

INSTITUTO UNIVERSITÁRIO EGAS MONIZ

MESTRADO INTEGRADO EM CIÊNCIAS FARMACÊUTICAS

UNRAVELLING SKIN HYDRATION – NEW TRENDS IN MOISTURIZING INGREDIENTS

Trabalho submetido por
Mariana Sousa Duarte
para a obtenção do grau de Mestre em Ciências Farmacêuticas

Novembro de 2024

INSTITUTO UNIVERSITÁRIO EGAS MONIZ

MESTRADO INTEGRADO EM CIÊNCIAS FARMACÊUTICAS

UNRAVELLING SKIN HYDRATION – NEW TRENDS IN MOISTURIZING INGREDIENTS

Trabalho submetido por
Mariana Sousa Duarte
para a obtenção do grau de Mestre em Ciências Farmacêuticas

Trabalho orientado por
Prof. Doutora Margarida Miranda

Novembro de 2024

Dedicatória

Aos meus avós.

Agradecimentos

Em primeiro lugar, quero agradecer à Egas Moniz School of Health & Science, por ter sido a minha segunda casa ao longo destes 5 anos e também por todas as aprendizagens que tive durante o meu percurso académico.

À minha orientadora, Prof. Doutora Margarida Miranda, por todas as orientações, dedicação e empatia, um obrigado nunca será o suficiente!

À Farmácia Cravidão e ao Hospital da Luz Lisboa, por me terem proporcionado a oportunidade de aprender ao lado de excelentes profissionais.

Às minhas colegas Ana Carolina, Catarina, Beatriz A., Beatriz M. e Mariana, foi um privilégio por vos ter conhecido e por fazerem parte do meu dia-a-dia durante estes anos. Nunca me vou esquecer por tudo o que passámos. Finalmente somos farmacêuticas!

Às minhas amigas Catarina e Mariana, por me acompanharem desde o secundário e por terem estado sempre a torcer por mim! Sem vocês nada disto seria a mesma coisa.

Às minhas amigas Ana e Inês, pela amizade e paciência que tiveram para mim durante este percurso, obrigada por terem sempre acreditado que eu seria capaz.

À minha querida amiga Beatriz, por ter sido o meu braço direito desde sempre, por nunca ter desistido de mim e pela força que sempre me transmitiu.

Ao meu namorado, por todo o amor, calma e apoio que me transmitiu ao longo deste tempo.

À minha família, especialmente ao meu pai e à minha mãe, por todos os esforços que fizeram para que eu conseguisse cumprir o meu sonho.

Por fim, um agradecimento muito especial aos meus avós, que foram um pilar importante para mim durante toda esta jornada. Avô, espero que estejas orgulhoso.

Abstract

The skin is a dynamic organ that plays a crucial role in human health and well-being. It is the main organ in contact with the environment and external agents, so it is extremely important to keep the skin barrier hydrated.

Moisturizers are topical products that play a fundamental role in any skin care routine, helping to improve and maintain the skin's barrier function. Their mechanism of action is to minimize transepidermal water loss (TEWL) by forming a hydrolipidic film on the skin.

Moisturizers can be classified as hydrophilic (humectants) or lipophilic (emollients or occlusives). Humectants, thanks to their hygroscopic nature, are able to capture water, attracting it to the inner layers of the dermis. Occlusives, on the other hand, due to their lipid properties, form a physical barrier that reduces water evaporation. Emollients occupy the space between the cells of the *stratum corneum* (corneocytes), increasing cell cohesion and controlling TEWL.

The cosmetics market has evolved substantially, incorporating innovative ingredients to meet consumer needs. In 2022, Portugal ranked 14th in the European Union, with cosmetics consumption estimated to be 1488 million euros.

The popularization of social media and the internet has made consumers more aware of the potential risks associated with the use of various chemicals in cosmetics. Although these substances are legally regulated, with substantial studies on their safety, an increasingly number of consumers nowadays tend to prefer more natural products in cosmetics, especially in the ones that are used in a daily basis. In response to this market need, there has been a considerable increase in the demand for products that not only satisfy their aesthetic needs, but also that display a more natural and sustainable composition. In response, the cosmetics industry has invested significantly resources in developing products based on vegetable raw materials and other more sustainable resources.

Keywords: skin; cosmetics; moisturizers; sustainability.

Resumo

A pele é o principal órgão em contacto com o ambiente e agentes externos, sendo por isso extremamente importante manter a barreira cutânea hidratada.

Os hidratantes são produtos cosméticos e de higiene corporal que desempenham um papel fundamental em qualquer rotina de cuidados da pele, ajudando a melhorar e a manter a função de barreira cutânea. O seu mecanismo de ação consiste em minimizar a perda de água transepidérmica (TEWL), através da formação de um filme hidrolipídico na pele.

Os hidratantes podem ser classificados como hidrofílicos (humectantes) ou lipofílicos (emolientes ou oclusivos). Os humectantes, graças à sua natureza hidrosscópica, conseguem captar água, atraindo-a para as camadas internas da derme. Já os oclusivos, devido às suas propriedades lipídicas, formam uma barreira física que reduz a evaporação da água. Os emolientes ocupam o espaço entre as células do estrato córneo (corneócitos), aumentando a coesão celular e controlando a TEWL.

