Naturally emulsifying with biomimetic clinical benefits

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Choosing the right emulsifier remains a decision formulation chemists face at the onset of each project. The natural origin, global regulatory acceptance, functionality, robustness and compatibility with skin structures are all parameters that need to be carefully analysed when selecting an emulsifier. In addition, the impact of the emulsifier on the sensorial properties of the final formulation remains a key factor. This parameter often determines the acceptance of the cosmetic product by end consumers. Even though oils, emollients and thickeners may influence the emulsion characteristics, emulsifiers remain the cornerstone of a formulations aesthetics and functionality.

Through years of research, Innovacos has developed an expertise in polyglycerol technology. This knowhow led to a new generation of polyglycerol-based emulsifiers known as PolyAqul™. The first member of this family is PolyAqul-2W; an all naturally derived O/W emulsifying technology that was assigned the Ecocert and Cosmos certifications. It is made of a skilled combination of the components polyglyceryl-2 stearate, glyceryl stearate and stearyl alcohol. It is non-ionic and has self-emulsifying properties meaning it works independently of the HLB system and can create stable emulsions on its own without the need of co-emulsifiers or co-factors. Polyglycerol-based emulsifiers are not new in the field of cosmetics. However, Innovacos succeeded to reinvent the polyglycerol technology by fine tuning its chemistry. PolyAqul-2W (now referred to as ‘the polyglycerol-based emulsifier’) is manufactured using highly purified building blocks such as diglycerol and stearic acid. The glycerol moiety and the fatty acid are linked together in a solvent-free system while respecting a very precise molecular stoichiometry. Such a close control of the glyceryl-OH group density allows for a consistent polarity of the emulsifier (Fig 1). This becomes important for uniform emulsifying properties between each lot produced. Furthermore, the reaction is controlled to avoid the presence of free diglycerol to maintain optimal sensorial properties in the final emulsion. The technology of the polyglycerol-based emulsifier (patent pending) thus emerges from a unique knowledge of the polyglycerol molecule combined with a meticulously controlled manufacturing process.

Figure 1: Schematic representation of polyglyceryl-2 stearate. Stearic acid (C18) forms the lipophilic tail interacting with the oil phase and the polyglyceryl-2 moiety creates the hydrophilic head of the molecule interacting with the water phase.

Figure 2: Proposed molecular configuration of the components of PolyAqul-2W to create stable O/W emulsions.
Once each component of the polyglycerol-based emulsifier is obtained, they are assembled in a way to favour molecular interactions. We take advantage of the presence of oxygen molecules ‘O’ (present on polyglyceryl-2 and glyceryl stearate) and hydroxyl groups ‘OH’ (present on stearyl alcohol) that can attract each other through hydrogen electrostatic interactions. A lamellar-like structure can thus be formed in which molecular poles are spatially oriented. In this manner, the hydrophilic heads can interact with the external water phase while the lipophilic tails would merge with the oil thereby maximising the O/W emulsion (Fig 2).

This lamellar structure most likely translates into a highly organised system in the emulsion particularly at the oil/water interface. This is evidenced by the observation of liquid crystals at the periphery of oil droplets in a polyglycerol-based emulsifier emulsion (Fig 3). In such an emulsion, liquid crystals (typically lyotrophic) self-organise during the homogenisation and cooling phase and are indicative of a molecular orientational order as depicted in Figure 2. Liquid crystal structures possess the dual property of a liquid (fluidity) and that of a solid (structure). It is the latter property that endows liquid crystals with the birefringence characteristic – the ability to bend polarised light. The seemingly discrete liquid crystal structures as seen in Figure 3b are not limited to the immediate vicinity of the oil droplets but would also extend – though in a lesser organised manner – in the continuous water phase.

This creates a sort of three-dimensional crystalline meshwork in the emulsion that actively contributes to the rheology and the stability of it. In turn, this would restrict the movement of oil droplets keeping them apart to prevent coalescence. In addition to impart stability to the emulsion, the fluidity and dynamism of this meshwork contributes to the sensorial properties of the formulation upon application on the skin.

