/or bio-mimetic ingredients with medium for cellular culture is one of the pioneers mark in this domain.