O mercado cosmético tem registado uma evolução substancial, na última década, sendo que se revela uma tendência cada vez maior para a incorporação de ingredientes inovadores, de carácter mais sustentável. Em 2022, Portugal ocupava o 14º lugar na União Europeia, com um consumo de cosméticos avaliado em 1488 milhões de euros.

A popularização das redes sociais e da internet sensibilizou os consumidores para os riscos potenciais associados à utilização de vários produtos químicos nos cosméticos. Embora estas substâncias estejam legalmente aprovadas, com segurança e eficácia comprovada, uma percentagem significativa de consumidores prefere ingredientes de origem natural, especialmente em produtos aplicados diariamente. Em resposta a esta necessidade do mercado, registou-se um aumento considerável da procura de produtos que satisfaçam não só as suas necessidades estéticas, mas que tenham uma composição natural e sustentável. Por isso, a indústria cosmética tem investido no desenvolvimento de produtos à base de matérias-primas vegetais e outros recursos mais sustentáveis.

Palavras-chave: pele; cosméticos; hidratantes; sustentabilidade.

Index

Dedicatória.....	i
Agradecimentos	ii
Abstract.....	1
Resumo	2
List of Figures.....	5
List of Tables	7
Abbreviations.....	8
1. Introduction	9
1.1. Composition and function of the skin barrier	9
1.2. Physiological Processes Involved in Skin Hydration	13
1.3. Hydration in cosmetics	17
1.4. Cosmetic products	21
1.5. Objectives	21
1.6. Methods	22
2. Traditional ingredients used in moisturizers	23
3. State of the art ingredients used in moisturizers.....	25
3.1. Hyaluronic acid	25
3.2. Ceramides	32
4. New Trends In Moisturizing Ingredients: By Products Of Plant Origin....	39
4.1. <i>Vitis vinifera (L)</i>	39
4.2. Algae	47
5. Conclusions and Future Perspective.....	57
References.....	59

List of Figures

Figure 1 – The layers of the skin. Adapted from (Meza, 2018).	9
Figure 2 – Structure of the epidermis. Adapted from (OpenStax, 2012).	10
Figure 3 – Physiological mechanisms of skin hydration. Adapted from (Barel et al., 2009).	14
Figure 4 – Bilayer arrangement of skin lipids. Adapted from (Voegeli, 2007).	16
Figure 5 – Main functions of a moisturizing product. Adapted from (Z. D. Draelos, 2018).	17
Figure 6 – Action mechanisms of moisturizers. Adapted from (Barnes et al., 2021). ...	19
Figure 7 - Emollients classification. Adapted from (Purnamawati et al., 2017).	20
Figure 8 – Molecular structure of hyaluronic acid. Figure adapted from (Fakhari & Berkland, 2013).	25
Figure 9 – Applications of HA and its derivatives. Adapted from (Fallacara et al., 2018).	27
Figure 10 – HA applications in cosmetics. Adapted from (Bukhari et al., 2018).	28
Figure 11 – HA action mechanisms. Adapted from (Juncan et al., 2021).....	29
Figure 12 – Basic structure of ceramides. Adapted from (Meckfessel & Brandt, 2014).	32
Figure 13 – Applications of ceramides in skin disorders. Adapted from (Kahraman et al., 2019).	34
Figure 14 – Mechanism of action of ceramides in skin hydration. Adapted from Freepik.	36
Figure 15 – Chemical structure of some examples of phenolic compounds. Adapted from (Zhou et al., 2022).	42
Figure 16 – Applications of <i>Vitis vinifera</i> (L). Adapted from (Sharafan et al., 2023). ..	43
Figure 17 – Algae classifications. Adapted from (Dini, 2023).	48
Figure 18 – Micro and macroalgae as mainstream bioactive compounds. Adapted from (Aslam et al., 2021).	49
Figure 19 – Applications of algal biomass. Figure adapted from Comissão Europeia (2022).	50

Figure 20 – Algae metabolites nutricosmetic potentialities. Adapted from (Dini, 2023).
..... 51

Figure 21 – Graphical abstract: Unravelling Skin Hydration – New Trends in
Moisturizing Ingredients..... 58

List of Tables

Table 1 – Chemical composition of natural moisturizing factor. Adapted from (Rawlings & Harding, 2004).	14
Table 2 – Common moisturizers and their effects on the skin. Adapted from (Barnes et al., 2021).	18
Table 3 – Examples of tissues and fluids containing HA. Adapted from (Chang et al., 2021).	26
Table 4 – Examples of products with HA and its derivatives that target skin hydration.	31
Table 5 – Nomenclature of the different classes of ceramides. Adapted from (Fujii, 2021).	33
Table 6 – Examples of ceramide-based moisturizing products.	38
Table 7 – Different chemical groups of polyphenols identified in different fruit parts. Adapted from (Nassiri-Asl & Hosseinzadeh, 2016).	40
Table 8 – Examples of grape-based moisturizing products.	46
Table 9 – Examples of algae-based moisturizing products.	54
Table 10 – Comparative analysis of the ingredients used in moisturizing cosmetic formulations that have been discussed throughout this work.	56

