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Plant Bioactives and Nanotechnology: The New Frontier for Personalized Dermatological Treatment

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The skin, the largest organ of the human body, performs vital functions as a protective barrier against external aggressions, thermal regulation, and sensory perception. However, it is constantly exposed to intrinsic and extrinsic factors that can compromise its health and appearance, such as ultraviolet radiation, pollution, oxidative stress, and inflammatory processes. The search for effective solutions for maintaining skin integrity and treating its various conditions has driven innovation in dermatology and cosmetology (BAUMANN, 2009).

Traditionally, dermatological formulations use synthetic ingredients or conventional plant extracts. While many of these components demonstrate efficacy, they often face challenges related to stability, solubility, limited skin permeation, and potential for irritation. The complexity of the epidermal barrier, composed of multiple layers of cells and lipids, restricts the penetration of active molecules, decreasing their bioavailability at the site of action (ELIAS, 2005).

In parallel, a paradigm shift in healthcare is observed, with a growing appreciation for personalization. The understanding that each individual possesses a unique genetic makeup, skin microbiome, and lifestyle has led to a demand for treatments that consider these particularities. The "one-size-fits-all" approach is increasingly questioned, making way for tailored therapies that promise greater efficacy and a lower incidence of adverse effects (ZHANG et al., 2020).

In this scenario of innovation and demand for more sophisticated solutions, plant-derived bioactives emerge as promising sources of compounds with antioxidant, anti-inflammatory, antimicrobial, and rejuvenating properties. Nature offers a vast array of phytochemicals with proven therapeutic potential. However, the full exploitation of these natural resources is often limited by their low stability and solubility in aqueous formulations, in addition to the difficulty in efficiently crossing the skin barrier (GOYAL et al., 2020).

It is at this point that nanotechnology becomes a revolutionary vector. By manipulating materials at the nanometer scale (1 to 100 nanometers), it is possible to develop delivery systems that encapsulate, protect, and precisely target bioactives to the deeper layers of the skin, optimizing their action and minimizing undesirable effects. The strategic combination of plant bioactives with intelligent nanocarriers therefore represents a new frontier for the development of personalized dermatological treatments that are more effective and safer (MOHANTY; SAHOO, 2020).

This article aims to explore the synergy between plant bioactives, nanotechnology, and personalization in skin treatment. It will address the benefits of plant bioactives, the role of *in vitro* plant cell culture in obtaining these actives, advancements in nanotechnology in dermatology, how this combination optimizes active delivery, and how personalization, driven by diagnostic technologies and artificial intelligence, is shaping the future of skin care. Finally, the challenges and future perspectives for this area of research and development will be discussed.

LITERATURE REVIEW

PLANT BIOACTIVES AND THEIR BENEFITS FOR THE SKIN

Plant bioactives are chemical compounds produced by plants that possess biological activity and can confer benefits to human health. In dermatology, their use dates back to ancient civilizations, but modern science has made it possible to isolate, characterize, and prove the properties of a vast range of these phytochemicals. They are valued for their natural origin, perceived lower toxicity, and multifunctionality (SRIVASTAVA et al., 2019).

Among the main classes of plant bioactives with dermatological relevance, the following stand out:

- **Polyphenols and Flavonoids:** Found in teas, red fruits, grapes, and cocoa, these are potent antioxidants that neutralize free radicals, protecting the skin from oxidative damage induced by UV radiation and pollution. They also possess anti-inflammatory and photoprotective properties, aiding in the prevention of premature aging and reduction of redness (AFONSO et al., 2020).
- **Carotenoids:** Present in carrots, tomatoes, and algae, such as beta-carotene and astaxanthin, they act as internal antioxidants and photoprotectors, absorbing UV light and dissipating energy, in addition to imparting a healthy skin tone (KUMAR et al., 2021).
- **Vitamin C (Ascorbic Acid):** Abundant in citrus fruits and acerola, it is essential for collagen synthesis and has brightening and antioxidant actions (BURKE, 2007).
- **Vitamin E (Tocopherols):** Found in vegetable oils, it is a lipid-soluble antioxidant that protects cell membranes (BURKE, 2007).
- **Triterpenes and Saponins:** Present in plants like *Centella asiatica* (asiaticoside, madecassoside), they promote wound healing, stimulate collagen and elastin synthesis, and possess anti-inflammatory effects, being widely used in products for sensitive and damaged skin (BYUN et al., 2019).
- **Alkaloids and Terpenes:** Some, such as resveratrol (present in grape skin), exhibit anti-aging properties by activating sirtuins, enzymes associated with cellular longevity, and protecting against oxidative stress (PÉREZ-SÁNCHEZ et al., 2020).

