Chemistry:
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CONTENTS

CHAPTER 1

Dendrimers: Synthesis, Properties, and Applications of Monodisperse Macromolecules

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Introduction

Dendrimers are a well-characterized kind of synthetic macromolecule displaying a uniformly defined, monodisperse, globular structure that provides them with the scope for relevant applications in fields of biomedicine and materials science (Pérez-Ferreiro, Abelairas, Criado, Gómez, & Mosque-ra, 2023) (Abbasi et al., 2014). The branched and tree-like arrangement of its spherical structure, with a core, repetitive branched units, and a large number of functional peripheral groups, makes these macromolecules peculiar with respect to linear or randomly branched polymers (Pérez-Ferreiro, Abelairas, Criado, Gómez, & Mosquera, 2023). From this fabulous structural precision arises the possibility of treating adequately their physicochemical properties adequately, leading to controlled interactions of their final applications inside the various biological systems and of particular materials (Bizzarri et al., 2021). Such structural control exposes some possibilities of performances in such fields as drug delivery, medical imaging, catalysis, etc. (Lyu, Ding, Tintaru, & Peng, 2020).

Definition and Historical Context

The word "dendrimer" is a portmanteau originating from the Greek words "dendron" (tree/branch) and "meros" (part) which aptly reflects their tree-like or highly branched morphology (Kwan & Leung, 2020). The first reported synthesis of such macromolecules can be traced back to Vögtle in 1978, who called them "cascade molecules" (Huang, Kao, Selvaraj, & Peng, 2022). It was, however, the pioneering work of Tomalia et al. in 1985 on poly(amidoamine) dendrimers and, independently of each other, Newkome et al., which brought dendrimer chemistry into the limelight and thereafter laid the groundwork for modern dendrimer synthesis and characterization (Fréchet, 2002). Subsequently, Fréchet's development of the convergent synthetic method has provided an alternative approach, with some of the drawbacks of the initial divergent approach addressed (Mirsharghi, Boas, Heegaard, & Nyström, 2016). Collectively, these important developments defined the basic tenets of modern dendrimer chemistry, providing methodologies for their controlled, stepwise synthesis, which permitted a high degree of control of their structural integrity and macroscopic properties

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(Mirsharghi, Boas, Heegaard, & Nyström, 2016; Chawla, Kaushik, Singh, & Manila, 2020). These breakthroughs permitted the design of highly specialized macromolecules with tunable features, which is paramount to their diverse applications (Singh, Dar, & Hashmi, 2014). This precise architectural control over the dendrimer structure, including its core, branching units, and peripheral functional groups, has a direct effect on their physicochemical properties and thus their utility in a variety of research and technological areas (Potluri, Ramulu, & Pardhasaradhi, 2004) (Klajnert-Maculewicz & Bryszewska, 2001).

Structural Framework of Dendrimers

The basic structure of dendrimers is composed of three areas: an initiator core, radially arranged branching units, and an outer layer of peripheral functional groups (Mendes, Pan, Torchilin, 2017). This structure, looking like spherical, hyper-branched trees, their size, shape, the outer surface chemistry, and consequently, their ability to interact in numerous situations are all determined (Mittal et al., 2021). The central core, or starting core of the molecular structure, determines the overall symmetry of the dendrimer and provides anchor points for later generations of branches (Mukherjee, Mukherjee, Abourehab, Sahebkar, Kesharwani, 2022). The branches, often termed "generations", radiate away and in number (if each branch double or triple in number), and each subsequent generation, or increase in number, will tend to increase the molecular density and the overall diameter of the dendrimer (Vilanueva, Guzmán, Villanueva, 2016). The earlier poly (amidoamine) dendrimers synthesised by Tomalia et al., are examples of the increase in generations of dendrimers, whereby, from the first generation (G1 - G6) increases in known and reliable increments of the molecular weights are present, with apparent increase in the physical dimensions because of the apparent exponential increase in the branch units (Lyu, Ding, Tintaru, Peng, 2020) (Xiao et al., 2020). The "generation number" gives a basis for this generation process. Each time the generation increases by 1 unit, an additional generation of branch units having their origin in the previous generation is produced, so progressively altering the size of the dendrimer and the density of the terminal groups present (Enríquez-Cabrera et al., 2020). For example, the G6 dendrimer has a much larger molecular weight and a greater number of terminal groups than the G1 (Torres-Pérez et al., 2020). The progressive growth produces highly monodisperse macromolecular substances with a narrow molecular weight range, which differentiates them from the conventional polymers where a very different state of polydispersity is a frequent phenomenon (Jebbawi, Fruchon, Turrin, Blanzat, Poupot, 2020) (Lloveras, Liko, Muñoz-Gómez, Veciana, Vidal-Gancedo, 2020). The peripheral portions with many modifications, prepared of functional groups, can be opened for chemical substitutition, thus allowing for the production of both solubility, biocompatibility and targeted molecular recognition, for special applications to be made (Caminade, Beraa, Laurent, Delavaux-Nicot, Hajjaji, 2019) (Oyeniyi, Abdurahma, 2019) (Vashist, 2013). These peripheral groups are important for conjugation to therapeutic agents, imaging moieties or targeting ligands, and their use in drug delivery and diagnostic applications (Wu, Ficker, Christensen, Trohopoulos, & Moghimi, 2015) (Agrahari, Singh, Mukherjee, & Tiwari, 2020). The results of these exponential increases in peripheral functionalities at each generation have a significant effect on the stability, solubility, flexibility and chemical reactivity of the dendrimer, extending to the overall shapes in space and on the surface (Chawla, Kaushik, Singh, & Manila, 2020). With increasing dendrimer generations the macromolecule changes from a flexible, open and amorphous structure, to one that resembles a more solid, compact form, approximately spherical in structure, that allows the encapsulation of the guest molecules in these branches of the dendrimer (Sorroza-Martínez et al., 2020) (Algar et al., 2021). This structural development is important as with greater dendrimer generations there will usually be exhibited a very close shell pattern of density, density being maximum to the core and reducing as one proceeds towards the periphery (Morgado et al., 2021). Systematically, a study of dendrimers of G3 to G5 will show a plateau of the repeating units as they appear along the molecule, this indicates a density of high localization, therefore less atomic mobility (Morgado et al., 2021). This shell density is particularly evident in G4 and G5 dendrimers and gives a heavy back-folding with terminal groups, even bringing some terminal groups towards the core, while in overall structure, tending to produce more density towards the outer regions (Morgado et al., 2021). This complicated structural shape therefore of the dendrimers, where the internal spaces and multitude of surface developments can be accurately engineered, gives dendrimers the versatility not seen in other polymeric systems, for the envelopment of active compounds and specific molecules in molecular interactions (Gaballu et al., 2018) (Lenz, Mladek, Likos, Kahl, & Blaak, 2010) (Morgado et al., 2021).