Abbreviations

AD – Atopic dermatitis

AQP3 – Water channel aquaporin-3

CERs – Ceramides

CosIng – Cosmetics Ingredients

EMA-HMPC – Committee on Herbal Medicinal Products in the European Medicines Agency's

EU – European Union

FA – Fatty acid

FD&C Act – Federal Food, Drug and Cosmetic Act

FDA – Food and Drug Administration

GAG – Glycosaminoglycan

HA – Hyaluronic acid

HFs – Hair Follicles

HMW-HA – High molecular weight HA

INCI – International Nomenclature Cosmetic Ingredient

LMW-HA – Low molecular weight HA

MMW-HA – Medium molecular weight HA

NaHA – Sodium hyaluronate

NMF – Natural moisturizing factor

OA – Osteoarthritis

pCERs – Pseudoceramide

PUFAs – Polyunsaturated fatty acids

RCT – Randomized controlled trial

SB – Sphingoid base

SC – Stratum Corneum

TEWL – Transepidermal Water Loss

vHMW-HA – Very high-molecular weight HA

1. Introduction

1.1. Composition and function of the skin barrier

The skin, the largest organ in the human body, represents approximately 16% of the body's weight and displays an extensive surface area, estimated to be around 2 m² (Castro et al., 2023). As depicted in Figure 1, structurally, the skin presents three distinct tissue layers: (i) epidermis, which is the outermost layer; (ii) dermis; and finally (iii) hypodermis, which is the deepest (Gilaberte et al., 2016). In what regards the skin's main functions, its primary role is to be the body's first line of defense against the surrounding environment. By being both a physical and chemical barrier, the skin offers essential protection against a variety of invasive agents, including pathogenic microorganisms, toxic agents and even ultraviolet radiation (Yousef et al., 2024). Furthermore, due to its bidirectional functionality, the skin also acts as a mediator between the body and the exterior. The skin is capable of control the water loss, electrolytes, and other constituents from the milieu interior while, and at the same time, reduce the entry of harmful or unwanted xenobiotics from the environment (M. Brown et al., 2024).

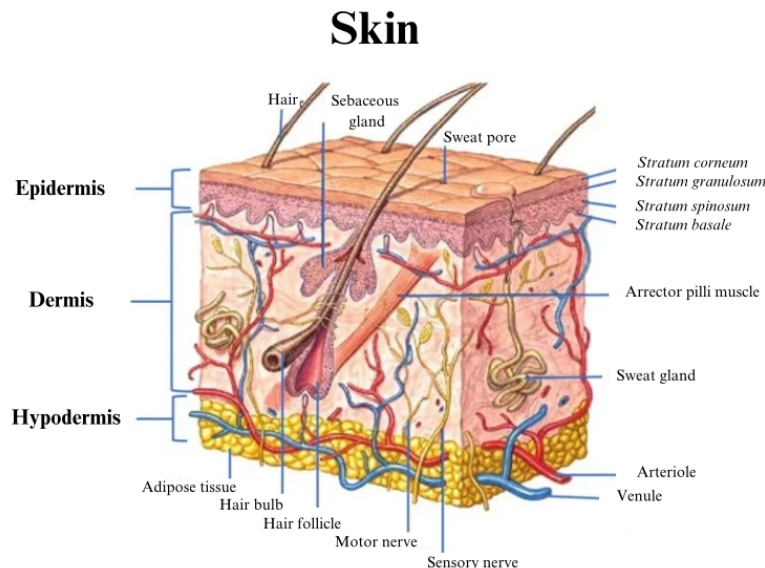


Figure 1 – The layers of the skin. Adapted from (Meza, 2018).

1.1.1. Epidermis

The epidermis is the top layer of the skin and its main function is to form a barrier between the body's internal structures and the external environment. This layer is also responsible for metabolising xenobiotics, as well as to promote the synthesis of melanin in melanocytes, the cells responsible for skin pigmentation and sun protection (Nunes et al., 2017).

Four distinct strata can be observed in the epidermis: *Stratum germinativum* or *basale*, *Stratum spinosum*, *Stratum granulosum* and *Stratum corneum* (Figure 2) (Baroni et al., 2012). A further layer, the *stratum lucidum*, is seen in the soles of the feet and palms of the hands, since these regard more thickened skin regions. However, *stratum lucidum* is difficult to notice, even microscopically (Freeman & Sonthalia, 2023).