**Formulation performances**

The molecularity and structural characteristics of the polyglycerol-based emulsifier make it a highly versatile emulsifier. Indeed, it can be added in concentrations between 1% and 5% in the water phase as well as in the oil phase when formulating O/W systems. Adding it to the oil phase results in a relatively higher viscosity emulsion compared to when incorporated to the water phase (Fig 4). The density of oil droplets is higher when the emulsifier is added in the oil phase. In that case, the average diameter of the oil droplets is 2.0 µm. On the contrary, incorporation of the polyglycerol-based emulsifier directly into the water phase produces a relatively lower density of oil droplets with a higher average diameter of 3.5 µm. This feature of the polyglycerol-based emulsifier is advantageous to create formulations with different viscosity levels without the addition of rheology modifiers. Yet, the polyglycerol-based emulsifier is compatible with a variety of thickeners or jellifying agents. Regarding the type of the lipid phase, the polyglycerol-based emulsifier is compatible with oils of different polarity and chemistry such as vegetable oils, esters, mineral oils and silicones. Furthermore, increasing the oil phase concentration is another way to modify the viscosity of the final emulsion. For instance, increasing the concentration of sweet almond oil from 5% to 20% brings the emulsion viscosity from 7000 to 18000 cps, respectively. Those characteristics of the polyglycerol-based emulsifier allow for the creation of emulsions with various viscosity levels and textures from sprayable lotions to rich creams and butters.

The robustness of the polyglycerol-based emulsifier was observed in different pH and electrolyte environments. Emulsions made with the emulsifier were shown to sustain a pH range between 4 to 9 after an incubation at 50°C for 30 days. Furthermore, the polyglycerol-based emulsifier tolerates the presence of monovalent or divalent electrolytes in the emulsion. For instance, the viscosity and the stability of the emulsion were not affected in the presence of up to 3% NaCl (Table 1) even after 30 days at 50°C.

The polyglycerol-based emulsifier was...
Biomimetic clinical benefits

After having characterised its emulsifying properties, we wanted to explore how the polyglycerol-based emulsifier can provide benefits to the skin especially toward the skin barrier function. The skin barrier function has two main physiological functions: preventing excessive water loss and impeding the intrusion of foreign particles such as pathogens, pollutants and allergens to viable layers of the skin. Moreover, it protects from physical insults and is involved in body thermoregulation. A weak barrier function would eventually lead to skin dryness and skin hypersensitivity. An optimal skin barrier is thus important to restrict outward and inward movements preserving skin and body homeostasis. The skin barrier function resides in the stratum corneum and is a complex histological and molecular structure that mainly rely on fully differentiated keratinocytes (called corneocytes) embedded in an intercellular lipid matrix. This arrangement is often referred to as the brick-and-mortar model. The lipid matrix consists of cholesterol, ceramides and fatty acids intermingled together. Numerous studies have been carried out with the goal to unravel the architecture of the lipid matrix of the skin barrier function. While the formation of a lamellar bilayer lipid matrix is acknowledged, several results point toward the co-existence of a crystalline gel and a fluid phase. Those structural characteristics are responsible for the semi-permissive water movement and protection against mechanical abrasions as well as the plasticity needed to cope with skin stretching and compression. The barrier function does not only rely on the intercellular lipid matrix of the stratum corneum but is complemented by other lipids originating from the pilosebaceous unit. Secreted triglycerides deposited at the surface of the skin are separated into glycerol and fatty acids by lipases. As mentioned above, fatty acids are an important component of the intercorneocyte lipid matrix interacting with ceramides and cholesterol. Fatty acids catalysed from skin surface triglycerides can diffuse back into the skin and intermix with the extracellular lipid matrix of the stratum corneum contributing to the skin barrier function. Furthermore, triglyceride-derived glycerol also actively participates in the skin barrier function. Topically added glycerol has been shown to restore skin barrier function and stabilise the lipid crystalline structure of the barrier extracellular lipid matrix and enhance the stratum corneum hydration. Interesteringly, the glycerol and fatty acids catalytically released from the triglycerides produced by the pilosebaceous unit bring to mind a similarity with the polyglycerol

Table 1: Electrolyte tolerance of PolyAquel-2W. The emulsifier (5%) was added in the oil phase that was subsequently emulsified with a water phase. NaCl was added in the emulsion. Viscosity was measured with a Brookfield apparatus, RVDV-I Prime, Sp 92, 10 rpm.

<table>
<thead>
<tr>
<th>% NaCl</th>
<th>Viscosity (cPs)*</th>
<th>Stability (1 month at 50°C)</th>
</tr>
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<tbody>
<tr>
<td>0 (control)</td>
<td>10 400</td>
<td>✓</td>
</tr>
<tr>
<td>0.5</td>
<td>11 200</td>
<td>✓</td>
</tr>
<tr>
<td>1.0</td>
<td>11 700</td>
<td>✓</td>
</tr>
<tr>
<td>2.0</td>
<td>11 200</td>
<td>✓</td>
</tr>
<tr>
<td>3.0</td>
<td>11 000</td>
<td>✓</td>
</tr>
</tbody>
</table>

Table 2: Comparison of PolyAquel-2W with other polyglycerol-based emulsifiers. Emulsion stability was assessed by verifying absence of phase separation after 30 days at 50°C. Viscosity was measured with a Brookfield apparatus, RVDV-I Prime, Sp 92, 10 rpm.

