



Imperative Role of Natural Product Chemistry in Cosmeceutical R&D - Phytonanocosmeceuticals*

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Abstract

Natural product chemistry has always been attractive for drug and cosmetic industries as natural products can address these industries very well. By consumer demand, the cosmetic industry is looking for innovative, safer, more effective, and environmentally friendly products. In this sense, a relatively new concept of cosmetics has emerged under “cosmeceuticals or dermocosmetics/medcosmetics”. Cosmeceuticals are briefly defined as a subclass of cosmetics that contain drug active substances or bioactive natural products with enhanced efficacy for therapeutic or cosmetic purposes. They are also described as a combination of cosmetics and pharmaceuticals or medical-grade cosmetics, which particularly enhance skin penetration and the restorative effect of active ingredients in cosmetic formulations. On the other hand, nanotechnology has become another exciting area in cosmetics as nanoformulations enhance skin penetration. Therefore, we have been working on research and development of novel phyto-based cosmeceuticals *via* extensive screening studies on plant extracts and purely natural substances using *in vitro* (enzyme inhibition, etc.), *in silico* (molecular docking and toxicity screening), and cell-based assays. In this regard, an anti-acne formulation based on a number of plant extracts tested against *Propionibacterium acnes* has been developed by our group. Besides, an antimicrobial formulation as an oral spray for mouth defense is currently a commercial product. We have also been studying nanofiber formulations loaded with plant extract with wound healing effects. All our ongoing studies on discovering novel active natural ingredients for cosmeceutical purposes have so far yielded three patents and four patent applications and commercialized a final product. In the present mini review, examples of phyto-based nanocosmeceuticals and nanoingredients will be underlined.

Key Words: Natural product chemistry, phytocompound, nanocosmetic, cosmeceuticals

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1. Introduction

Phytocosmetics, also known as plant-based cosmetics, represent a fascinating and rapidly growing beauty and skincare industry segment. In today's world, where consumers increasingly seek natural, eco-

friendly, and sustainable alternatives, phytocosmetics have emerged as a compelling choice. These products harness the power of botanical extracts, plant-based ingredients, and natural compounds to promote healthy and radiant skin, hair, and overall well-being. With a deep-rooted

connection to traditional herbal remedies and a focus on the inherent benefits of plants, phytocosmetics offer a holistic approach to beauty that emphasizes the harmony between nature and human skin care (Ahmed et al., 2022). Botanical ingredients in cosmetics are natural, plant-based substances commonly used in skincare, haircare, and beauty products (Mohammad et al., 2018). These ingredients have gained popularity in the cosmetic industry due to their perceived safety, efficacy, and the growing consumer demand for natural and eco-friendly beauty solutions (Kanlayavattanukul and Lourith, 2018). In the current mini review, we will briefly mention the relationship between botanical compounds and nanomaterials in cosmetic formulations.

2. Botanical ingredients in cosmetics

Botanical ingredients, known for their potential to benefit the skin, encompass a wide variety of plant extracts, oils, and powders derived from sources like herbs, fruits, flowers, seeds, and roots. Examples include aloe, lavender oil, chamomile extract, green tea extract, and many more. They can offer antioxidant protection, anti-inflammatory properties, hydration, skin-soothing, and anti-aging effects, etc. (Antignac et al., 2011; Ferreira et al., 2021). Various plants have unique properties that cater to specific skincare needs (Lianza et al., 2020; Goyal et al., 2022). Some botanicals, like *Rosa canina* L. (rosehip) and *Melaleuca alternifolia* (Maiden & Betche) Cheel. (tea tree) oils, are recognized for their anti-aging and acne-fighting properties (Segueni et al., 2022). They can also help reduce the appearance of wrinkles and blemishes.