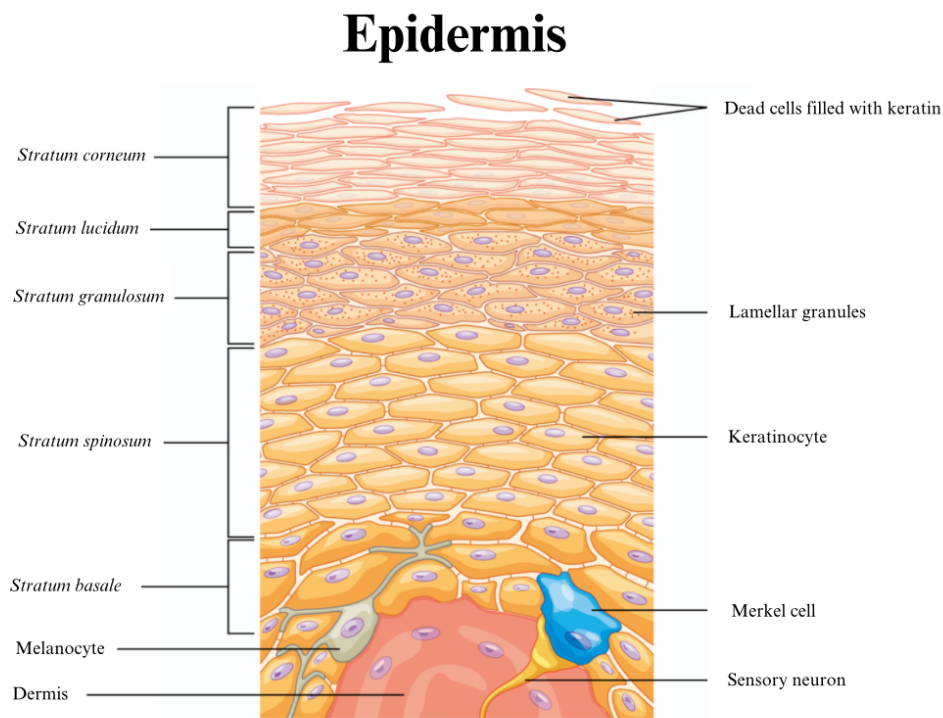


Figure 2 – Structure of the epidermis. Adapted from (OpenStax, 2012).

The non-viable epidermis, or better known as the *stratum corneum*, is essentially composed of a layer of protein-rich dead cells (corneocytes), which are embedded in a lipid matrix. This lipidic matrix is essentially composed by three main lipid classes: cholesterol, ceramides and free fatty acids (FFAs), which all play a key role in

maintaining the skin's hydration. These components will be presented in more detail in the following sections (Nunes et al., 2017). On the other hand, corneocytes are flat, hexagonal structures that contain keratin and are surrounded by a protein-reinforced envelope. This structure mainly regards a wide range of proteins, such as involucrin, loricrin, filaggrin, proline-rich proteins and keratolinin (Barel et al., 2009). The corneocytes of the *stratum corneum* arise from the differentiation of keratinocytes located in the *stratum granulosum*. Keratinocytes are the most abundant cells in the epidermis and are responsible for producing keratin, which gives the skin its resistance and impermeability (Tortora & Derrickson, 2016). As keratinocytes divide and migrate towards the outer layers of the skin, a process known as differentiation, these cells change their cellular content and morphology. Just below the *stratum corneum*, is the *stratum lucidum*, which is made of flattened cells without a nucleus (Freeman & Sonthalia, 2023).

The viable epidermis is made up of all the remaining layers. Then, there is the *stratum granulosum*, which is made up of cells that are continuously degenerating. These cells contain keratohyalin granules, which play an essential role in forming the epidermis lipid barrier (Barbieri et al., 2014; Seeley et al., 2011). The *stratum spinosum*, or better known as the Malpighian layer, consists of cells that are in the process of active cell division. In greater numbers, there are keratinocytes (which will later give rise to corneocytes), Langerhans cells (which play a key role in immune mechanisms and are considered macrophages) and melanocytes (Yousef et al., 2024). Finally, there is the basal layer, which is made up of 'stem cells' that continually divide to produce new cells in the epidermis. These cells gradually migrate to the uppermost layer of the skin, maturing over a period of 14 days. In the *stratum corneum*, they remain for another 14 days until they are eliminated from epidermis (a process known as cell turnover, which takes around 28 days) (American Skin Association, 2020; Brown et al., 2024). In this layer, there is another specialized cell type – the Merkel cell, which has a predominant role in tactile sensation, as well as in the transmission of sensory signals to the nervous system. Merkel cells display these functions due to their connection with nerve endings, present in the dermal side of the basement membrane and commonly found around the touch-sensitive sites of the body, such as the lips and fingertips (M. Brown et al., 2024; Woo et al., 2015).

1.1.2. Dermis

The dermis regards the mean layer of the skin, between the epidermis and the hypodermis. Its thickness is highly dependent on the body site, but usually it is about 3-5 mm thick (M. Brown et al., 2024). The main function of this layer is to strength, support and provide flexibility to the skin. Anatomically, the dermis is made up of two heterogenous layers: a lower (reticular) and upper (papillary) (M. Brown et al., 2024). The reticular layer is rich in collagen fibers, which are arranged parallel to the skin's surface (T. M. Brown & Krishnamurthy, 2022; Chanda & Singh, 2023). This layer is responsible for supporting the blood vessels, lymphatics, nerves, hair follicles (HFs), sebaceous glands, as well as the sweat glands. It is mainly composed by connective tissue, more specifically collagen fibers, that provide for mechanical strength, as well as elastic fibers for flexibility. These fibers are embedded in an amorphous gel-like matrix that also contains water, glycoproteins and glycosaminoglycans (e.g., hyaluronic acid and dermatan sulfate) with small amounts of heparan sulfate and chondroitin sulfate (M. Brown et al., 2024). On the other hand, the papillary layer is composed by loosely arranged collagen fibers, that seek to increase the surface area between the dermis and epidermis. Furthermore, this layer contains terminal networks of capillaries, that actively promote the exchange of nutrients, waste products and oxygen (M. Brown et al., 2024).