Physicochemical Properties

Dendrimers have a special set of physical and chemical properties driven by their unique, repetitively branched, highly ordered structure (Szota et al., 2024), which include specific molecular weight, high monodispersity, high degree of surface functionality, etc. This architectural control leads to good control of their dimensions on the molecular nanoscale as well as the chemistry taking place at their surface, which, in turn, allows for selective interaction with biological systems and different materials (Pandita et al., 2014). Monodispersity means reliable activity is obtained, a significant factor when size and distribution control is important in applications such as targeted drug delivery (Sandoval-Yáñez &

Castro, 2020) applications. Moreover, the monodisperse size gives predictable pharmacokinetic and pharmacodynamic properties with low variability from batch to batch (Zhang et al., 2024). Also, the exact molecular mass and spherical shape of dendrimers, particularly that of the PAMAM dendrimers, allows for a comparison with biological macromolecules such as proteins as G3, G4 and G5 PAMAM dendrimers have the approximate sizes of insulin, cytochrome C and hemoglobin, respectively (Gaballu et al., 2018). The many different surface functional groups that can be modified impart the possibility of tuning various properties of the product, so crucial for optimizing biological properties and performance as materials with respect to solubility, charge and reactivity (Gaballu et al., 2018). The different generations of dendrimers have a marked influence on their flexibility, degree of encapsulation as well as biological properties (Wang et al., 2018). For example, often the higher generations have a dense core construction rather than a dense shell, since structures of the outer terminal groups fold back towards the core due to entropy considerations to leading to a more compact, hard-sphere-like conformation (Blaak, Lehmann, & Likos, 2008). The internal arrangement in the structure may influence the different aspects, e.g., the internal cavities for encapsulation and distribution of the charge effect on the surface of result products (Fréchet, 2002). The polyvalent nature and internal cavities of these nanostructures also account for their properties as pharmaceutical excipients and increase the solubility of drugs poorly soluble in water as well as biologically active conjugates (Santos, Veiga, & Figueiras, 2019; Mittal et al., 2021). Apart from drug delivery, they possess optical properties including intrinsic fluorescence, which allows for their further applications in diagnostic imaging as well as particle dimension determinations (Mittal et al., 2021). The pKa values of the amine groups of the dendrimers, particularly the primary amines of PAMAM dendrimers and tertiary amines located inwards, critically influence their biological and physical properties and interactions taking place in the various physiological media. (Asandei et al., 2017). For instance, the pKa of tertiary amines (~9.5-10.5) or primary amines (~5.5-7.0) will determine the protonation state and thus determine the net charge of the dendrimers as well as aggregation, and interactions with biological membranes and proteins (Laskar & Dufès, 2021) (Wang et al., 2018). This subsequently has a major influence on the uptake and biodisponibility, and therapeutic efficacies and net toxicity effects, clearance of the systemically transmitted drugs (Cheng & Xu, 2008) (Fernandes et al., 2021).

Synthetic Strategies

To fine-tune a dendrimer's architecture and its resulting properties, chemists must turn to tactics that fall into three broad camps: divergent routes, convergent routes and hybrid combinations (Patra et al., 2018). Each approach carries its set of trade-offs in terms of scalability, purity and the level of precision it can achieve. The divergent growth route, kicking off from a core and branching outward makes it possible to crank out batches of dendrimers. Yet in practice, it often stumbles over reactions and the birth of glitches a problem that gets worse as you push into higher generations (Torres-Pérez et al., 2021). To stave off the creeping accumulation of these flaws -flaws that would otherwise erode the monodispersity and functional performance of the end product- the protocol leans on purification after each step. In contrast the convergent route pulls together pre-crafted fragments (dendrons), toward a central core. This grants control and reduces defects since the smaller intermediates are easier to purify (García-Álvarez & Martínez-García 2021). The drawback, however, is that the method is generally less scalable for production and can become increasingly tangled when targeting high-generation dendrimers. Hybrid strategies, solid-phase synthesis being an example, blend the strengths of convergent routes yielding a workable compromise, between scale-up potential and exact structural fidelity, especially when crafting higher-generation dendrimers that bear precise functional groups. This combined divergent/convergent tactic, often dubbed the double-stage convergent approach mitigates many of the constraints by generating the building blocks divergently and then piecing them together convergently (Lyu, Ding, Tintaru, & Peng, 2020). In the years, click chemistry has surged to the forefront as an appealing avenue, for dendrimer synthesis, furnishing rapid, efficient assembly under mild near-physiological conditions while retaining an impressive level of fidelity (Huang, Kao, Selvaraj, & Peng, 2022). When these cutting-edge synthetic tactics are combined with the evolution of purification protocols, they become indispensable for surmounting the obstacles that accompany dendrimer fabrication, especially when the ambition is to translate the process to large-scale clinical or industrial settings (Xiao et al., 2022). Even though the convergent route falters in scalability and yields as the dendrimer generations climb it still proves indispensable for fashioning dendrimers that are remarkably uniform and possess controlled molecular weights (Ajith, Almomani, El-hissi, & Husseini, 2023). By contrast, the divergent route scales up readily for synthesis yet its ability to preserve structural integrity and purity wanes with each additional generation, leading to a surge in defects and making purification increasingly problematic when reactions remain incomplete (Fréchet, 2002). So in practice, the divergent approach is broadly employed across a host of dendrimer types. Continues to be the favored technique for most dendrimers on the market (Mirsharghi, Boas, Heegaard, & Nyström, 2016).

Major Dendrimer Families

In turn, these different synthetic considerations have produced a number of important dendrimer families, which are typified by the chemical nature of their core molecule, branching units and peripheral species. The characteristics of these compounds greatly influence their physical and chemical character, biocompatibility and suitability for different applications. Poly(amidoamine) dendrimers represent by far the most studied and commercially available family, mainly due to their well defined structure, solubility in water and favourable function-alibity of their surface (Devi & Kumar, 2025). These poly(amido-amine) dendrimers, which arise from repetitive amidation and reduction reactions, contain, as core structure, ethylene-diamine, whereas the branching units consist of repeating units of methyl acrylate, ethylenediamine (Tang, 2017). Inside these dendrimers there exist large quantities of tertiary amine groups which have pKa values which vary from 4.0 - 6.0, and which thus dictate their protonation state and influence their tendency to encapsulate guest molecules by means of electro-static interactions, whilst the terminal primary amine groups (pKa approximately 9-10) constitute no with ample sites for conjugation and attach-ment of targeting ligands or therapeutic agents (Chen, Wang, Xie, & Gong, 2018). Poly(propyleneimino) dendrimers having an aliphatic nature with their polyamine branches, represent another of the important families and hence find application in many catalytic and materials sciences ot perhaps more publicised volumes due to their internal high density of aminal species (Ajith, Almomani, Elhissi, & Husseini, 2023) . In addition to PAMAM and PPI dendrimers, there do exist other families of specialized dendrimers such as polylysine dendrimers, which as the name suggests are based on peptide units , which in turn is supposedly of a biocompatible nature, carbosilane and phosphorus dendrimers, which are formed from the inclusion of inorganic elements, giving them stability and electronic properties. Although PAMAM dendr-mers are still widely used and investigated, especially in their pro-perties as carriers for delivery of drugs and or genes, however their divergently proposed method of manufacture whereby ethylene-diamined is used as basic core, and subject to stages, illicit structural defects in 29% of all productions upto the fifth generation of production (Gaballu et al, 2018) (Morgado et al., 2021), whereupon charactersitic heterogeneity of their structure can arise advantageously or disadvantageously in this case as with respect to their biological activity thus leading to a complication of cahracterization and purification of the resultant species before application in drug based bio-medical experiments (Morgado et al., 2021). Polypropyleneimino dendrimers much more advanced in manufacture, which are recognised more or less in aggregate by their root core diaminobutantine, possess vast property profiles, having a natural aliphatic nature facilitating a high density of secondary and primary amine functional groups, etc., which establish their suitability for applications in most diverse ranges of both biological and materials science applications (Ajith, Almomani, Elhissi, & Husseini, 2023; Saintmont et al, 2020). These dendrimers, having such characteristics are especially PAMAM and PPI dendrimers, gives great significance to their amine terminated surfaces, which has extreme affrontation and high sensitivity to ph variations in general which allows for limited release properties of encapsulated agents or cargo, and facile conjugation with the greatest variety of good targeting ligands (Marquez, Madu, & Lu, 2018)(Peltek, Muslimov, Zyuzin, & Timin, 2019).