Botanical ingredients are generally considered safer and have fewer side effects than synthetic chemicals, making them popular for individuals with sensitive or allergy-prone skin. Some plant extracts and natural molecules possess natural preservative properties, which can help

extend the shelf life of cosmetics without the need for synthetic preservatives (Papageorgiou et al., 2010; Novak et al., 2021; Rybczyńska-Tkaczyk et al., 2023). Sourcing botanical ingredients can be more sustainable and environmentally friendly than specific synthetic alternatives, aligning with the demand for eco-conscious beauty products (Serra et al., 2023). The consumer preference for natural and plant-based products has driven the cosmetics industry to include botanical ingredients in a wide range of products, from cleansers and moisturizers to shampoos and perfumes (Bauman et al., 2007). The efficacy and safety of botanical ingredients are often backed by scientific research and clinical studies (Avonto et al., 2018). Researchers investigate the bioactive compounds within these plants and their effects on the skin. The use of botanical ingredients in cosmetics is subject to regulatory oversight in various countries. Manufacturers must ensure that their products meet safety and labeling requirements.

3. Nanomaterial-based cosmetics

Nanotechnology is a multidisciplinary field of science, engineering, and technology that deals with nanoscale materials, devices, and systems, typically at the level of individual atoms and molecules. The prefix "nano" refers to one billionth of a meter or 10^{-9} meters, and nanotechnology involves working with structures and components that are typically between 1 and 100 nanometers in size. At the nanoscale, materials often exhibit unique and enhanced properties compared to their bulk counterparts. This can include changes in mechanical, electrical, thermal, optical, and chemical properties. Nanotechnology has revolutionized the field of medicine as well as cosmetics (Gupta et al., 2022; Basudkar et al., 2022). Nanotechnological drug dosage forms, often called nanomedicine or nanopharmaceuticals, represent a groundbreaking drug delivery and therapy

approach (Patra et al., 2018), which can be applied to cosmetic formulations. These innovative formulations utilize nanotechnology to design and manipulate drug/cosmetic-active carriers and delivery systems, enabling precise targeting and controlled release of therapeutic and dermocosmetic agents. Nanocosmetics, often referred to as nanotechnology-based cosmetics, represent an innovative and rapidly evolving sector of the beauty and skincare industry (Shokri, 2017; Vaishampayan and Rane, 2022). These products leverage nanotechnology, which involves working with materials at the nanoscale, to create novel and highly effective skin care solutions (Santos et al., 2019; Dubey et al., 2022). Nanocosmetics offer several unique features and advantages, including:

Enhanced penetration: Nanoparticles can penetrate the skin more effectively, allowing active ingredients to reach deeper layers (Bucci et al., 2018). This enhances the effectiveness of skin care products.

Improved stability: Nanotechnology can enhance the stability of certain ingredients, extending the shelf life of products and ensuring they remain effective over time (Zhang et al., 2023).

Targeted delivery: Nanoparticles can be designed to release active ingredients at specific times or locations, allowing for precise and targeted treatment of skin issues (Di Stefano, 2023).

Increased efficacy: The reduced particle size allows for a more even distribution of active ingredients on the skin, resulting in better overall efficacy (Patil et al., 2015; Rama & Ribeiro, 2023).

Cosmetic and aesthetic benefits: Nanocosmetics can provide aesthetic benefits such as smoother textures, better coverage, and improved color dispersion in makeup products (Zouboulis et al., 2019).

Reduced irritation: Nanoparticles can reduce the potential for skin irritation, making these products suitable for individuals with sensitive skin (Bai et al., 2023).

Nanocosmetics encompass a variety of product types that incorporate nanotechnology for enhanced performance, improved texture, and targeted effects (Raszewska-Famielec and Flieger, 2022). Some common types of nanocosmetic products are as follows:

Nanoparticle sunscreens: These sunscreens contain nanoparticles, such as zinc oxide or titanium dioxide, which provide effective UV protection without leaving a visible white residue on the skin. The small particle size allows for a cosmetically elegant appearance (Dréno et al., 2019; Lin et al., 2024).

Nanomaterial-based make-up: Nanotechnology is used to create makeup products like foundations, powders, and eyeshadows. Nanoparticles improve color dispersion and create a smoother, more even texture (Aziz et al., 2019; Santos et al., 2019).

Antiaging serum and creams: Anti-aging skincare products often incorporate nanoparticles to enhance the delivery of active ingredients like peptides, antioxidants, and retinoids (Bellu et al., 2021; Jin et al., 2023). This improves their penetration into the skin and effectiveness in reducing signs of aging.