Despite their vast potential, the use of plant bioactives in conventional dermatological formulations presents significant challenges. Many of these compounds are chemically unstable, sensitive to light, heat, and oxidation, which compromises their integrity and efficacy over time. Moreover, their low solubility in aqueous vehicles and their difficulty in permeating the complex skin barrier limit their bioavailability in the deeper layers of the skin, where their targets of action are often located (GUO et al., 2020). Overcoming these limitations is crucial for the full exploration of the true potential of these natural active ingredients.

The Fundamental Role of Pharmacognosy in the Selection and Validation of Plant Bioactives

The foundation for the development of any dermatological or cosmetic product of natural origin lies in the careful selection and scientific validation of plant bioactives. It is at this point that pharmacognosy, the science that studies drugs of natural origin, plays an irreplaceable role. Pharmacognosy not only identifies and characterizes the active compounds present in plants but also ensures their quality, purity, and consistency, crucial aspects for the safety and efficacy of formulations (EVANS, 2009).

The contributions of pharmacognosy to this field include:

- **Discovery and Screening:** Through ethnobotanical and phytochemical approaches, pharmacognosy investigates plants with a history of medicinal use or with untapped therapeutic potential. It allows for the identification of species and plant parts rich in phytochemicals with properties relevant to skin health, such as antioxidants, anti-inflammatories, antimicrobials, and collagen stimulators (RODRIGUES; LIMA, 2018).
- **Chemical Characterization and Standardization:** Once bioactives of interest are identified, pharmacognosy employs advanced analytical techniques (such as chromatography and spectrometry) to isolate, elucidate the chemical structure, and quantify these compounds. The standardization of plant extracts, ensuring they contain a consistent concentration of target bioactives, is fundamental for the reproducibility of biological effects and consumer safety (SIMÕES et al., 2017).
- **Quality Control and Safety:** Pharmacognosy establishes quality parameters for plant raw materials and their derivatives, including the detection of adulterations, the identification of contaminants (pesticides, heavy metals, mycotoxins), and the evaluation of bioactive stability. This rigor in quality control is essential to ensure that final products are safe and maintain their integrity over time (COSTA, 2015).
- **Validation of Biological Activity:** Although nanotechnology optimizes delivery, pharmacognosy contributes to the initial validation of the biological activity of bioactives, often in preliminary *in vitro* or *in vivo* models, confirming the therapeutic properties attributed to these compounds before their incorporation into advanced delivery systems (SRIVASTAVA et al., 2019).

Therefore, pharmacognosy serves as the scientific basis that ensures the quality, purity, and efficacy of plant bioactives, providing reliable and validated raw material that will subsequently be optimized by nanotechnology for personalized dermatological treatments.

IN VITRO PLANT CELL CULTURE FOR BIOACTIVE PRODUCTION

While traditional extraction of plant bioactives faces challenges such as seasonal variability, environmental impact of harvesting, and inconsistency in purity, *in vitro* plant cell culture emerges as a promising technology for the controlled and sustainable production of high-value phytochemicals (MURTHY; BHAT; GIRI, 2014).

In vitro plant cell culture involves the growth of plant cells, tissues, or organs in a sterile environment, using a nutritious culture medium and controlled conditions of light, temperature, and hormones. This technique can generate callus cultures (masses of undifferentiated cells), cell suspensions, or cultures of specific organs, such as roots and shoots (GEORGIEV et al., 2011).

The improvements and facilities provided by this technology are remarkable:

- **Sustainability and Reduced Environmental Impact:** It decreases reliance on harvesting wild or cultivated plants, protecting biodiversity and endangered species. Production can occur anywhere, regardless of climate or soil, reducing transportation costs and carbon footprint (MURTHY; BHAT; GIRI, 2014).

