

Emulsions Systems for Skin Care: From Macro to Nano-Formulations

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Aging of the skin, the largest human body's organ, is a gradual process that involves both intrinsic molecules (e.g. reactive oxygen species (ROS) [1] and environmental factors (e.g. ultraviolet radiation [2,3]. During this process, the skin appearance and functions are altered (e.g. stimulated release of collagenase, elastase and hyaluronidase from the extracellular matrix (ECM)) [1]. The signs of skin aging are visible in the form of wrinkles, uneven pigment appearance and skin atrophy [2]. An aged skin will decrease the social comfort and self-confidence [4].

Topical applications of cosmetics in the form of emulsions, often used in lotions and creams (e.g. sunscreens), contribute to retrieve certain rejuvenation and delay the physio-pathological aging process, in particular due to their content in anti-oxidants (e.g. polyphenols, vitamins C and E) [5-7].

Emulsion can be defined as a dispersed system which consists of small globules of dispersed phase of liquid (e.g. internal or discontinuous phase) that are distributed into an immiscible vehicle (i.e. dispersion medium *aka* external or continuous phase) [8]. An emulsifying agent (i.e. surfactant), known to possess both hydrophilic and hydrophobic groups (Figure 1), is routinely used to stabilize the emulsion [9-11]. The surfactant adsorbed at the water and oil interface reduces the interfacial tension and aids in distribution of small globules in dispersion medium [12].

Nowadays, two types of emulsion are commonly used in cosmetics [13-15], independently of the globule size: (i) the oil-in-water (O/W) type emulsion, which is used in general cosmetic and hydrophilic drug bases; (ii) the water-in-oil (W/O) type which is used for dry skin and as emollient (e.g. moisturizing creams).

O/W emulsion system consists in an oily internal phase (up to 55%) and an aqueous external phase (Figure 2). The emulsifier agent needs to be hydrophilic in nature and may be ionic or non-ionic [16]. Conversely, W/O emulsion system consists in an aqueous internal phase (up to 45%) and an oily external phase (Figure 3). The emulsifier agent needs to be lipophilic in nature [17].

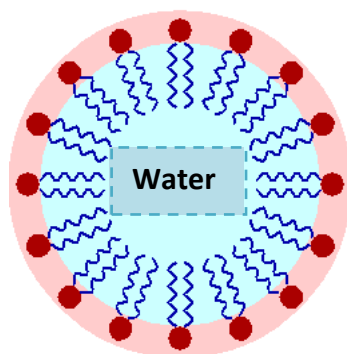


Figure 1: Schematic diagram of a micelle of oil in aqueous suspension. In this example, the surfactant molecule (e.g. emulsifier agent)' oil-soluble tails (i.e. hydrophobic groups) project into oil, while the water-soluble ends (i.e. hydrophilic groups) remain in contact with the water.

Another type of emulsion, rarely used due to its complexity in nature and instability issues, is known as multiple emulsions [18]. In such system, water-in-oil-in-water (W/O/W) emulsion (i.e. W/O plus hydrophilic emulsifier) or oil-in-water-in-oil (O/W/O) emulsion (i.e. O/W plus hydrophobic emulsifier) can be produced [12,19].

Additionally, we can distinguish three types of size-dependent

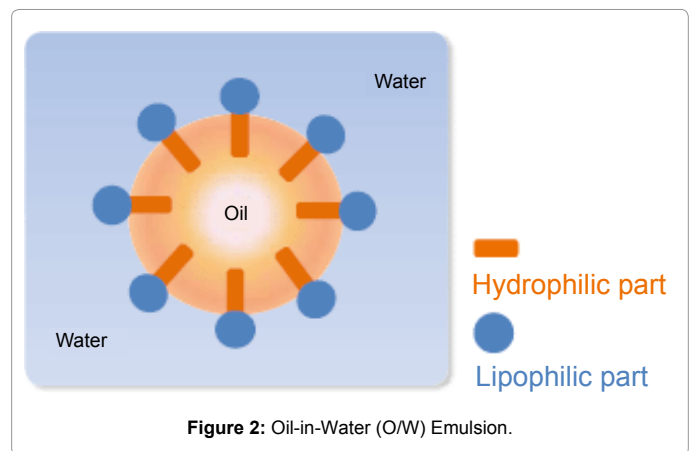


Figure 2: Oil-in-Water (O/W) Emulsion.

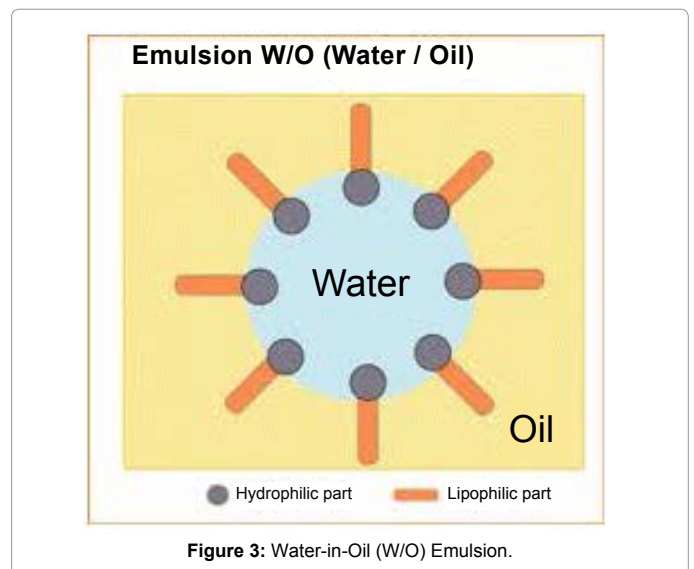


Figure 3: Water-in-Oil (W/O) Emulsion.

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emulsions: (i) the *macro-emulsions* (droplets of 1 to 100 μm of diameter), also known as conventional emulsions/colloids, are unstable in the sense that the droplets sediment or float, depending on the densities of the dispersed phase and dispersion medium, and in case they are not stabilized by adsorption of solid particles onto their surface (so-called Pickering stabilization) [8]; (ii) the *micro-emulsions* (droplets of 1-100 nm of diameter, usually between 10-50 nm), is an isotropic liquid system which, when compared to macro-emulsions, are more transparent, more uniform/homogeneous in size, less viscous, display lower interfacial tension due to use of co-surfactant (short chain alcohol) as well as higher thermodynamic stability and higher bioavailability [20-22]. In pharmaceutical care as well as in cosmetics, micro-emulsions gives the best option [8]; (iii) the *nano-emulsions* (droplets of 20 nm to 200 nm of diameter), likewise micro-emulsions, are transparent or translucent and are stable. Interestingly, they need less amount of emulsifying agent when compared to the micro-emulsions. Nano-emulsion systems have been recently used as a vehicle for drug delivery of non-steroidal anti-inflammatory drugs and steroids, targeted drug delivery of anti-cancer drugs and in cosmetics [23,24].

Eventually, the recent nano-emulsions systems constitute promising vehicles for the development of more efficient and safer theranostics and cosmetics.

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