Nanosome and liposome-based skin care: Nanosomes and liposomes are nanoscale carriers encapsulating active ingredients (Fakhravar et al., 2016; Cheng et al., 2020). They are used in a range of skincare products, such as moisturizers, serums, and creams, to improve ingredient delivery and stability.

Nanoemulsions: Nanoemulsions are used to create lightweight and easily absorbed cosmetic formulations (Ngan et al., 2015). They are commonly found in products like moisturizers, cleansers, and serums.

Nanoparticle-enhanced haircare: Nanotechnology is employed in hair care products to improve the delivery of vitamins, conditioners, and other beneficial ingredients to the hair and scalp. This can lead to healthier, more lustrous hair (Heng et al., 2011).

Nanogels and nanocapsules: These nanocarriers are used to encapsulate and deliver active ingredients in a controlled manner (Marchiori et al., 2017; Cardoso et al., 2019). They are commonly found in products designed for targeted skincare and treatments.

Nanoparticle-infused nail products: Some nail polishes and treatments incorporate nanoparticles for improved durability, shine, and wear resistance (Trombino et al., 2016; Flores et al., 2017).

Nanoparticle-containing fragrances: Nanotechnology is beneficial in creating fragrance formulations that provide longer-lasting scent, better adherence to the skin, and improved fragrance stability (Capasso Palmiero et al., 2020; Hu et al., 2021; Wang et al., 2022).

It is important to note that using nanotechnology in cosmetics has raised questions and concerns regarding safety and regulatory oversight. Some people worry about potential health risks associated with using nanoparticles in cosmetics, and regulatory agencies in various countries have implemented guidelines and regulations to ensure the safety of nanocosmetic products.

4. Conclusion

Nanotechnological dosage forms have significantly advanced the cosmetic industry, leading to the development of products that offer enhanced benefits and a more enjoyable user experience. As technology progresses, cosmetic companies need to balance innovation with rigorous safety testing to ensure the well-being of consumers. On the

other hand, using nanoparticles in various products has raised concerns about potential health and environmental risks. Ensuring the safety of nanotechnology is an ongoing challenge, and regulatory agencies are working to establish guidelines for the responsible use of nanomaterials. Consumers interested in nanocosmetics should be informed about the ingredients and technologies used in these products and any manufacturer safety assessments. As with any cosmetic purchase, individual skin type and potential sensitivities should be taken into account, when selecting and using nanocosmetic products.

Nanotechnology holds great promise for addressing complex challenges in various fields, such as creating more powerful and energy-efficient electronics, developing targeted drug therapies, and improving the efficiency of cosmetics. Nanotechnology continues to be a rapidly evolving field with far-reaching implications for science, industry, and society. Researchers, policymakers, and the public are all engaged in ongoing discussions about its potential and the responsible development of nanotechnology.