Characterization Techniques

Because of their structural intricacies and possibility of defects, particularly in higher generations, precise characterizations are necessary for dendrimers to ensure that they possess the requisite molecular structure and purity. Such techniques are necessary not only to confirm the presence of the desired molecular architecture, but also in regard to dispersion of properties and quality generally which are required to enable reproducible scientific and translational results. For these reasons, techniques such as Fourier Transform Infrared spectroscopy and nuclear magnetic resonance are frequently employed for the chemical verification of the presence of functional groups and integrity of structure in dendrimers (Prados, Barrios-Gumiel, Mata, Marina, & Garcia, 2021). More specifically, FTIR gives information on the presence of the characteristic bonds and functional bases, while NMR spectroscopy, when applied in the widely used leaves of (i.e., ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy for phosphorus-containing dendrimers), gives better information about the chemical environment and interconnectivity of atoms within the molecular structure of dendrimer (Majoral et al., 2021). Ultraviolet-visible spectroscopy is also applied to assess the extent of surface modifications and the presence of encapsulated chromophoric guests, while gel exclusion chromatographic methods and dynamic light scattering are utilized to determine molecular weight distribution, hydrodynamic diameter, etc., as well as for the required monodispersity of dendrimers owing to their potential structural heterogeneity (Torres-Pérez et al., 2021) (Chawla, Kaushik, Singh, & Manila, 2020). In addition to these, more sophisticated methods, including Transmission Electron Microscopy and Atomic Force Microscopy, are employed for the visualization of dendritic nanoparticles, in respect of their size and morphology, which give direct evidence of their size covering scales corresponding to the nanometer size range and surface topography. Other methods, such as small-angle X-ray scattering and small-angle neutron scattering, are powerful tools that can be employed in elucidating internal structure, shape or conformation of dendrimers in solution, and provide critical information with regard to the various parameters of structure, such as gyration radius and structural scattering length density (Mirsharghi, Boas, Hegaard, &

Nyström, 2016). Mass spectrometry, particularly MALDI-TOF MS, is widely employed to check the molecular weight and also to ensure the successful conjugation of different moieties to the periphery of dendrimers and thus the purity and functionalization efficiency of the dendrimer conjugates (Lesniak et al., 2024). These similarities of methods collectively serve to maintain the desired degree of control over the synthesis and modification of dendrimers, which is necessary for their utilization in sensitive, quantitatively defined areas, such as drug delivery and diagnostic applications (Caminade, Laurent, & Majoral, 2005; Torres-Pérez et al., 2021).

Applications of Dendrimers

The unique structural features of dendrimers, including their highly branched architecture, tunable surface functionality, and precise nanoscale dimensions, render them exceptionally versatile for a broad spectrum of advanced applications across biomedical and industrial sectors.

Biomedical Applications

Dendrimers are studied intensively for their biomedicinal potential in studies of drug delivery systems, gene therapy, and diagnostic imaging utilizing their ability to encapsulate and/or conjugate different therapeutic and imaging agents (Ahangarani-Farahani, Bodaghi-fard, & Asadbegi, 2022). These properties are due to their monodisperse characteristics, multi-valence, and well-defined globular structure. Moreover, dendrimers have a very good loading capacity and therefore, the ability to enhance the targeted delivery of their load into the body. This property of the dendrimers allows researchers to overcome many of the critical barriers to effective drug delivery (Noriega-Luna et al., 2014). For example, the polyamidoamine dendrimers through their well-defined nature and high loading capacity of bioactive compounds have been important in the controlled drug delivery, gene therapy and theragnostic studies (Torres-Pérez et al., 2021). These studies have demonstrated their properties as nanocarriers for a variety of different drugs with improved bioavailability and lower systemic toxicity due to their targeted delivery (Mittal et al., 2021). Other studies have also shown that dendrimers provide much greater solubility of drugs, and allow for drug release in a controlled manner, both of which are valuable properties in considering the therapeutic evaluations in the treatment of cancers and cardiovascular diseases (Sandoval-Yáñez & Castro, 2020) (Mhlwatika & Aderibigbe, 2018). It is also important to note that the surface chemistry of dendrimers is tunable and allows for the conjugation of targeting ligands to improve the targeted delivery of their bioactive vessels to diseased tissue and minimise side effects (Ajith, Almomani, Elhissi, & Husseini, 2023). Dendrimers are not only useful in drug delivery, but they are also of value for gene delivery, where they are useful to encapsulate and protect nucleic acids (DNA, RNA) for an efficient uptake and gene expression, which is important in gene therapy studies (Yang, Jia, & Yang, 2021). They are also useful molecules in gene delivery studies because of their ability to bind and protect nucleic acids and when their surfaces are charged positively so to also serve as effective vectors to aid in the process of transfections (Žmudová et al., 2023).

Industrial Applications

Apart from their biomedical uses, dendrimers are of considerable interest in industrial applications, where they can be utilized as catalysts, in advanced coatings, and in high-sensitivity sensor technologies, due to their structural benefits. Their nanosized structure and high surface area-to-volume ratio lead to increased activity and selectivity in a variety of catalytic applications. For example, dendrimers are excellent scaffolds for holding metal nanoparticles attainable in heterogeneous catalysts that are highly efficient, readily recyclable, stable, and excellent in performance (Huang, Kao, Selvaraj, & Peng, 2022). In like manner, their well-defined structure and peripheral groups lend them to infrastructure in advanced coatings, which afford improved durability, corrosion resistance, and tailored surface properties. In the sensor area, it is the high density of functional groups on the dendrimers' surface that enhances the molecular-recognition and signal-amplifying propensities, which lead to increased selectivity and sensitivity.

Challenges and Future Outlook

Dendrimers hold potentially exceptional value and versatility, though they face many serious issues limiting their clinical and industrial application, being due to a complicated and sophisticated method of synthesis which is laborious and thus expensive and difficult easily to obtain in large bulk (Li et al., 2022). In addition, the question of possible cytotoxicity, especially with cationic forms of dendrimers limits their possible application from the aspect of peculiar surface chemistry and construction such as is obtainable from surface modification techniques used (Li et al., 2022). Therefore, clinical and commercial use of dendrimers demands improved, easier and cheaper methods of synthesis and means for making them more compatible with biological systems and showing less toxicity (Contín et al., 2019) (Dhull et al., 2024).

Conclusion

In conclusion, dendrimers are an important class of synthetic macromolecules with superior structural precision and functional versatility. Dendrimers hold great promise for the future within a wide range of manifold enlightened scientific and technical fields (Villanueva, Guzmán, & Villanueva, 2016). Sufficient advances in the methods of generation of these structures, including solid phase methods, are an imperative in order to overcome present production obstacles and to increase the accessibility of these complex macromolecules for universal technical use (Huang, Kao, Selvaraj, & Peng, 2022). Biodegradable dendrimer designs and the generation of solid phase synthesis methods of appropriate scale are, however, paramount in order for future applications (Huang, Kao, Selvaraj, & Peng, 2022). Further, employment of new synthetic strategies, particularly those which involve convergent methodologies, could help in affording dendrimers which were asymmetric as well as those which incorporate mixed features which could lead to therapeutic advantage and to new properties (Chow, Mong, Nongrum, & Wan, 1998). Also, investigation of these types of structures should be the source of further knowledge of the long term stability, in vivo, and of degradation profiles, so that the safe and effective employment of these dendrimers may be ensured when applied therapeutically. The use of advanced methods of characterization will per?haps be of great importance for the complete understanding of the pharmacokinetics and pharmacodynamics of dendrimers and thus may help in providing a faster transition from the laboratory research to the clinical reality (Lyu, Ding, Tintaru, & Peng, 2020) (Pérez-Ferreiro, Abelairas, Criado, Gómez, & Mosquera, 2023).

