BIO Integration

Can Nanocrystals Help Create Our Dream Cosmetics?

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Abstract

Cosmetics have evolved beyond mere skin beautifying agents. Cosmetics are now combined with active ingredients to support skin health. This evolution underpins the emergence of dream cosmetics, where innovation is continuously pursued. Indeed, nanotechnology has responded in force to the notion of dream cosmetics. Nanocrystals are expected to overcome the barriers posed by issues, such as poor solubility of bioactive agents and skin penetration. Moreover, nanocrystals exhibit multiple features, making dream cosmetics achievable. However, the clinical translation of nanocrystals is hampered by concern of negative host responses associated with long-term use. Accordingly, screening by integrated omics is needed because because multiple omics offer comprehensive nanotoxicity evaluation by identifying new molecular pathways and toxicity markers.

Keywords

Cosmetics, nanocrystal, omics, solubility, toxicity.

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Essay

Everyone needs cosmetics, which has facilitated the continuous evolution of cosmetics across time and space. The use of cosmetics dates back to 10,000 BCE when Egyptians used cosmetics to enhance beauty, elevate social status, and for spiritual purposes. Recent developments have made cosmetics more accessible to people in all social strata and genders [1]. With the rise in digitalization, consumers are increasingly conscious about beauty, essentially making cosmetics a necessity, while advances in cosmetic manufacturing technology have ensured that products meet consumer needs. Cosmetics have become a significant economic product with the worldwide cosmetic market valued at $380.2 billion in 2019 and predicted to reach $463.5 billion by 2027 [2, 3]. There are many types of cosmetics with specific functions. Some cosmetic products have a single function (e.g., cleansing, cetaphil gentle skin cleanser; brightening, whitelab brightening day cream; moisturizing, olay regenerist retinol 24 night moisturizer; hydrating, wardah aloe multifunction gel; protective, biore UV aqua rich watery essence; brightening and hydrating agent, gush beauty glow getter moisturizer; cleansing, exfoliating, and brightening agent, ras luxury oils polish brightening & exfoliating face wash cleanser; nourishing and brightening, D'you hustle serum), while other types of cosmetics have double or even multiple functions. Dozens of cosmetics innovations are ongoing to meet consumer needs and satisfaction. Specifically, cosmeceuticals are a combination of cosmetic and therapeutic formulations with active ingredients that improve and maintain skin health after topical treatment [4]. Additionally, nanotechnology has been introduced to cosmetic formulations, offering better performance. The idea of reducing cosmetic materials into a nanoscale (i.e., one billionth of a meter) enhance skin penetration, provide a long-lasting effect, offer better UV protection, and improve finish quality. These advances are expected to benefit the business market [2]. As a result of the connection with the business market, the concept of dream cosmetics begins to resonate.

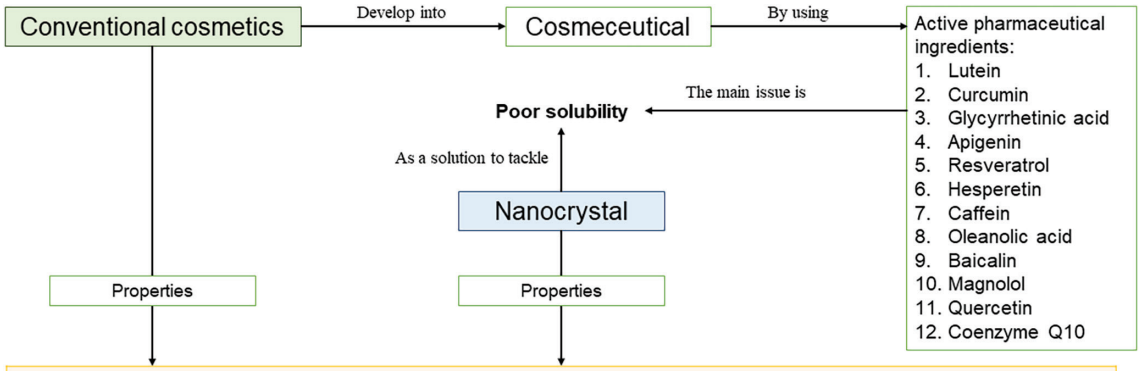
The term, dream cosmetic, defines agents that exhibit multiple enhanced bioactivities, especially antioxidant and anti-aging activities. Unfortunately, active ingredients used in cosmeceuticals, especially those from natural products, have low solubility in water, which leads to low bioavailability, skin penetration, and bioactivity [4]. This limitation diminishes the dream cosmetic formulation. In this case, nanocrystals,

as one of the nanotechnology-based delivery systems, may address the problem by enhancing the water solubility of active ingredients (see **Figure 1**). Nanocrystals are a type of nanoparticle composed of thousands of molecules joined together by surfactants without any polymers in a fixed pattern to form a group ranging in size from 1–1000 nm. Nanocrystals have a straightforward structure that enhances skin penetration against the stratum corneum barrier, making the nanocrystal more valuable in addition to improving solubility. Furthermore, preparation of nanocrystals is also simpler than other formulations [5].