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Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Ahmed, I.A., Mikail, M.A., Zamakshshari, N.H., Mustafa, M.R., Hashim, N.M., Othman, R., (2022). Trends and challenges in phytotherapy and phytocosmetics for skin aging. *Saudi Journal of Biological Sciences*, 29(8), 103363. <https://doi.org/10.1016/j.sjbs.2022.103363>
2. Antignac, E., Nohynek, G.J., Re, T., Clouzeau, J., Toutain, H. (2011). Safety of botanical ingredients in personal care products/cosmetics. *Food and Chemical Toxicology*, 49(2), 324-341. <https://doi.org/10.1016/j.fct.2010.11.022>
3. Avonto, C., Chittiboyina, A.G., Sadrieh, N., Vukmanovic, S., Khan, I.A. (2018). In chemico skin sensitization risk assessment of botanical ingredients. *Journal of Applied Toxicology*, 8(7), 1047-1053. <https://doi.org/10.1002/jat.3614>
4. Aziz, Z.A.A., Mohd-Nasir, H., Ahmad, A., Setapar, S.H.M., Peng, W.L., *et al.* (2019). Role of nanotechnology for design and development of cosmeceutical: application in makeup and skin care. *Frontiers in Chemistry*, 7, 739. <https://doi.org/10.3389/fchem.2019.00739>
5. Bai, D., Hu, F., Xu, H., Huang, J., Wu, C., *et al.* (2023). High stability and low irritation of retinol propionate and hydroxypinacolone retinoate supramolecular nanoparticles with effective anti-wrinkle efficacy. *Pharmaceutics*, 15(3), 731. <https://doi.org/10.3390/pharmaceutics15030731>
6. Basudkar, V., Gharat, S.A., Momin, M.M., Shringarpure, M. (2022). A review of anti-aging nanoformulations: recent developments in excipients for nanocosmeceuticals and regulatory guidelines. *Critical Reviews in Therapeutic Drug Carrier Systems*, 39(3), 45-97. <https://doi.org/10.1615/CritRevTherDrugCarrierSyst.2021039544>
7. Baumann, L. (2007). Botanical ingredients in cosmeceuticals. *Journal of Drugs in Dermatology*, 6(11), 1084-1088 (doi not available).
8. Bellu, E., Medici, S., Coradduzza, D., Cruciani, S., Amler, E., (2021). Nanomaterials in skin regeneration and rejuvenation. *International Journal of Molecular Sciences*, 22(13), 7095. <https://doi.org/10.3390/ijms22137095>
9. Bucci, P., Prieto, M.J., Milla, L., Calienni, M.N., Martinez, L., *et al.* (2018). Skin penetration and UV-damage prevention by nanoberrries. *Journal of Cosmetic Dermatology*, 17(5), 889-899. <https://doi.org/10.1111/jocd.12436>
10. Capasso Palmiero, U., Ilare, J., Romani, C., Moscatelli, D., Sponchioni, M. (2020). Surfactant-free and rinsing-resistant biodegradable nanoparticles with high adsorption on natural fibers for the long-lasting release of fragrances. *Colloids and Surfaces B: Biointerfaces*, 190, 110926. <https://doi.org/10.1016/j.colsurfb.2020.110926>
11. Cardoso, A.M., de Oliveira, E.G., Coradini, K., Bruinsmann, F.A., Aguirre, T., *et al.* (2019). Chitosan hydrogels containing nanoencapsulated phenytoin for cutaneous use: skin permeation/penetration and efficacy in wound healing. *Material Science and Engineering C*, 96, 205-217. <https://doi.org/10.1016/j.msec.2018.11.013>
12. Cheng, Y.C., Li, T.S., Su, H.L., Lee, P.C., Wang, H.D. (2020). Transdermal delivery systems of natural products applied to skin therapy and care. *Molecules*, 25(21), 5051. <https://doi.org/10.3390/molecules25215051>
13. Di Stefano, A. (2023). Nanotechnology in targeted drug delivery. *International Journal of Molecular Sciences*, 24(9), 8194. <https://doi.org/10.3390/ijms24098194>
14. Dréno, B., Alexis, A., Chuberre, B., Marinovich, M. (2019). Safety of titanium dioxide nanoparticles in cosmetics. *Journal of European Academy of Dermatology and Venereology*, 33(Suppl 7), 34-46. <https://doi.org/10.1111/jdv.15943>
15. Dubey, S.K., Dey, A., Singhvi, G., Pandey, M.M., Singh, V., *et al.* (2022). Emerging trends of nanotechnology in advanced cosmetics. *Colloids and Surfaces B: Biointerfaces*, 214, 112440. <https://doi.org/10.1016/j.colsurfb.2022.112440>
16. Fakhrahar, Z., Ebrahimnejad, P., Daraee, H., Akbarzadeh, A. (2016). Nanoliposomes: synthesis methods and applications in cosmetics. *Journal of Cosmetic and Laser Therapy*, 18(3), 174-181. <https://doi.org/10.3109/14764172.2015.1039040>
17. Ferreira, M.S., Magalhães, M.C., Oliveira, R., Sousa-Lobo, J.M., Almeida, I.F. (2021). Trends in the use of botanicals in anti-aging cosmetics. *Molecules*, 26(12), 3584. <https://doi.org/10.3390/molecules26123584>
18. Flores, F.C., Rosso, R.S., Cruz, L., Beck, R.C., Silva, C.B. (2017). An innovative polysaccharide nanobased nail formulation for improvement of onychomycosis treatment. *European Journal of Pharmaceutical Sciences*, 100, 56-63. <https://doi.org/10.1016/j.ejps.2016.12.043>
19. Goyal, A., Sharma, A., Kaur, J., Kumari, S., Garg, M., *et al.* (2022). Bioactive-based cosmeceuticals: an update on emerging trends. *Molecules*, 27(3), 828. <https://doi.org/10.3390/molecules27030828>
20. Gupta, V., Mohapatra, S., Mishra, H., Farooq, U., Kumar, K., *et al.* (2022). Nanotechnology in cosmetics and cosmeceuticals-a review of latest advancements. *Gels*, 8(3), 173. <https://doi.org/10.3390/gels8030173>
21. Heng, B.C., Zhao, X., Tan, E.C., Khamis, N., Assodani, A., *et al.* (2011). Evaluation of the