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CHAPTER 2

Natural and Environmental Friendly Cosmetic Raw Materials

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INTRODUCTION

Nowadays, there is an increase in the use of cosmetic products made with natural and organic raw materials as an alternative to synthetic cosmetics using chemical substances. The main reason for the increase in interest in natural or organic cosmetics is the upbringing of new generations with an ecological environment and a sense of responsibility, resulting in the emergence of a consumer segment that establishes a connection between health and nature. Moreover, today's consumers are bombarded with information through social media such as internet advertisements and television programs, and are encouraged to make their own cosmetics with natural materials. While the use of natural and organic products prevents the harmful side effects of synthetic chemicals, this group of products conveys a message of cleanliness and hygiene to the consumer.

Most of green cosmetics for the reasons mentioned above, the personal care industry also responds to the increasing demand of the consumer by introducing many products to the market with organic and natural claims every year. These products can be 100% organic or 100% natural, as well as being produced with organic or natural content. The global natural and organic personal care market was $12 billion in 2017, and reached a market size of $29.9 billion in 2021 [1,2].

The mst important discussion topic regarding this group of cosmetics is whether the products actually possess the natural, organic, or environmentally-friendly, sustainable characteristics they claim to have, as well as product safety. The terms 'natural','organic', or'green' on cosmetic product labels not only indicate restricted use of synthetic raw materials, but also convey a message of health and environmental-friendliness. Research shows that organic product consumers are greatly influenced by packaging and labeling.

For example, a 2011 survey in France found that stating over 75% organic content on the organic shampoo packaging influenced consumer preference despite the price increase.

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Likewise, a 2018 survey in the UK revealed that consumers lacked a clear understanding of green cosmetics, despite their feedback on desiring safe, organic, and recyclable packaging.

Since the cosmetics market actually contains many unsustainable, so-called 'green marketing' (greenwashing) products, it is important to raise consumer awareness to distinguish these. Indicating on the label how much of the product's content is natural/organic, and having this content certified by international organizations, can increase the safety and reliability of such products and help prevent greenwashing.another advantage is the contribution of the certificate to sustainability in line with the requests in the regulations of the organizations.

In this review, the issue of natural and organic cosmetics, which has become an important tendency in cosmetics and a commercial market, has been discussed. After the definition of the concepts of green and sustainability in cosmetics is given and the definition of sustainability, the legal status of these cosmetic products and the relevant definitions of which organizations are certified by the organizations and the relevant definitions in the certificates and guidelines were explained. Green chemistry principles are taken into consideration in the production of green cosmetics. Used accordingly Raw materials, preferred production methods, difficulties encountered in production and packaging materials were informed about the effects of reducing water and plastic use in green cosmetics in terms of sustainability in terms of sustainability on waste management.

Green approach to cosmetics

Although the concept of cosmetics and sustainability seems to be very different at first glance, green cosmetics are avoided from the use of synthetic raw materials, adaptation to green chemistry principles, carbon foot and waste management are produced with sustainability approach due to the attention of the sustainability approach [4].

Global warming and increasing environmental pollution, the abundance of storage areas for cosmetic companies that offer new products every year, the fact that cosmetic products become waste by filling their shelf life at the end of a certain period of time, and the discussion of the safety of chemical content used in cosmetic products in social media are the causes of this approach in the cosmetic industry. In addition, the “Corporate Social Respponsibility; which began in the United States in the 1920s (USA) in the 1920s and expanded the scope of the 1960s in 1960s and added environmental problems to the working strategies of the companies, is among the reasons for the“ green and organic cosmetic brands of natural and organic cosmetic brands in the early 2000s.

The concept of green chemistry, which aims at economic, social and environmental sustainability, forms the basis of the definition of green cosmetics. The US Environmental Protection Agency (EPA) defines sustainability as conditions that ensure the productive harmony of humans and nature; the protection of natural resources and ensuring access to water, materials, resources and social and economic needs for future generations by sufficiently reducing the human impact on the environment [6].

In general, in the context of the green approach in cosmetics, sustainability is achieved by using biodegradable packaging, reducing the use of synthetic raw materials and plastic packaging, developing reusable products or packaging, developing multi-benefit products, using recyclable materials, and producing less toxic substances for the environment. When natural or organic cosmetics are evaluated in this respect, it is seen that sustainability is also encouraged by the certifying organizations. For example, the COSMOS standard encourages the sourcing of raw materials from organic agriculture, respecting biodiversity, using natural resources responsibly, ensuring that the processes and manufacturing are clean, and being respectful of human health and the environment. Similarly, the Ecocert Greenlife standard aims to ensure environmentally friendly production processes, better management of existing energy and natural resources (water, air, soil fertility), and product quality and safety [7,8].

Green Cosmetics Legal Status

The European Union and the US Food and Drug Administration (FDA) directives do not have direct legal sanctions on the production and marketing of green cosmetics. There are no standardized definitions in existing regulations for such products. Therefore, such products are generally classified as 'natural' or 'naturally derived' by the cosmetics market, considering the natural or nature-derived nature of their functional ingredients. In addition, the term 'green' is used instead of 'natural' or 'organic'[3].

There are different standards used by different countries regarding green cosmetics. However, this situation is confusing for consumers and also creates problems in the formulation design of green cosmetic products. Therefore, the COSMOS standard, which is a common standard used in the definition of this group of cosmetic raw materials and products, has been established [9]. Another problem encountered in green cosmetics is the difference in standards for natural and organic cosmetic products between the US and Europe. In the US, natural and organic claims are seen as different claims with different formulation philosophies, while in Europe, organic and natural standards are intertwined A[1]Among the most well-known of these natural and organic cosmetic standards, which are widely used and defined as non-state market-driven, are Natrue (Belgium), BDIH (Germany), Ecocert Greenlife (France), CosmeBio (France), Soil Association (UK) and ICEA (Italy), as well as the COSMOS standard that has emerged from the harmonization of these standards.

Although it is global, it is used more in Europe. In addition, there are different organizations that provide organic/natural certification such as IBD in Brazil, NASAA in Australia, and JAS in Japan [9-11]. The certificates provided by these organizations aim to standardize not only the issues related to raw materials and the processes applied to them, production, storage, packaging, and labeling to improve the final product quality, but also energy consumption and waste management. Each standardization organization has its own regulations in this regard, and a certificate logo used on the packaging is given when the product is certified [4].

In the USA, certificates for organic cosmetics are provided by organizations such as NOP (National Organic Program) established under the USDA (United States Department of Agriculture), NSF/ANSI organic personal care products standard, OASIS (Organic and Sustainable Industry Standards), and NPA (Natural Products Association) [9].

The FDA has not defined organic cosmetics. However, organic cosmetics defined by NOP in the 'Code of Federal Regulations' must meet both the USDA organic claim requirements and the FDA cosmetic product labeling and safety requirements [12]. In addition, NOP regulations provide certification that the agricultural contents are produced under conditions that meet the definition. Among the international USDA/NOP certification providers are organizations such as Ecocert (France), ETKO (Turkey), ICEA (Italy), IBD (Brazil), NASAA (Australia), Pro-cert (Canada), BIOH (Greece) [13].

Natural and Organic Standards

In addition, the presence of the logos of these certificates on the label allows consumers to more easily obtain information about the raw materials, production and packagin marketing method, called 'green marketing', uses green color, plant or flower images, or words like 'natural' and 'environmentally friendly' on the packaging to appeal to consumer perception. However, in such products without any official documents, the product is often not as sustainable as claimed. For the reasons listed above, it is important to obtain certification from standardization organizations for natural and organic cosmetics and to include these certification logos on the label. The natural and organic standardization bodies and the requirements for the certificates they issue, which are frequently seen in green cosmetics, are explained below:

COSMOS

The COSMOS (COSMetics Organic Standard) Standard was established in 2002 in Nuremberg by BDIH, Cosmebio, Ecocert Greenlife, ICEA, Soil Association and the later withdrawn BioForum, with the aim of harmonizing organic natural standards in Europe. This standard evaluates differently the raw materials from different natural sources that have undergone physical or chemical processing, water, minerals and synthetic (petrochemical) products [3, 9, 10]. COSMOS is an organization that successfully harmonized the requirements of multiple standardization bodies [10].