The combination of media milling and homogenization techniques can produce nanocrystals, while the introduction into topical formulations, such as creams, lotions, and liposomal dispersions, has been done repeatedly [5, 6]. Nanocrystals are reported to enhance the bioactivity performance of several active ingredients, such as flavonoids, lutein, beta-carotene, and coenzyme Q10, by improving water solubility [4]. The first marketed products include Juvedical® Age-decoder Cream, which is made from rutin by Juvena (St. Margrethen, Switzerland), and Cellular Serum Platinum Rare, which is made from hesperidin by La Prairie (Montreux, Switzerland). Both formulations bear antioxidant, chelating, and anti-aging properties [5], and both are followed by formulations of other nanocrystal-related cosmetics [7–15]. **Table 1** provides further examples of bioactive compounds made into nanocrystal. Accordingly, nanocrystals enable cosmetic production with multiple performances.

In addition to the benefits of nanocrystals for cosmetics, nanocrystal prominence remains confined largely to research with clinical application still relatively limited. Not only are there technological bottlenecks and rapid expansion of the market scale but legal approval is lagging and concern of toxicity with long-term use has hampered nanocrystal application [5]. Once again, those issues cast doubt on the use of nanocrystals in formulating dream cosmetics. The alteration in physicochemical properties due to nanosize leads to toxicity and warrants thorough study.

To effectively address issues of toxicity, integrated omics studies have emerged as a prudent strategy. Omics represent a holistic assessment of biological molecules that shed light on the diverse roles within biological processes. Omics



Differentiation	
Particle size	Conventional cosmetics typically contain larger particles, whereas nanocrystals has size ranging from 1 to 1000 nm.
Solubility	Nanocrystals exhibit enhanced solubility of active ingredients in water compared to conventional cosmetics.
Stability	Nanocrystals tend to be more stable and less prone to degradation than conventional cosmetics.
Penetration	Nanocrystals can penetrate skin more effectively due to their small size and high solubility, potentially leading to better delivery of active ingredients compared to conventional cosmetics.

Figure 1 Nanocrystal-based cosmetics offer better performance over conventional cosmetics because solubility of active pharmaceutical ingredients is improved.

Table 1 Record of Nanocrystal Application in Biomedical Research

Nanocrystal-Containing Active Pharmaceutical Ingredient	Benefit of Formulation	Reference
Quercetin	Enhanced *in vitro* antioxidant activity	[7]
Apigenin	Rapid dissolution rate	[8]
Baicalein	Improved stability	[9]
Rutin	High dissolution and bioavailability	[10]
	High ex vitro skin permeability (3–5-fold) and antioxidant activity (60%)	[11]
Lutein	Better skin penetration (60%)	[12]
Hesperetin	Increased release rate (1.79-fold), and anti-inflammatory and antioxidant enzyme activities	[13]
	Improved skin penetration and stability of active product	[14]
Hesperidin	With long-lasting antioxidant activity and stability enhancement	[15]

encompass genomics, epigenomics, miRNomics, transcriptomics, proteomics, phosphoproteomics, and metabolomics. In contrast, integrated or multi-omics methodologies integrate single omics approaches. Compared to singular omics analyses, integrated omics offer a more nuanced and comprehensive understanding of nanotoxicity, identifying novel molecular pathways and key markers of toxicity with heightened sensitivity. This integrative approach facilitates the seamless flow of information across omics layers, which bridges the divide between genotype and phenotype in the context of nanotoxicity. Numerous studies have corroborated the efficacy of this approach [16–18], underscoring the manifold benefits. Therefore, utilization of integrated omics to assess nanocrystal toxicity is imperative. Furthermore, in the endeavor to advance nanocrystal cosmetics into nanocrystal-based cosmeceuticals, integrated omics unveil intricate toxicological mechanisms and cellular responses that conventional nanotoxicity evaluations may not detect. Moreover, in the pursuit of elevating nanocrystal-based cosmetics to nanocrystal-based cosmeceuticals, this approach provides nuanced insight into the temporal aspects of nanotoxicity, encompassing both early acute reactions and delayed responses to nanocrystals. Ultimately, integrated omics may rapidly pave the way for transforming the concept of dream cosmetics into a reality.

In conclusion, nanocrystals can contribute to formulating dream cosmetics. These products offer dual benefits, combining skin beautification with health maintenance, without concerns about the solubility of active ingredients. Toxicity-related issues associated with nanocrystals can be addressed through comprehensive toxicity screening utilizing integrated omic studies.

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