- cytotoxic and inflammatory potential of differentially shaped zinc oxide nanoparticles. *Archives in Toxicology*, 85(12), 1517-1528. <https://doi.org/10.1007/s00204-011-0722-1>
22. Hu, J., Zhang, J., Li, L., Bao, X., Deng, W., *et al.* (2021). Chitosan-coated organosilica nanoparticles as a dual responsive delivery system of natural fragrance for axillary odor problem. *Carbohydrate Polymers*, 269, 118277. <https://doi.org/10.1016/j.carbpol.2021.118277>
23. Jin, S., Wang, Y., Wu, X., Li, Z., Zhu, L., *et al.* (2023). Young exosome bio-nanoparticles restore aging-impaired tendon stem/progenitor cell function and reparative capacity. *Advanced Materials*, 35(18), e2211602. <https://doi.org/10.1002/adma.202211602>
24. Kanlayavattanukul, M. and Lourith, N., (2018). Skin hyperpigmentation treatment using herbs: a review of clinical evidences. *Journal of Cosmetic and Laser Therapy*, 20(2), 123-131. <https://doi.org/10.1080/14764172.2017.1368666>
25. Lianza, M., Mandrone, M., Chiocchio, I., Tomasi, P., Marincich, L., *et al.* (2020). Screening of ninety herbal products of commercial interest as potential ingredients for phytocosmetics. *Journal of Enzyme Inhibition and Medicinal Chemistry*, 35(1), 1287-1291. <https://doi.org/10.1080/14756366.2020.1774571>
26. Lin, C.H., Lin, M.H., Chung, Y.K., Alalaiwe, A., Hung, C.F., *et al.* (2024). Exploring the potential of the nano-based sunscreens and antioxidants for preventing and treating skin photoaging. *Chemosphere*, 347, 140702. <https://doi.org/10.1016/j.chemosphere.2023.140702>
27. Marchiori, M.C.L., Rigon, C., Camponogara, C., Oliveira, S.M., Cruz, L. (2017). Hydrogel containing silibinin-loaded pomegranate oil based nanocapsules exhibits anti-inflammatory effects on skin damage UVB radiation-induced in mice. *Journal of Photochemistry and Photobiology B*, 170, 25-32. <https://doi.org/10.1016/j.jphotobiol.2017.03.015>
28. Mohammad, I.S., Naveed, M., Ijaz, S., Shumzaid, M., Hassan, S., *et al.* (2018). Phytocosmeceutical formulation development, characterization and its *in-vivo* investigations. *Biomedicine & Pharmacotherapy*, 107, 806-817. <https://doi.org/10.1016/j.biopha.2018.08.024>
29. Ngan, C.L., Basri, M., Tripathy, M., Abedi Karjiban, R., Abdul-Malek, E. (2015). Skin intervention of fullerene-integrated nanoemulsion in structural and collagen regeneration against skin aging. *European Journal of Pharmaceutical Sciences*, 70, 22-28. <https://doi.org/10.1016/j.ejps.2015.01.006>
30. Nowak, K., Jabłońska, E., Ratajczak-Wrona, W. (2021). Controversy around parabens: Alternative strategies for preservative use in cosmetics and personal care products. *Environmental Research*, 198, 110488. <https://doi.org/10.1016/j.envres.2020.110488>
31. Papageorgiou, S., Varvaresou, A., Tsirivas, E., Demetzos, C. (2010). New alternatives to cosmetics preservation. *Journal of Cosmetic Sciences*, 61(2), 107-123.
32. Patil, S., Vhora, I., Amrutiya, J., Lalani, R., Misra, A. (2015). Role of nanotechnology in delivery of protein and peptide drugs. *Current Pharmaceutical Design*, 21(29), 4155-73. <https://doi.org/10.2174/1381612821666150901095722>
33. Patra, J.K., Das, G., Fraceto, L.F., Campos, E.V.R., Rodriguez-Torres, M.D.P., *et al.* (2018). Nano based drug delivery systems: recent developments and future prospects. *Journal of Nanobiotechnology*, 16(1), 71. <https://doi.org/10.1186/s12951-018-0392-8>
34. Rama, B., Ribeiro, A.J. (2023). Role of nanotechnology in the prolonged release of drugs by the subcutaneous route. *Expert Opinion in Drug Delivery*, 20(5), 559-577. <https://doi.org/10.1080/17425247.2023.2214362>
35. Raszewska-Famielec, M. and Flieger, J. (2022). Nanoparticles for topical application in the treatment of skin dysfunctions-an overview of dermo-cosmetic and dermatological products. *International Journal of Molecular Sciences*, 23(24), 15980. <https://doi.org/10.3390/ijms232415980>
36. Rybczyńska-Tkaczyk, K., Grenda, A., Jakubczyk, A., Kiersnowska, K., Bik-Małodzińska, M. (2023). Natural compounds with antimicrobial properties in cosmetics. *Pathogens*, 12(2), 320. <https://www.mdpi.com/2076-0817/12/2/320>
37. Santos, A.C., Morais, F., Simões, A., Pereira, I., Sequeira, J.A.D., *et al.* (2019). Nanotechnology for the development of new cosmetic formulations. *Expert Opinion in Drug Delivery*, 16(4), 313-330. <https://doi.org/10.1080/17425247.2019.1585426>
38. Segueni, N., Akkal, S., Benlabed, K., Nieto, G. (2022). Potential use of propolis in phytocosmetic as phytotherapeutic constituent. *Molecules*, 27(18), 5833. <https://doi.org/10.3390/molecules27185833>
39. Serra, M., Casas, A., Teixeira, J.A., Barros, A.N. (2023). Revealing the beauty potential of grape stems: harnessing phenolic compounds for cosmetics. *International Journal of Molecular Sciences*, 24(14), 11751. <https://doi.org/10.3390/ijms241411751>