- **Purity and Consistency:** It eliminates contamination by pesticides, heavy metals, and microorganisms present in the natural environment. It ensures a standardized and consistent chemical profile of bioactives, essential for the reproducibility of product quality and efficacy (GEORGIEV et al., 2011).
- **Controlled and Optimized Biosynthesis:** Culture conditions (medium composition, elicitor addition, light spectrum) can be manipulated to stimulate specific metabolic pathways, increasing the production of desired secondary metabolites. This allows for higher yields of specific compounds compared to the whole plant (VERPOORTE; ALFERMANN, 2002).
- **Independence from Environmental Factors:** Production is not affected by climatic, seasonal, or geographical variations, ensuring a continuous and predictable supply of bioactives (MURTHY; BHAT; GIRI, 2014).
- **Discovery of New Compounds:** Manipulation of culture conditions can induce the production of new compounds or compounds in atypical concentrations, paving the way for the discovery of novel bioactives (GEORGIEV et al., 2011).
- **Industrial Scalability:** Bioreactors enable large-scale production of plant cells and their metabolites in a contained and controlled environment, facilitating the transition from research to industrial application (GEORGIEV et al., 2011).

Key applications in dermatology and cosmetology include:

- **Source of Bioactives from Rare or Endangered Plants:** Allows access to valuable compounds from species that are difficult to cultivate or are under environmental protection.
- **Production of High-Value Compounds:** Obtaining polyphenols, flavonoids, triterpenes, growth factors, and peptides with high purity.
- **"Plant Stem Cell" Extracts:** Although the term is popularized, it refers to extracts from undifferentiated plant cells cultured *in vitro*, which are valued for their regenerative, antioxidant, and skin-protective properties.
- **Examples:** Production of asiaticoside from *Centella asiatica*, ginsenosides from Ginseng, Argan peptides, and leontopodic acid from Edelweiss through cell cultures.

The high purity and consistency of *in vitro* produced bioactives make them ideal candidates for nanoencapsulation, further optimizing the synergy with advanced delivery technologies.

NANOTECHNOLOGY IN DERMATOLOGY

Nanotechnology, defined as the science and engineering of materials at the nanometer scale, has revolutionized various fields, and dermatology is no exception. The ability to manipulate matter at such small dimensions allows for the creation of innovative delivery systems, known as nanocarriers, that overcome skin barriers and optimize the action of active ingredients (PATIL et al., 2018).

Nanocarriers offer multiple advantages over traditional formulations:

- **Increased Skin Permeation:** Due to their reduced size, nanoparticles can more easily penetrate through hair follicles, sweat glands, and, to some extent, through the stratum corneum, reaching the deeper layers of the epidermis and dermis (MOHANTY; SAHOO, 2020).
- **Active Ingredient Protection:** Encapsulation protects sensitive bioactives from degradation by external factors such as light, oxygen, and temperature, extending their shelf life and maintaining their potency (CHEN et al., 2021).
- **Controlled and Sustained Release:** Nanocarriers can be designed to release the active ingredient gradually and continuously, maintaining therapeutic concentrations for longer periods and reducing application frequency (ZHANG et al., 2020).
- **Reduced Irritation and Toxicity:** By targeting the active ingredient to the site of action and reducing its concentration on the skin surface, nanotechnology can minimize adverse effects and irritations, making formulations safer and better tolerated (GOYAL et al., 2020).
- **Improved Stability and Solubility:** Lipophilic compounds can be solubilized in aqueous nanocarriers, and vice versa, facilitating their incorporation into different types of formulations and increasing their stability (MOHANTY; SAHOO, 2020).

Various types of nanocarriers are employed in dermatology:

Liposomes: Spherical vesicles formed by one or more lipid bilayers, capable of encapsulating both hydrophilic and lipophilic active ingredients. They are biocompatible and biodegradable, mimicking the structure of cell membranes (CHEN et al., 2021).