The dermis also possesses sensory receptors, responsible for receiving stimuli from the outside environment and feel pressure, pain and temperature (Castro et al., 2023; Gilaberte et al., 2016; Sociedade Portuguesa de Dermatologia e Venereologia, n.d.).

1.1.3. Hypodermis

The hypodermis, also known as subcutaneous tissue, is the deepest layer of the skin and its thickness can vary depending on the anatomical region, reaching up to 3 cm in the abdomen (Institute for Quality and Efficiency in Health Care, 2022). This layer is fundamentally made up of fat microglobules and fibrous collagen, but also blood vessels, lymphatic vessels and nerves (Jepps et al., 2013). Its function includes protection against physical trauma to the underlying tissues, storing energy, insulating the skin and providing a connection between the underlying structures, such as muscles and bones. (Jepps et al., 2013; Olatunji & Das, 2015). Like the other layers of the skin, its thickness

varies between individuals and can be influenced by factors such as gender, race, age and the anatomical region (Olatunji & Das, 2015).

1.2. Physiological Processes Involved in Skin Hydration

The hydration of the epidermis highly conditions both the appearance, as well as the physical properties of the skin. Skin hydration is influenced by various parameters, namely external humidity, skin structure, lipid and protein composition, the skin's barrier properties and also by the concentration of hygroscopic molecules, better known as natural moisturizing factors (NMF) (Hara-Chikuma & Verkman, 2008).

Natural moisturizing factors (NMF) are located exclusively in the *stratum corneum*, more specifically inside mature corneocytes. These compounds derive from the filaggrin, which as previously detailed, comprises a protein present in the viable epidermis. Through the hydrolyzation of this protein, a complex mixture of hygroscopic free amino acids, amino acid derivatives and salts is formed, which together constitute the NMF. Their composition, depicted in Table 1, mainly regards a mixture of natural hygroscopic molecules, being the majority amino acids and related compounds. These compounds account for 20 to 30% of the dry weight of the *stratum corneum* and play a key role in maintaining the water content of the *stratum corneum*, as well as to contribute to the skin barrier function (Bonté, 2011; M. Brown et al., 2024).

As hygroscopic molecules, NMFs have the ability to bind to water molecules, absorbing them and dissolving in the moisturizing water itself. This process is essential for maintaining hydration inside the corneocytes, which in turn keeps the *stratum corneum* and its outer layers moisturized. Not all the components of NMF are located inside the corneocytes, being sugars, urea and especially lactates mainly present outside these cells (Rawlings & Harding, 2004).

Table 1 – Chemical composition of natural moisturizing factor. Adapted from (Rawlings & Harding, 2004).

Chemical	Composition (%)
Free amino acids	40
Pyrrolidone carboxylic acid	12
Lactate	12
Sugars	8.5
Urea	7
Chloride	6
Sodium	5
Potassium	4
Ammonia, uric acid, glucosamine and creatine	1.5
Calcium	1.5
Magnesium	1.5
Phosphate	0.5
Citrate and formate	0.5

Skin hydration was only associated with the presence of NMF, but over time, other pathways for skin hydration have been discovered (Figure 3). These include: (i) the presence of endogenous glycerol as a natural humectant; (ii) the bilayer arrangement of skin lipids, as well as; (iii) the presence of tight junctions (TJ) in the *stratum granulosum* of the epidermis (Barel et al., 2009; Bonté, 2011). In the next sections, these mechanisms will be detailed.

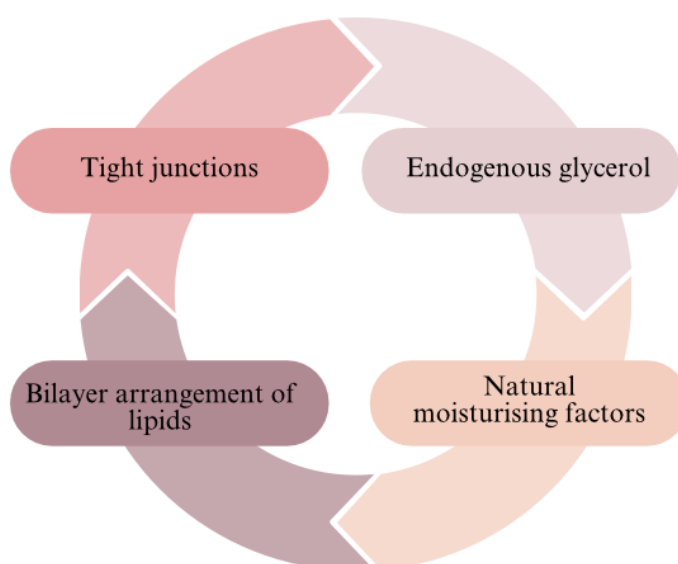


Figure 3 – Physiological mechanisms of skin hydration. Adapted from (Barel et al., 2009).

Glycerol acts as an endogenous humectant, which is capable of diffusing osmotically into the *stratum corneum* and the underlying epidermis. This process enables water uptake, thus promoting a reservoir effect that enhances the skin's ability to retain water (Z. Draelos, 2012). In fact, there is a protein that regulates the transport of water and glycerol between the *stratum corneum* and viable epidermis – aquaporin-3 water channel (AQP3) (Bonté, 2011; Z. Draelos, 2012). This is the most abundant aquaporin in the epidermis and is able to cross the membrane 6 times to form a pore, allowing the selective passage of these compounds (Bollag et al., 2020).