40. Shokri, J. (2017). Nanocosmetics: benefits and risks. *Bioimpacts*, 7(4), 207-208. <https://doi.org/10.15171/bi.2017.24>
41. Trombino, S., Mellace, S., Cassano, R. (2016). Solid lipid nanoparticles for antifungal drugs delivery for topical applications. *Therapeutic Delivery*, 7(9), 639-647. <https://doi.org/10.4155/tde-2016-0040>.
42. Vaishampayan, P. and Rane, M.M. (2022). Herbal nanocosmeceuticals: a review on cosmeceutical innovation. *Journal of Cosmetic Dermatology*, 21(11), 5464-5483. <https://doi.org/10.1111/jocd.15238>
43. Wang, W., Qiu, X., Dong, Q., Wang, J., Hao, Q., *et al.* (2022). Nanocapsule-based reactive nano-fragrances with slow-release and antibacterial performances for applications of commodities. *Journal of Biomedical Nanotechnology*, 18(4), 1138-1145. <https://doi.org/10.1166/jbn.2022.3329>
44. Zhang, L., Yao, L., Zhao, F., Yu, A., Zhou, Y., *et al.* (2023). Protein and peptide-based nanotechnology for enhancing stability, bioactivity, and delivery of anthocyanins. *Advance Healthcare Materials*, 12(25), e2300473. <https://doi.org/10.1002/adhm.202300473>
45. Zouboulis, C.C., Ganceviciene, R., Liakou, A.I., Theodoridis, A., Elewa, R., *et al.* (2019). Aesthetic aspects of skin aging, prevention, and local treatment. *Clinical Dermatology*, 37(4), 365-372. <https://doi.org/10.1016/j.clindermatol.2019.04.002>.