- **Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs):** Represent an evolution of liposomes, being more stable and with greater encapsulation capacity. SLNs are formed by a solid lipid matrix, while NLCs incorporate liquid lipids into the solid matrix, offering greater flexibility and loading capacity (GOYAL et al., 2020).
- **Nanoemulsions:** Oil-in-water (or vice versa) dispersions with nanometer-scale droplets, which provide high stability and transparency. They facilitate the permeation of lipophilic active ingredients and provide a pleasant skin feel (MOHANTY; SAHOO, 2020).
- **Polymeric Nanoparticles:** Formed by biodegradable polymers, they can be designed for controlled and targeted release, being versatile for encapsulating a wide range of active ingredients (PATIL et al., 2018).

Despite remarkable advances, the application of nanotechnology in dermatology is not without challenges. Issues related to the safety of nanomaterials, such as their potential long-term toxicity, bioaccumulation, and environmental impact, are still subjects of intense research and debate. The regulation of these products is complex and varies among different countries, requiring rigorous safety and efficacy studies before widespread commercialization. Standardization of production and quality control at an industrial scale also represent obstacles to be overcome (ZHANG et al., 2020). Nevertheless, the potential for innovation and patient benefits continues to drive research and development in this area.

THE SYNERGY BETWEEN PLANT BIOACTIVES AND NANOTECHNOLOGY

The combination of plant bioactives with nanotechnology represents a powerful strategy to optimize the performance of dermatological products. Nanocarrier delivery directly addresses the main limitations of crude plant extracts and isolated phytochemicals, elevating their efficacy to a new level (GOYAL et al., 2020).

The synergy manifests in several aspects:

- **Enhanced Protection:** Many plant bioactives, such as vitamin C and polyphenols, are extremely sensitive to oxidation and light. Encapsulation in nanocarriers, such as liposomes or lipid nanoparticles, creates a physical barrier that protects them from environmental degradation, ensuring that a greater quantity of the active ingredient reaches its site of action intact (CHEN et al., 2021).
- **Increased Solubility and Stability:** Lipophilic phytochemicals, such as carotenoids and some flavonoids, have low solubility in aqueous formulations, hindering their incorporation and homogeneity. Nanocarriers like nanoemulsions or NLCs can solubilize these compounds, allowing their uniform dispersion and increasing the stability of the final formulation (MOHANTY; SAHOO, 2020).
- **Improved Permeation and Bioavailability:** The skin barrier is a challenge for most molecules. Nanocarriers, due to their size and lipid composition, can interact more efficiently with the stratum corneum, facilitating the delivery of encapsulated bioactives into the deeper layers of the epidermis and dermis. This results in greater bioavailability of the active ingredient at the site where it needs to act, whether to stimulate collagen production, modulate inflammation, or protect against oxidative stress (PATIL et al., 2018).
- **Targeted and Sustained Release:** The engineering of nanocarriers allows for the development of intelligent delivery systems. For example, nanoparticles can be functionalized to release their content in response to specific skin stimuli, such as pH changes in inflamed areas or the presence of certain enzymes. This targeted and sustained release optimizes efficacy and reduces the need for frequent applications (ZHANG et al., 2020).

Promising application examples include the encapsulation of green tea extracts (rich in catechins) in nanoparticles to increase their antioxidant and anti-inflammatory action in skin exposed to UV radiation (AFONSO et al., 2020), or the formulation of resveratrol in liposomes to improve its stability and penetration, enhancing its anti-aging effects (PÉREZ-SÁNCHEZ et al., 2020). The combination of curcumin, a potent anti-inflammatory derived from turmeric, with lipid nanoparticles has demonstrated superior efficacy in treating inflammatory skin conditions compared to free curcumin (SRIVASTAVA et al., 2019).

This synergistic approach not only enhances the efficacy of plant bioactives but also paves the way for the development of dermatological products with optimized safety profiles, by allowing the use of lower concentrations of active ingredients with greater biological impact.

PERSONALIZATION IN DERMATOLOGICAL TREATMENT

CONCEPT OF PERSONALIZED MEDICINE IN DERMATOLOGY

Personalized medicine, or precision medicine, represents an evolution in healthcare, moving away from a generalized approach to focus on the individual characteristics of each patient. In dermatology, this concept gains particular relevance, as each person's skin is unique, influenced by a complex interaction of genetic, environmental, and lifestyle factors (ZHANG et al., 2020).