Currently, there are 12 different authorized certification providers for the COSMOS standard. These are ETKO and IFC Global operating in Turkey,ACO in Australia, Bureau Veritas, Ecocert Greenlife and Cosmecert SASU in France, IONC in Germany, ICEA i n Italy, Control Union Korea Co. and KTR in South Korea, CAAE in Spain, and Soil Association in the United Kingdom [14].

Ecocert Greenlife

Ecocert Greenlife, founded in 1981 in France, is a leading certification and inspection body for organic products in Europe. It certifies both natural and organic products. While it is active in more than 80 countries today, it is originally based in France, where it certifies Approximately provides certificates for its 70s. Ecocert promotes organic farming, the sustainability of raw material sources, and other environmental initiatives [3,9].

CosmeBio

CosmeBio is an organization that provides ecological and organic certification. It was established in France in collaboration with Ecocert and the Ministry of Agriculture. It has two different certifications, Biolabel and Ecolabel. Biolabel provides organic certification similar to Ecocert, while Ecolabel provides a natural certification similar to Ecocert [3].

Soil Association

The Soil Association, established in England in 1967, is the first organization to provide organic certification. In addition to organic agriculture and food, it has also been providing certification in areas such as textiles and cosmetics since 2002.

The certificates issued by the Soil Association only cover organic cosmetics and related agricultural and food products. According to this standard, 95% of the agricultural content must be organic. Only water and substances required for processing can be non-organic. Water is considered a natural product, so products containing water are not considered 100% organic. Organic content products require 70-95% organic content, and this must be indicated on the label [3].

ICEA

ICEA, established in Italy in 2002 with the support of the Ministry of Organic Agriculture, is an organization that provides organic certification. In addition, it also provides standardization for packaging. ICEA provides vegan certification (ICEAVEGAN and ICEA VEGETARIAN) not only for cosmetics but also for the food sector. The use of GMOs is prohibited in this certification [3].NaTrue (The International Natural and Organic Cosmetics Association) is a non-profit organization established in 2008 to create legal definitions for natural and organic cosmetics, based on the complexity in the recognition of cosmetic products. Its founding members Weleda, Wala-Heilmittel, Logocos, Laverana, Santaverde and Primavera are also the founders of another standard, BDIH [9]. NaTrue has also signed an agreement oncertification criteria with IBD (Instituto Biodinâmico, Brazil).

For a cosmetic product group to be able to carry a certification label, at least 75% of the products belonging to a particular brand (or sub-brand) must be certified. If there are products certified by another certification standard, they can be included in the 75%calculation for the first 2 years to obtain the NaTrue certification. After this period, the brand must have 75% of its products certified by NaTrue.

IBD

IBD (Instituto Biodinâmico, Brazil) is an organic certification provider located in Latin America. It is accredited by IFOAM (International Federation of Organic Agriculture Movements), ISO/IEC 17065 (European market regulation CE 834/2007), Demeter (international market), USDA/NOP (North American market) and SISORG (Brazil Organic Conformity Assessment System), and is therefore a globally recognized certification. While similar to NaTrue in terms of requirements, this certification does not accept water as an input [15].

BDIH

BDIH (Bundesverband Deutscher Industrie- und Handelsunternehmen) is a German/European standard established in Mannheim, Germany, that only provides natural certification. It has played a role in the establishment of IONC GmbH and the COSMOS standard. Its founding members are the cosmetic companies Weleda, Wala, Logocos, Laverana, Santaverde and Primavera. Due to the import volume of German-origin natural cosmetic products, BDIH is the leading natural cosmetic certification in Europe.

This is one of the organizations. Although it does not issue organic product certificates, it verifies the organic status of the raw materials in certified products [9].

The basic requirements of some standards commonly encountered in natural and organic cosmetics are compared in Table 1 [9,16,17]. Some common certification logos in Turkey and Europe are given in Figure 1.

In addition to the standards mentioned above, another organization that provides guidelines for natural and organic cosmetics is the International Organization forStandardization (ISO). ISO is an international standard with member organizations around the world.

The federation of their establishments. The 'ISO 16128-Guidelines on Technical Definitions and Criteria for Natural and Organic Ingredients and Products' standard prepared by ISO technical committees provides guidelines on definitions and criteria for natural and organic cosmetic ingredients and products, and these guidelines are specific to the cosmetics industry.

The ISO 16128 standard consists of two parts. The first part, 16128-1:2016, is a guide on technical definitions and criteria for natural and organic cosmetic contents and products. ISO 16128-2:2017 explains the approaches for calculating the natural, naturally-derived, organic and organic source for the content categories defined in ISO 16128-1 [3,18].

Unlike other certifications, the ISO 16128 standard does not include labeling claims for end consumers and claims related to sustainability. Minimum threshold values are also not specified. The aim here is for the raw materials to meet the natural criteria and to indicate the natural or organic content of the finished product in quantity [3].

Legal Status of Natural and Organic Cosmetics in Turkey

The limits on the content of organic cosmetics in Turkey are determined in the Guide on Natural and Organic Cosmetic Ingredient and Product Claims prepared by the Turkish Medicines and Medical Devices Agency (TİTCK) based on Articles 6 and 10 of the 25823 numbered Cosmetics Regulation dated 23.05.2005 [19]. According to the guide, a n 'Organic/Ecological Cosmetic Product' is a finished cosmetic product composed of at least 95% by weight of organic/ecological cosmetic ingredients produced in accordance with the principles of organic agricultural activities, proving that it meets the requirements of being organic from raw material to finished product [19].

The guide provides detailed explanations on the extraction agents, auxiliary substances, minimum natural/organic substance percentages byproduct category, claims and warnings regarding labels and promotional materials, and the required documents for the finished product, that can be used in the production of natural and organic cosmetics.

In the guide, animal-derived components, except for plant, inorganic-mineral or dead vertebrates, are defined as natural cosmetic ingredients, and natural cosmetic ingredients derived through biotechnological processes are also defined as such. Organic cosmetic ingredients must be produced in accordance with the principles of organic farming activities. Natural cosmetic products containing natural and derived natural cosmetic ingredients are classified as Level 1, while natural cosmetic products containing organic ingredients are classified as Level 2. Level 2 includes finished cosmetic products that meet the definition of natural cosmetic products and are made using at least 70% natural ingredients or derived natural ingredients that are produced in accordance with organic farming principles or directly obtained from nature. Level 3 defines organic cosmetic products, which are finished cosmetic products that meet the definition of natural cosmetic products and contain at least 95% natural ingredients or derived natural ingredients that are produced in accordance with organic farming principles or directly obtained from nature. According to Article 7 of the guideline, it is required that necessary certification by internationally recognized certification bodies is made, proving that manufacturers comply with the guideline requirements for natural cosmetic products.

In the certification of natural and/or organic cosmetic components and products, internationally recognized harmonized standards (TS ISO 16128-1/ISO 16128-1, ISO 16128-2) and the criteria of internationally recognized certification bodies are taken into account. Misleading statements should not be included in the commercial name of the product. It is also possible to obtain Ecocert, Cosmos, USDA/NOP certificates through the certification bodies ETKO (Ecological Agriculture and Control Organization) and IFC Global (International First Certification Global) operating in Turkey.