Other physiological mechanism that helps to regulate skin hydration reports to the lamellar or bilayer arrangement of skin lipids. Their specific spatial conformation, regardless of their specific nature, acts as a natural barrier to water permeability. In the skin, there is a significant gradient in the chemical potential of water between the viable epidermis, where the water content is approximately 70 % by weight, and the junction between the *stratum granulosum* and the *stratum corneum*, where the water content drops to 15 to 30 %. From this sharp gradient, the distribution of lipids in overlapping bilayers forms a continuous region in the *stratum corneum*, which is an efficient way of reducing skin water loss. Water molecules trying to move out of the *stratum corneum* need to cross the path provided by the lipid bilayer structure. In addition, fully mature corneocytes increase the tortuosity of the pathway, prolonging the diffusional path of the water. Thus, the combination of the ordered lamellar arrangement of intercellular lipids and the increased diffusional path determined by corneocytes significantly contributes to an increased retention of water molecules in the epidermis, and subsequently to a reduction in transepidermal water loss (TEWL) (Barel et al., 2009).

Figure 4 shows the brick-and-mortar model, that is helpful to understand the structure of the *stratum corneum* , with the bricks being the corneocytes and the "mortar" being the lipids that made up the skin barrier.

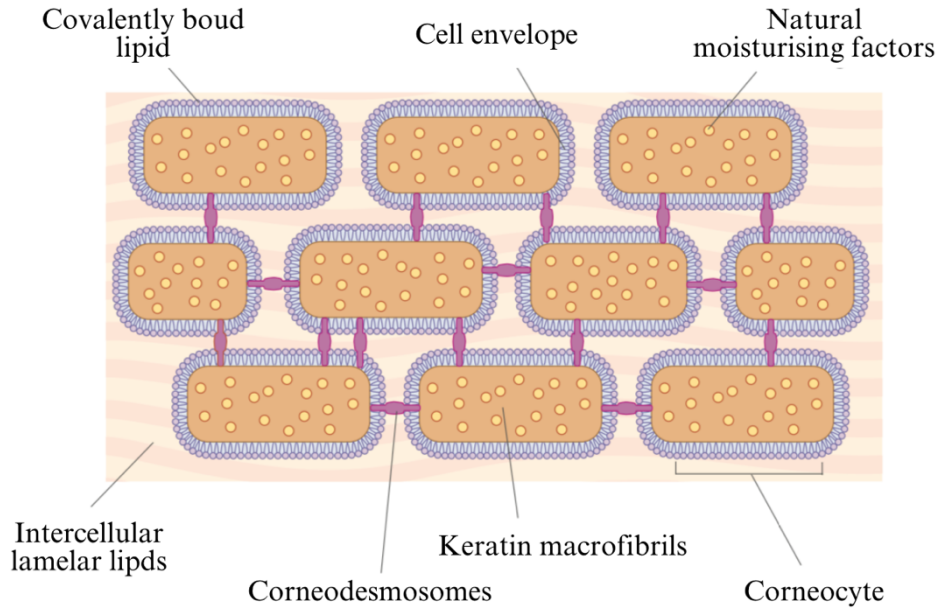


Figure 4 – Bilayer arrangement of skin lipids. Adapted from (Voegeli, 2007).

Other mechanism that contributes to the maintenance of skin hydration concerns the presence of tight junctions in the *stratum granulosum*. These structures are made up of transmembrane proteins such as claudins, occludins and junctional adhesion molecules (JAMs), as well as proteins from the TJ plate (*zonula occludens*). The interaction between these proteins forms a semi-permeable barrier to adjacent cell membranes, which impairs the water passage through the intercellular space of the *stratum granulosum*. Thus, tight junctions contribute to the skin's barrier function and to a decrease in TEWL (Barel et al., 2009; Bäslér et al., 2016).

Although these physiological skin mechanisms contribute to maintaining hydration, it is necessary to moisturize the skin with products designed for this purpose. The daily use of moisturizers improves the softness, hydration and flexibility of the skin, preserving the skin barrier and preventing TEWL (Purnamawati et al., 2017). To ensure adherence, it is that the cosmetic product displays pleasant sensory properties. Therefore, these characteristics, such as rapid absorption, spreadability and a feeling of softness, are crucial when developing moisturizing formulations (A. L. Wagemaker et al., 2013; Brown et al., 2024).

1.3. Hydration in cosmetics

From the patient/consumer point of view, topical moisturizers should cover 4 basic needs: (i) provide softness to the skin; (ii) increase skin hydration; (iii) improve skin appearance and finally (iv) provide beneficial ingredients to the skin's surface (Figure 5) (Z. D. Draelos, 2018).