The fundamental premise of personalized dermatology is that the efficacy of a treatment can be significantly optimized when the formulation and care regimen are adapted to the individual's specific needs. This contrasts with the traditional model, where products are developed for broad skin types (dry, oily, sensitive) or common conditions, without considering the biological nuances of each person.

Factors that make each individual's skin unique and justify personalization include:

- **Genetics:** Genetic polymorphisms can influence collagen production, antioxidant capacity, inflammatory response, sensitivity to certain ingredients, and predisposition to conditions such as acne, rosacea, or premature aging (BAUMANN, 2009).
- **Skin Microbiome:** The community of microorganisms inhabiting the skin surface (bacteria, fungi, viruses) plays a crucial role in skin barrier health and immune response modulation. Imbalances in the microbiome (dysbiosis) are associated with various dermatological conditions, such as acne, atopic dermatitis, and psoriasis (ELIAS, 2005).
- **Lifestyle and Environmental Exposure:** Diet, stress levels, smoking, exposure to pollution and UV radiation, and sleep habits directly impact skin health and appearance, varying significantly among individuals (SRIVASTAVA et al., 2019).
- **Physiological Characteristics:** Skin type (oily, dry, combination), phototype, sensitivity, presence of specific conditions (acne, hyperpigmentation, wrinkles), and age are determining factors for the selection of active ingredients and formulations (BAUMANN, 2009).

Personalization therefore seeks to go beyond simple categorization, using detailed data to create an accurate skin profile and, from it, formulate products containing the ideal active ingredients in appropriate concentrations, delivered optimally for the individual in question. This not only maximizes efficacy but also minimizes the risk of adverse reactions, as unnecessary or potentially irritating ingredients can be excluded from the formulation (ZHANG et al., 2020).

ENABLING TECHNOLOGIES FOR PERSONALIZATION

The realization of personalized dermatology depends on the advancement and integration of various technologies that enable the collection, analysis, and interpretation of an individual's biological and environmental data.

- **Genomics and Proteomics:** DNA and protein expression analysis in the skin can reveal genetic predispositions to certain conditions, the capacity to respond to specific active ingredients, and enzymatic deficiencies affecting skin health. This information allows for the selection of ingredients that act on specific biological pathways, optimizing treatment efficacy (BAUMANN, 2009).
- **Skin Microbiome Analysis:** Genetic sequencing techniques enable the identification of the composition and diversity of the skin's microbiota. Based on this data, specific probiotics, prebiotics, or postbiotics can be selected to help restore microbiome balance and strengthen the skin barrier (ELIAS, 2005).
- **Advanced Skin Diagnosis:** High-resolution imaging devices, spectroscopy, biosensors, and bioimpedance analyses can provide detailed information on hydration, oiliness, elasticity, pigmentation, inflammation, and sun damage in real-time. This objective data guides formulation and allows for monitoring treatment response (SRIVASTAVA et al., 2019).
- **Artificial Intelligence (AI) and Big Data:** AI plays a crucial role in analyzing and interpreting the vast amount of data generated by the above technologies. Machine learning algorithms can identify complex patterns, predict skin response to:

- different ingredients, and recommend personalized formulations. Big Data allows for the storage and processing of information from millions of users, continuously refining personalization models (ZHANG et al., 2020).
- **3D Printing and Robotics:** Although still in early stages, 3D printing may, in the future, allow for the small-scale manufacturing of personalized dermatological products with optimized geometries and structures for active ingredient release. Robotics can automate the formulation and mixing process of ingredients, ensuring precision and reproducibility (GOYAL et al., 2020).

The integration of these technologies enables the creation of a "skin passport" for each individual, a detailed profile that serves as the basis for truly personalized product formulation.

THE ROLE OF NANOTECHNOLOGY IN PERSONALIZED DELIVERY

Nanotechnology not only enhances the delivery of active ingredients but also plays a fundamental role in achieving personalization at a molecular level. The ability to design nanocarriers with specific characteristics allows for active ingredient delivery that adapts to the dynamic conditions and unique needs of each skin (MOHANTY; SAHOO, 2020).