Commonly Encountered Definitions in Green Cosmetics

In natural cosmetics, the fact that raw materials are obtained from natural sources means that these cosmetics do not contain unnatural components such as colorants, synthetic chemicals, petrochemical-derived raw materials. However, this is not enough for organic products. In this group of formulations, raw materials obtained through controlled organic farming must be used. In accordance with Good Agricultural and Collection Practices (GACP)

However, a natural component is not necessarily organic [4]. Also, when it comes to natural and organic products, different definitions as explained below may be encountered depending on the amount of natural or organic raw materials in the product. For the consumer to overcome marketing deceptions, they need to know the differences in these definitions [21].

Synthetic Content

Synthetic raw materials are substances or materials produced by chemical processes and not naturally occurring.

Natural Content

Natural raw materials are substances and materials harvested, extracted or collected from natural sources and then processed without chemical reactions. In this direction, the material undergoes physical processes such as washing, coloring, distillation, grinding, purification or concentration 'without chemical reaction'. The production of cosmetic raw materials through biotechnological methods or fermentation can also be included in these definitions.

Naturally Derived Ingredient

Naturally derived ingredients are obtained by using a natural raw material as the starting point of a chemical process to produce a new chemical that does not exist in nature or the original material.

Natural Identical Content

To produce a material that is natural identical, a synthetic substance is usually used instead of a natural starting material. For example, L-menthol is usually produced synthetically instead of being extracted from peppermint oils; synthetically produced ceramide-like structures are better accepted than animal-derived ceramides.

Organic

They are natural contents derived from organic farming methods. Organic farming is a form of agriculture that prevents the use of synthetic fertilizers, pesticides, plant growth regulators and animal feed additives. The products of producing farms must be certified in order to be used as cosmetic ingredients.

The common point of definitions such as natural, organic, and herbal cosmetics is that they are produced with materials found in nature. What is expected from these cosmetics is that they are produced using clean technology with responsible use of natural resources, and presented in biodegradable or reusable packaging, in short, that they are environmentally friendly [4,22].

Raw Materials Used in Green Cosmetics

The raw materials preferred in the production of green cosmetics are selected considering natural/sustainable options. Synthetic or petrochemical-derived raw materials, chemicals that may have allergy or irritation potential or that may cause endocrine system problems are not preferred in this group of cosmetic products. The risky raw materials in cosmetics include parabens, mineral oils, aluminum, triclosan and phthalates used in packaging [23].

Parabens are weakly absorbed through the skin, and their estrogenic effect increases depending on the length and branching of the alkyl side chain. Methyl paraben shows the weakest estrogenic effect among paraben derivatives. Hydroxybenzoic acid, the common metabolite of all parabens, is inactive under in vitro conditions.

Especially butyl paraben causes DNA damage, but methyl and ethyl parabens are carcinogenic No evidence has been found regarding the effect. According to the Scientific Committee on Consumer Safety (SCCS), methyl and ethyl parabens can be used safely in cosmetics up to 0.4% alone and up to 0.8% in combined use for human health [23].

Similarly, it is reported that the toxicity potential of saturated or alkylated hydrocarbons present in trace amounts in mineral oils is not high. According to the European Chemicals Agency (ECHA), if pharmaceutical-grade mineral oil is used in cosmetics, there is no carcinogenic risk associated with hydrocarbon residues [23]. However, even if purified, hydrocarbons have the potential to cause irritation and allergies, and due to the importance of reducing petroleum-based products for sustainability, this group of chemicals is not preferred in green certifications.

In general, when examining green standards, it is seen that in addition to natural and organic raw materials collected from nature in a controlled manner, physically processed natural substances and raw materials derived from natural sources through chemical reaction are also accepted. However, the chemical processes permitted by the certifications are limited. For example, in COSMOS and NaTrue certification, processes such as acetylation, amidation, condensation, dehydrogenation, dimerization, esterification, glycosidation, hydrogenation, hydrolysis, saponification, oxidation, and neutralization are accepted; while ethoxylated or propoxylated (alkoxylation) raw materials, bleaching, phosphation and polymerization are among the prohibited processes. The chemical processes to be applied to the raw material must not disrupt the ecological balance due to the sustainability policy, and must be sensitive in terms of energy consumption and waste .

These are processes. The criterion sought in these methods is also sensitivity in terms of ecological balance, energy use and waste management. Physical processes frequently encountered in green cosmetics include centrifugation, evaporation by distillation or blowing, purification by filtration/ultrafiltration or dialysis and ion exchange, freezing, grinding, lyophilization, maceration, infusion, percolation, UV sterilization, ultrasonication and vacuum pumping [16].

Natural and organic raw materials that can be used instead of synthetics When looking at the raw material groups used in the production of natural and organiccosmetics, it is seen that emollients, emulsifiers and surfactants, antioxidants, antimicrobial preservatives and solvents are frequently used.

Emollients

Natural vegetable oils and their esters are frequently used as fatty raw materials with emollient properties that soften and moisturize the skin. These oils are raw materials rich in natural fatty acids/triglycerides [21,24].

Emulsifiers and Surfactants

Lecithin, a phospholipid obtained from soybeans, egg yolk or sunflower seeds, is a good natural option. Lecithin derivatives such as hydrogenated lecithin or sucrose, glucose,sorbitan, glyceryl or polyglyceryl esters, alkyl glucoside mixtures, inulin lauryl carbamate, olive oil esters and their mixtures can be used. Likewise, as natural anionic emulsifiers, raw materials such as glyceryl stearate citrate, acyl glutamates,acyllactylates, acyl phosphates obtained by esterification of hydrophilic acids (such as citric, lactic, glutamic) and natural fatty alcohols and fatty acids and glycerin can be used [21]. Anionic surfactants such as sodium laureth sulfate (SLS) that are commonly used in products like shampoo and shower gel are not preferred in green cosmetics due to their detergent effect. However, if SLS is non-ethoxylated (SLES), it can be acceptable. Some standards like Ecocert allow the use of amphoteric substances that act as foaming agents in this group of cosmetics. Cocoamidopropyl betaine (CAPB) derived from coconut oil can be used in combination with SLES as an amphoteric surfactant to reduce the irritation potential on the skin.

Biodegradable fatty alcohols derived from coconut or palm oil, and alkyl polyglucosides (such as coco, lauryl, decyl and capryl/caprylic derivatives) derived from corn or potato-based glucose, as well as saponins extracted from plants like Yucca glauca or Quillaja saponaria, can be used due to their surfactant properties. However, extracts rich in saponins are generally quite colored and it is difficult to formulate an acceptable foam [21].

Silicones

Silicons, which are among the limited raw materials used in green cosmetics, give a slippery feel to products and increase spreadability on the skin. In green cosmetics, marine and

plant-based silicons are used as a few natural alternatives. For example, Chondrus crispus extract, a chitosan derivative derived from fungus (chitosan succinamide), and milk thistle extract (Silybum marianum ethyl ester) can be listed. They are designed to provide a natural silicon-like feel, like a non-occlusive protective film, in water-rich products such as emulsions [21].

Polymer

Natural derivatives of polymers used for thickening, emulsion or suspension stabilization purposes are preferred in green cosmetics. Natural polymers such as xanthan gum (fermentation derivative), Irish moss (Crondus crispus), corn starch (Zea mays), microcrystalline cellulose, Tara gum (Caesalpiniaspinosa gum) and acacia (Acacia senegal), algae and clays can be given as examples. The biggest disadvantage of many of these materials is that they can give a sticky feel on the skin or have the potential to create a fibrous appearance in the product. Another challenge is to achieve a clear appearance when used with surfactants [21].

Solvent and humectans

Glycols such as propylene or all -threatened glycols are widely used and influenced by the substances that are widely used to extract botanical materials. Propylene glycol is an oil derivative that is believed to penetrate the skin and possibly weaken protein and cellular structures. Instead of glycerin, water, alcohol, such as other appropriate water or natural oils are preferred in green cosmetics. As a green alternative, solvents can be obtained by fermentation from a few. For example, propandiol is produced by fermentation from corn sugar. Glycols derived from biofermentation are also available and pentholine glycols [21].