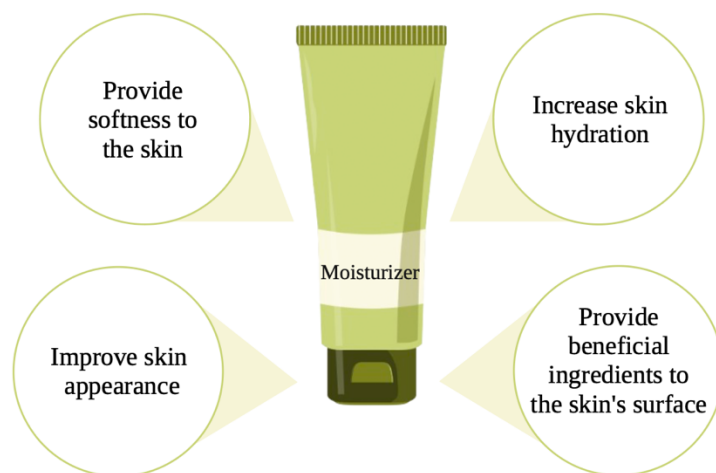


Figure 5 – Main functions of a moisturizing product. Adapted from (Z. D. Draelos, 2018).

The process to adequately select the most suitable moisturizer for each individual often relies on a process of trial and error, depending on consumer preferences, as well as skin characteristics. Nevertheless, the pharmacist role in the selection of such products may be extremely relevant, as they are often the first source of advice for users with mild dermatological diseases (Fabbro et al., 2014).

Pharmacists are widely recognized as an accessible source of health advice. A study by Harvey and colleagues reported that since the beginning of the COVID-19 pandemic, users are increasingly turning to their community pharmacy for more effective and timely advice (Harvey et al., 2024).

Most moisturizers available on the market are regulated as cosmetics, however they may also be classified as pharmaceutical products or medical devices. When regulated as pharmaceutical products or medical devices, moisturizers can be marketed for the treatment or prevention of certain pathologies (i.e. atopic dermatitis, psoriasis, ichthyosis). In fact, moisturizers highly contribute to the relieve of dermatological symptoms ranging from dryness, stretching to itching. Furthermore, moisturizers also increase skin flexibility and thereby contribute to restore the defective skin barrier that

characterizes a wide range of skin diseases (M. Brown et al., 2024). Due to the appointed reasons, in recent years there has been a significant increase in the number of formulations certified as medical devices in Europe for the treatment of dermatological diseases (Lodén, 2016). These dermatological products are widely prescribed due to their proven efficacy in the prevention, as well as in the treatment of various dermatological conditions (Mawazi et al., 2022).

Moisturizers can be divided into two main types: lipophilic or hydrophilic. Hydrophilic moisturizers, also known as humectants, attract and retain water on the skin's surface. On the other hand, lipophilic moisturizers, can be subdivided into emollients, which soften and smooth the skin, and occlusives, which form a barrier to reduce TEWL (Figure 6) (Barnes et al., 2021).

An ideal moisturizing product should have an appropriate balance of proportions between occlusive compounds, humectants and emollients. In order to restore and maintain skin hydration, it is essential that these ingredients are present in sufficient quantities to create a favorable environment to repair the skin barrier (Mawazi et al., 2022). Table 2 depicts the existing classes of moisturizers, their effects on the skin, as well as raw material examples.

Table 2 – Common moisturizers and their effects on the skin. Adapted from (Barnes et al., 2021).

Moisturizer Class	Effects on the skin	Examples
Humectants	Low molecular weight substances, which are responsible for attracting and holding the water	Glycerin, gelatin, propylene glycol, butylene glycol, panthenol, sorbitol, urea, hyaluronic acid, glycolic acid, lactic acid and sodium pyrrolidine carboxylic acid
Emollients	Saturated and unsaturated variable length hydrocarbons. The substances enhance the softness of the skin by filling the spaces in between the corneocytes	Cholesterol, squalene, linoleic acid, stearic acid, oleic acid and fatty alcohols
Occludents	Oils and waxes, which act through the formation of an inert layer, that physically blocks TEWL	White soft paraffin/petrolatum, beeswax, mineral oil, dimethicone, lanolin, carnauba wax, cetyl alcohol, and caprylic/capric triglyceride

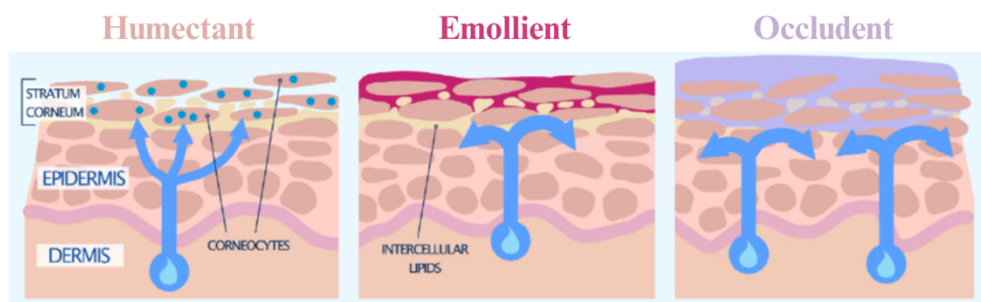


Figure 6 – Action mechanisms of moisturizers. Adapted from (Barnes et al., 2021).

Humectants are substances that attract and retain water on the skin's surface. These compounds are able to increase water absorption, from the deeper layers of the skin, into the epidermis. However, this process can increase TEWL due to evaporation. To reduce this effect, they are often combined with occlusive agents, which help to improve the barrier function of the epidermis and, consequently, skin hydration (Purnamawati et al., 2017; Rajkumar et al., 2023).