- **Responsive Release Systems:** Nanocarriers can be designed to be "intelligent," releasing their content in response to specific stimuli that vary from person to person or according to skin condition. For example:
  - **pH-sensitive:** In inflamed or acne-prone areas, skin pH can be altered. pH-sensitive nanoparticles can release anti-inflammatory or antimicrobial active ingredients only in these regions, minimizing exposure to healthy areas (PATIL et al., 2018).
  - **Enzyme-responsive:** The presence of certain enzymes in excess (such as metalloproteinases in aged skin) can trigger the release of active ingredients that inhibit these enzymes or stimulate collagen production (ZHANG et al., 2020).
  - **Temperature-sensitive:** In febrile conditions or areas with localized inflammation, skin temperature may increase, activating the release of soothing or antipyretic active ingredients encapsulated in thermosensitive nanocarriers (GOYAL et al., 2020).
- **Specific Cellular Targeting:** Nanoparticles can be functionalized with ligands that bind to specific receptors present on certain skin cell types, such as keratinocytes, fibroblasts, or melanocytes. This allows bioactives to be preferentially delivered to target cells, maximizing efficacy and reducing the total required dose. For example, brightening active ingredients can be specifically targeted to melanocytes in cases of hyperpigmentation (SRIVASTAVA et al., 2019).

- **Adaptation to Individual Skin Barrier:** The integrity and lipid composition of the stratum corneum vary among individuals and can be compromised in certain conditions (dry skin, dermatitis). Nanocarriers can be adapted to optimize permeation in different barrier states, ensuring that active ingredients reach where they are needed, regardless of the user's specific skin characteristics (ELIAS, 2005).
- **Modular Formulations:** Nanotechnology facilitates the creation of "building blocks" for formulations. Different nanocarriers, each containing a specific bioactive, can be combined in varied proportions to create a personalized final formulation. This allows unprecedented flexibility in creating on-demand products, adapted to the individual's skin profile (MOHANTY; SAHOO, 2020).

The integration of nanotechnology with advanced diagnostics and artificial intelligence allows personalization to go beyond ingredient selection, encompassing how these ingredients are delivered and activated in the skin, making the treatment truly adapted to each person's biological and dynamic needs.

CHALLENGES AND FUTURE PERSPECTIVES

CHALLENGES

Despite the immense potential of combining plant bioactives, nanotechnology, and personalization in dermatology, several challenges need to be overcome for this approach to reach its full maturity and become widely accessible.

- **Regulation and Safety of Nanomaterials:** The primary concern lies in the safety of nanomaterials. Although many studies indicate the safety of specific nanocarriers, the lack of global and harmonized regulation for nanoparticles in cosmetic and dermatological products creates uncertainty. Issues such as long-term toxicity, potential bioaccumulation in internal organs, interaction with complex biological systems, and environmental impact after disposal still require more research and clear guidelines (ZHANG et al., 2020). The distinction between nanoparticles that remain on the skin surface and those that penetrate deeper layers or the bloodstream is crucial for risk assessment.

- **Production Cost and Scalability:** The development and production of nanocarriers and personalized formulations are complex and currently high-cost processes. Research and development of new nanosystems, optimization of encapsulation processes, and industrial-scale manufacturing require significant investments in technology and infrastructure. This can make final products inaccessible to most consumers, limiting their widespread adoption (GOYAL et al., 2020).
- **Standardization and Quality Control:** The complexity of nanotechnological formulations and the variability of plant bioactives make standardization and quality control difficult. Ensuring the uniformity of nanoparticle size, encapsulation stability, purity of bioactives, and reproducibility of personalized formulation across different batches is a considerable technical challenge (MOHANTY; SAHOO, 2020).
- **Consumer Acceptance:** Despite growing interest in natural and personalized products, there may be resistance or distrust from consumers regarding nanotechnology, due to the perception of "chemicals" or a lack of understanding about what nanomaterials are and how they work. Transparent communication and public education are essential to build trust (PATIL et al., 2018).
- **Need for More Robust Clinical Studies:** Although promising studies exist, most are still in preclinical phases or small-scale clinical studies. Randomized, double-blind, placebo-controlled clinical trials, involving large populations and long-term follow-up, are needed to prove the superior safety and efficacy of personalized nanotechnological formulations with plant bioactives (SRIVASTAVA et al., 2019).