Odor components

In green cosmetics, mixtures of essential oils, oleoresin and other natural aromatic compounds are used instead of synthetic odor compounds. FDA accepts essential oils as cosmetic raw materials and does not require additional leave for odor substances. However, odor mixtures should comply with the arrangements of odor allergens that essential oils may drink and IFRA (International Fragrance Association; International FragranceAssociation), which define their maximum limits [21,25].

ISO standards encodes each essential oil content with separate certification. For example Rosmarinus officinalis L. ISO 1324: 1988 ile sertifikalandırılır. ISO Technical Committee (ISO/TC54) also standardizes the analytical methods required for the specifications and controls of all essential oils [25]. For extraction of flavours supercritic carbondioxide extraction is used [21].

Antioxidants

Natural Vitamin E component alpha-tocopherol and vitamin E-rich oils can be cited as alternatives to synthetic antioxidants. Rosemary (Rosemary) extract or oil is also widely used [21]. At the same time, all marine organisms contain vitamins, especially in high amounts in macro and micro algae. Algae are particularly rich in vitamins E and C and provitamin A (β-carotene) [26]. In addition, the avenanthramides found in oats; pomegranate polyphenols (ellagic acid and punicalagin); oligomericproanthocyanidins rich in polyphenol derivatives from malted barley extract and sesame (Sesamum indicum) oil rich in ferulic acid and sesamin and sesamolin can be cited as natural antioxidants [21].

Colouring agents

In cosmetic formulations, a range of oil-soluble or water-soluble natural coloring materials, usually from the food industry, are used. Natural colors are mainly obtained from plant seeds (such as annatto); roots or rhizomes (such as turmeric); sugars (caramel); leaves and stems (such as spinach); flowers (such as lutein from Tagetes); vegetables (such as red cabbage, red beet juice and carrot oil extract); fruits (grape juice); and algae (beta carotene). Carmine, a red color, is also technically natural, but from an animal source (cochineal insect).ot accepted due to being obtained from natural sources and the risk of allergies. Mineral pigments approved by Ecocert Greenlife, pearlescent and mica-based shimmering particles are used for decorative cosmetics [21].

UV Absorbers

As of now, there are no naturally derived sun protection ingredients allowed by European Union or US regulations. Most natural sunscreen product manufacturers use inorganic UV protective materials such as titanium dioxide (TiO2) and zinc oxide (ZnO). UV-absorbing plant extracts rich in phytochemicals can be utilized, but they cannot be used as the sole sunscreen component. Examples include black tea (Camellia sinensis), aloe (Aloevera), ginkgo (Ginkgo biloba) leaves, pomegranate (Punica granatum) and tomato (Solanum lycopersicum) fruits, curcumin (Curcuma longa) rhizome, propolis resin, avocado (Persea americana) and grape (Vitis vinifera) seeds, and Peruvian maca (Lepidium meyenii) [21,27].

pH arrangements

Sodium or potassium hydroxide used to set pH in formulations is considered synthetic in terms of certification. A more natural, but more expensive alternative, l-arginine amino acids, alpha hydroxy acids such as lactic or citric acid obtained from natural sources can be used [21].

Waterfall Makers

Ethylene diamine tetra acetic acid (EDTA), which is frequently used in cosmetics, is among the suspicious raw materials in terms of environment and human health. Instead of EDTA, fitic acid or sodium salt in the bodies of hazelnuts, seeds and cereals can be used. However, the costs of these substances are quite high. Another possibility is to use ethylene diamine dysucinic acid (EDDS), which is produced from aspartic acid, although not natural, unlike EDTA [21].

Preservatives

Microbial deterioration in cosmetic formulations may lead to physical deterioration of the product, or pathogenic presence in the product may pose a threat to consumer safety.

Chemical protectors are added to cosmetics, drugs and foods to protect against microbial contamination. However, in recent years, many questions about whether traditional/chemical protectors are safe. Consumers have pushed the doubts about chemical preservatives, especially paraben derivatives, to seek alternative approaches for the protection of cosmetics [28]. These approaches will be mentioned in the following parts of the compilation.

Cosmeceutical raw materials

In natural and organic cosmetics, botanical, marine and microbial raw materials are used due to their anti-aging effects. Among the frequently encountered marine raw materials are antioxidant-rich marine algae such as Laminaria digitata, Kappaphycus alvarezii and Chondrus crispus [29]. Collagen and chitosan derived from marine sources, as well as proteins and peptides obtained from algae such as Porphyra, Wakame,Spirulina, Chlorella, are also examples of natural cosmeceutical raw materials [21].

Among the natural cosmeceutical raw materials are seed oils extracted from the fruit of Pentaclethra macroloba (Pracaxi), emollient vegetable oils such as coconut, jojoba and argan, cosmeceutical actives derived from halophilic microorganisms such as Ectoin, glycoin obtained from Myrothamnusflabellifolia, and beta glucan derived from oats [21,30-32].any food ingredients such as tea, coffee, grapes, lemons, and coconut also contain various natural actives. Most of these cosmeceutical actives, which have antioxidant effects, are used for nutricosmetic purposes. Examples of commonly encountered nutricosmetic components, the foods they are found in, and their areas of use are given in paper [33].

The organic raw materials obtained by standardizing the conditions such as seed diversity, growth environment and fertilizer use, non-use of pesticides, drying and storage in organic

agriculture carried out in accordance with good agricultural practices, and the finished products in which these raw materials are used, are certified by standardization The extraction method used in raw material procurement also affects the product. Natural materials such as any form of water or ethyl alcohol, glycerin, vegetable oils should be used for extraction. If other solvents need to be used, these solvents must be recycled and completely removed from the finished product. The use of aromatic,alkoxylated,

halogenated, nitrogen or sulfur-based solvents is not permitted in the production of organically certified products [16].The most preferred method in terms of sustainability is the use of supercritical fluid extraction and supercritical solvents, which are in line with green chemistry principles. In supercritical fluid extraction, the substance dissolves in the liquid and is then separated from the liquid by reducing the pressure. Supercritical solvents are consideredenvironmentally friendly as they reduce the use of organic solvents. The most commonly used supercritical solvent in extraction processes is carbon dioxide (CO2).

In COSMOScertification, all extractions using water or a third solvent, including supercritical CO2 extraction, are required to be carried out using natural materials.Another challenge encountered in developing green cosmetic formulations is themicrobiological preservation of the product. The use of synthetic preservatives is limited in green cosmetics, and different standards have different requirements for preservatives.Among them, the Ecocert standard still allows phenoxyethanol and parabens, provided that the purchased materials only. The BDIH standard allows the use of some synthetic preservatives such as organic acids, their salts and ethyl esters (benzoic acid, salicylic acid, sorbic acid) and benzyl alcohol, using the term 'nature-identical'. Similarly to Ecocert, the NaTrue standard also allows nature-identical preservatives such as benzoic acid, salicylic acid, sorbic acid, and sulfation, hydrogenation and synthetically protected components using the term 'nature-identical'.The approach towards preservatives in natural and organic cosmetics is to manufacture preservative-free or self-preserving products. Preservative-free cosmetics envisage the use of sterilization and/or appropriate packaging design to reduce or eliminate chemical preservatives in the product. However, this approach is insufficient in highly dosedpackaged and high water content natural formulations

[37]. In such formulations, the self-preserving product approach, which also includes the use of natural compounds with antimicrobial effects or multifunctional raw materials instead of synthetic chemicalpreservatives, is preferred today.The self-preserving product approach aims to create an environment in cosmetics that inhibits microbial growth or kills microorganisms. Compliance with Good Manufacturing

Practice (GMP) requirements such as water filtration, microbial testing of raw materials, and equipment disinfection can significantly reduce potential contamination risks. Additionally, approaches such as preferring oil-in-water emulsion type in production, pH control of the environment, and reducing the water content in the formulation are also beneficial. Due to the need for water for microorganisms to grow, reducing the free water in the formulation through the addition of polyols, protein hydrolysates, amino acids, salts, and hydrocolloids, defined as water activity, and achieving a low water activity value also helps to prevent microbial growth in cosmetics [28,37]. Air-free packaging is also frequently preferred in self-preserving cosmetics [37].