<table>
<thead>
<tr>
<th>Emulsifier</th>
<th>Vegetable oil</th>
<th>Viscosity (cPs)*</th>
<th>Stability (1 month at 50°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3%</td>
<td>Polyglycerol-3-Distearate</td>
<td>12%</td>
<td>3 600</td>
</tr>
<tr>
<td></td>
<td>Polyglycerol-3-Methylglucose Distearate</td>
<td></td>
<td>1 550</td>
</tr>
<tr>
<td></td>
<td>PolyAquel™-2W</td>
<td></td>
<td>6 300</td>
</tr>
<tr>
<td>5%</td>
<td>Polyglycerol-3-Distearate</td>
<td>20%</td>
<td>5 350</td>
</tr>
<tr>
<td></td>
<td>Polyglycerol-3-Methylglucose Distearate</td>
<td></td>
<td>3 250</td>
</tr>
<tr>
<td></td>
<td>PolyAquel™-2W</td>
<td></td>
<td>18 000</td>
</tr>
</tbody>
</table>

Figure 5: Clinical benefits of PolyAquel-2W. A, In the preventive effect protocol, subjects (10) were applied with a formulation made of 5% PolyAquel-2W in 95% water (hereafter referred to as a PolyAquel-2W water gel) or a control made of cetearyl alcohol, ceteareth-20 and polyacrylate as a jellifying agent (2 mg/cm²) for a period of 10 days. Twenty-four hours after the last application, TEWL was measured (Tewameter 300® - Courage+Khazaka, electronic GmBH) to obtain a baseline value. After measurement, subjects were exposed to a solar simulator (UVA/B). TEWL was again measured 24 hours after UV exposure.

B, In the repair action protocol, subjects were first exposed to UVA/B and TEWL was measured 24 hours after to obtain a reference value. Immediately after the reference measurement, subjects were applied with the water gel or the control formulation. One single application of each formulation was made. TEWL was re-assessed 30 minutes, 1 hour, 2 hours and 24 hours after formulation applications. Solar simulator exposure was done at 1.5X the minimal erythema dose. All protocols were under dermatologist supervision. *p<0.05; **p<0.01
derivatives of fatty acids present in the polyglycerol-based emulsifier. In addition to this molecular resemblance, the ability of the polyglycerol-based emulsifier to form liquid crystals extends the analogy with the skin barrier lipid matrix to a more structural level. The molecular and structural biomimicry features of the polyglycerol-based emulsifier led us to clinically verify its potential benefits on the skin barrier function challenged with UV. UV radiation is a ubiquitous skin stressor that has been shown to negatively impact the epidermal lipid synthesis and the skin barrier integrity.15,16

The polyglycerol-based emulsifier was applied topically as a water gel consisting of 5% polyglycerol-based emulsifier and 95% water. The water gel is odourless, stable and has a viscosity in the vicinity of 10,000 cps. The clinical trial was twofold and designed as both ‘preventive effect’ and ‘repair action’ protocols. In the preventive effect protocol the water gel was applied daily, for a period of 10 days, prior to UVA/B exposure. In the case of the repair action protocol, the water gel was applied, only once, 24 hours after UVA/B stress. Pre-treating the skin with the water gel significantly reduces the UVA/B-induced increase in TEWL compared to a control (Fig 5a). When applied post-UVA/B the water gel rapidly brings down TEWL (Fig 5b). There is a significant reduction of the UV-induced increase in TEWL readily 30 minutes upon water gel application. The repair action of the polyglycerol-based emulsifier water gel builds up upon time as

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**Figure 6:** Proposed model for the biomimetic action of PolyAqual-2W in maintaining and repairing the integrity of the skin barrier lipid matrix.
The proposed mechanisms of action are further supported by our clinical results showing prevention and repair of the skin barrier function integrity upon UV-induced damage. Indeed, a unique trait of PolyAqual-2W resides in its ability to improve skin barrier function homeostasis. This most likely relies on a skin biomimicry concept put forward by its molecular organization and the formation of tridimensional liquid crystal structures. Interestingly, when added in a completely anhydrous system, PolyAqual-2W generates birefringent – thus highly organized – lamellar structures (Fig 7) evocative of the bi-layer organisation of the skin barrier lipid matrix.5

The robustness and clinical efficacy of PolyAqual-2W ally with the possibility to create formulations endowed with unique properties and benefits. The availability of PolyAqual-2W to all chemists and cosmétologists is likely to open new frontiers in designing multi-functional and efficacious formulations.6

References