- **Infrastructure for Personalization:** The implementation of truly personalized treatments requires robust infrastructure for data collection (genomics, microbiome, skin diagnosis), AI analysis, and, potentially, on-demand product manufacturing at retail points or specialized laboratories. The logistics and integration of these systems are complex (ZHANG et al., 2020).

FUTURE PERSPECTIVES

Despite the challenges, the future of personalized dermatology with plant bioactives and nanotechnology is extremely promising, with several potential development areas.

- **Smarter and Multifunctional Nanocarriers:** The next generation of nanocarriers will be even more sophisticated, capable of responding to multiple stimuli (pH, temperature, enzymes, light) and delivering different bioactives sequentially or simultaneously to optimize biological response. The development of nanosystems that interact more precisely with the skin microbiome is also an area of great interest (CHEN et al., 2021).
- **Total Integration of Diagnosis and Formulation:** The trend is towards the complete integration of advanced diagnostic devices (portable and home-use) with AI platforms that, in real-time, will analyze the skin profile and current needs, generating a personalized formulation that can be produced in smart dispensers at home or in specialized pharmacies. This will democratize access to tailored treatments (BAUMANN, 2009).
- **Advances in Understanding Nanomaterial-Skin Interaction:** In-depth research on how nanomaterials interact with skin cells, the immune system, and the skin microbiome at a molecular level will enable the design of even safer and more effective nanosystems, minimizing any potential risks (ELIAS, 2005).
- **Expansion to Chronic Skin Diseases:** Beyond aesthetic and anti-aging care, nanotechnology and personalization have vast potential in treating chronic skin diseases such as psoriasis, atopic dermatitis, rosacea, and melasma. Targeted delivery of drugs and anti-inflammatory or immunomodulatory bioactives can revolutionize the management of these conditions, reducing systemic side effects (SRIVASTAVA et al., 2019).
- **Biomanufacturing and Sustainability:** The development of more sustainable biomanufacturing processes for nanomaterials and plant bioactives, using green chemistry and biotechnology principles, will be crucial to ensure the environmental viability of this technology in the long term (GOYAL et al., 2020).
- **Telemedicine and Digital Dermatology:** Telemedicine and digital platforms will facilitate consultations with dermatologists, who can interpret skin diagnostic data and adjust personalized formulations remotely, making care more accessible and convenient (ZHANG et al., 2020).

In summary, the convergence of plant bioactives, nanotechnology, and personalization is paving the way for an unprecedented era of dermatological treatments, where science and nature unite to offer highly effective solutions adapted to the uniqueness of each individual.

CONCLUSION

The journey towards more effective and truly personalized skin care finds a promising and innovative path in the fusion of plant bioactives and nanotechnology. This article has demonstrated how plant-derived bioactives, with their rich diversity of therapeutic properties, can have their potential fully exploited. *In vitro* plant cell culture offers a controlled, sustainable, and high-purity source for these phytochemicals, overcoming the limitations of traditional extraction. Subsequently, nanotechnology, by encapsulating and delivering these bioactives via nanocarriers, overcomes barriers of stability, solubility, and skin permeation, optimizing not only bioavailability but also enabling controlled and targeted release, minimizing undesirable effects.

Personalization, driven by advancements in genomics, skin microbiome analysis, advanced diagnostics, and artificial intelligence, elevates this synergy to a new level. By understanding the biological uniqueness of each skin, it is possible to formulate tailored treatments that act on specific pathways and respond to the individual's dynamic conditions. Nanotechnology, in this context, acts as a crucial enabler, allowing the creation of intelligent delivery systems that adapt to specific skin stimuli, ensuring the right active ingredient reaches the right place at the right time.

Although significant challenges, such as regulation, production costs, and the need for more robust clinical studies, still persist, the future prospects are encouraging. The development of smarter and multifunctional nanocarriers, the full integration between diagnosis and formulation, and the expansion into the treatment of chronic skin diseases are just some of the directions this research and development area is taking.

Ultimately, the combination of plant bioactives, nanotechnology, and personalization represents a redefinition of the skin care paradigm. It not only promises more effective and safer products but also a future where skin health and beauty are treated with the precision and individuality each person deserves, incessantly challenging the status quo of generalized approaches and paving the way for truly biointelligent solutions.

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