One of the basic approaches in its preparation is the other. Among the frequently encountered examples due to their protective efficacy are the volatile oils and extracts obtained from plants such as Rosmarinus officinalis, Lavandula officinalis, Pteronia incana, Artemisia afra, Thymus vulgaris, Eucalyptus globulus, Laurus nobilis, Salvia officinalis and Melaleuca alternifolia [28]. Raw materials such as glyceryl caprylate, glyceryl caprate,glycerylundecylenate, phenylethyl alcohol, sodium anisate/sodium levulinate, which are not permitted as preservatives in the regulations but have secondary protective effects, are also among the multifunctional raw materials encountered in natural cosmetics [21].

Although they have antimicrobial activity, natural substances are insufficient for the broad-spectrum protection required in large-scale manufacturing. Most of these substances are not active against the Pseudomonas species and other Gram-negative bacteria, which are the main sources of water-borne contamination in cosmetic production, or very high concentrations of essential oils are required for antimicrobial effect. Poor miscibility of natural materials in emulsions, incompatibility with other cosmetic raw materials, and safety risks due to irritation also pose problems. Furthermore, using a natural preservative in a cosmetic product is quite expensive [21].

Packaging in Green Cosmetics

In recent years, due to global warming, environmentally friendly (eco-friendly) or green packaging has gained importance and its preference by consumers has increased.Therefore, sustainable cosmetic manufacturers also use environmentally-friendly labels prescribed by their certifications on their products, strengthening their preference by consumers and their image in the market [38].Environmentally friendly packaging can be examined in two groups: biodegradablepackaging or recyclable, refillable packaging (recycle, refillable/reuse). In terms of cost and efficiency, biodegradable materials are often preferred [38].Among the materials frequently used in environmentally friendly cosmetic packagingproducts are cellulose acetate, cellulose, ceramics, glass, metals such as aluminum, iron, stainless steel, paper/cardboard, polyethylene, polyethylene terephthalate, polyethylene terephthalate glycol, polylactic acid, polypropylene, rubber, wood, and other 100%non-GMO sourced materials [16,34]. In recent years, the market has seen examples of refillable packaging, and bamboo is generally the packaging preference of organic makeup brands.

Green packaging has advantages such as having less impact on the environment and global warming, reducing costs in the long run through recycling and less packaging production, saving energy, having less interaction with the formulation compared to the classic materials (especially plastics), and increasing brand image and preference. However, there are also disadvantages such as the high cost of the starting material and some being insufficient in protecting the product from environmental conditions, microbial contamination, and mechanical aspects [38].

Sustainability and Waste Management in Green Cosmetics

Sustainability refers to the life cycle of a product. Although the scope is more comprehensive than the responsible use of agricultural resources expressed by natural, organic or green words and not using synthetic raw materials, the concept of sustainability in cosmetics produced with allegations such as green and organic is important [3].Sustainable cosmetics are prepared with green chemistry principles. Green chemistry is the design of chemical products and processes to reduce or eliminate the use and production of dangerous substances. By intervening in the processes and substances that make up pollution with the principles of green chemistry, it is aimed to minimize or remove the formation of pollution and to save recycling and energy [39,40]. In this context, water used, packaging and plastic wastes are expected to be minimized and waste is expected to be soluble in nature.The use of water in the green cosmetic industry is an important issue. Many formulations contain water. According to ISO 16128-1 regulations and many of the natural/organic standards, water is a natural content and includes water obtained from plants such as extract or juice as well as pure water used in formulations. In addition, water, organic agriculture and production, which is the initial step in organic products, in the production of energy used in processes such as cooling and heating,

Equipment cleaning is also required. It is not possible to use zero water in the life cycle and supply chain of a cosmetic product. However, among the goals of green cosmetic companies is to protect clean water sources and reduce the water footprint [41]. For example, supercritical fluid extraction is also a frequently preferred method because it reduces water use. Reducing the use of plastic in packaging is also a factor that reduces water consumption. For example, plastic packaging materials such as high density polyethylene are not sustainable in terms of sustainability as they require large amounts of water consumption in their production [41].

According to the EU's Packaging and Packaging Waste Directive (94/62/EC), packaging must be produced in the minimum volume and weight required for the safety, hygiene and

acceptance of the entire product by the consumer; harmful or hazardous components must be kept to a minimum and must be reused, recycled and/or recovered after use. Nowadays, many cosmetic companies prefer plastic packaging that can be recycled after consumer use. The most widely used 100% recyclable plastic is polyethylene terephthalate (PET). The advantage of using PET is that, although it still requires water for its production and recycling, it is produced using naturally occurring ethylene glycol and terephthalic acid.

It is a biodegradable resin. Another alternative to PET packaging is the use of certified renewable polypropylene (PP) packaging material. The advantage of renewable PP packaging is that it cannot be visually distinguished from fossil fuel-based plastics byconsumers [41]. In the certifications given to green products, it is generally recommended to reduce packaging, replace it with recycled or renewable source-based alternatives, and design packaging with the most suitable size and weight with the least resources [16,17,41].

Another issue where green cosmetics align with green chemistry principles is the biodegradability of waste. One of the most important problems created by waste chemicals in the ecosystem is microplastics . Microplastics are particles made of plastic materials less than 5 mm in size, forming the micro-sized fraction of plastic waste. The cosmetics industry uses plastic components in a wide variety of products . These plastic materials are synthetic, non-biodegradable and insoluble in water, composed of polymers mixed with additives to provide the desired properties and functionality to the materials. Most microplastic waste is invisible to the naked eye, and is transported to rivers and seas through rinsing products containing plastics and household wastewater. These microplastics that cause environmental pollution can remain in nature for centuries without decomposing.

Production with green chemistry principles, the preference for reusable or recyclable packaging, the reduction of plastic content in products or the use of plastic-free components, can reduce microplastic emissions in green cosmetics. The concept of zero waste is also important for sustainable cosmetics companies today

CONCLUSION AND DISCUSSION

The desire to transfer natural resources to future generations and health problems caused by synthetic raw materials and products have made sustainability important in cosmetics today. The use of natural and/or organic raw materials, the standardization of these raw materials and finished products are among the most important issues in these cosmeticproducts presented alongside environmentally friendly, sustainable, natural or organic expressions.While there are regulatory and related standardization bodies in almost every countrytoday, it is possible to come across European standards such as COSMOS and Ecocert, as well as NaTrue, ICEA, Soil Association and BDIH in many countries including our country. From the point of view of Turkey, organic and/or natural certification can be obtained from organizations such as ETKO and IFC Global, including the USDA/NOP standard of the USA. These standards and the Guide on Natural and Organic Cosmetic Ingredient and Product Claims published by TİTCK provide information on the raw materials and packaging materials allowed to be used in green cosmetics, physical or chemical processes, and the calculation of the natural/organic content percentage in the product. Another common certification for natural and organic cosmetic contents and products is the ISO 16128 standard. It is required that the certification logos obtained from the relevant organization be provided on the product packaging for the organic or natural definitions of cosmeticproducts. This is necessary to ensure that consumers are properly informed and to show that the product is produced in accordance with green chemistry principles, with minimal environmental waste.

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