Many humectants are the same molecules that form NMF (i.e. lactic acid, pyrrolidone acid). These are composed of a mixture of hygroscopic and soluble low molecular weight substances, and as previously referred play a key role in moisturizing the *stratum corneum* (Barnes et al., 2021; Purnamawati et al., 2017; Rajkumar et al., 2023).

Occlusive agents play a fundamental role in maintaining the *stratum corneum* hydration, through the reduction of TEWL, and at the same time by allowing the transfer of water that is necessary for normal skin function (Mawazi et al., 2022). This class of moisturizers is made up of substances that do not have hydroxyl functional groups in their chemical structure. This chemical absence provides the hydrophobic properties, characteristic of this class. Given their lack of chemical affinity with water molecules, these compounds are unable to attract or retain water directly on the skin's surface (Mawazi et al., 2022). However, their effectiveness lies in their ability to form uniform, hydrophobic films on the skin, which act as a physical barrier, retaining the moisture inside and preventing it from evaporating into the atmosphere (Z. D. Draelos, 2013; Mawazi et al., 2022).

Emollients are mainly made up of long-chain saturated fatty acids, such as stearic acid, linoleic acid, oleic acid and fatty alcohols obtained from natural fats/oils (i.e. wool grease, palm oil, coconut oil) (Barnes et al., 2021; Purnamawati et al., 2017).

The number of double bonds in a fatty acid and their distribution along the carbon chain are among the most important characteristics in an emollient. In turn, its molecular weight can be used to distinguish it from an occlusive product (Mawazi et al., 2022).

The action mechanism of emollients mainly relies on their ability to replicate the intracellular bilayers of the *stratum corneum*, filling in the spaces between the corneocytes. This ultimately improves the skin's feeling of lubricity and glide (Barnes et al., 2021). As a result, there will be an increase in the skin's softness and plasticity, which significantly improves the skin texture and overall appearance. In addition, emollients have important effects on the skin's barrier function, membrane fluidity and cell signaling, by enhancing skin repair and permeability (Barnes et al., 2021; Purnamawati et al., 2017).

Figure 7 shows examples of ingredients used in emollient formulations and their respective classifications.

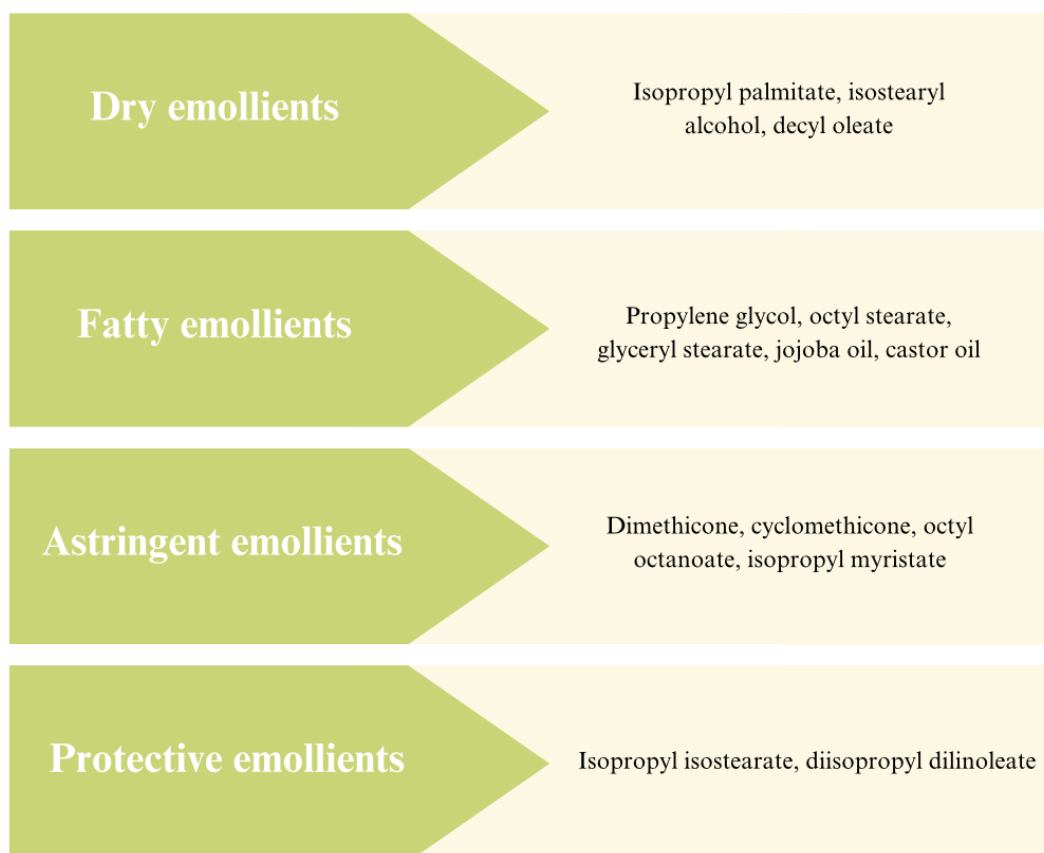


Figure 7 - Emollients classification. Adapted from (Purnamawati et al., 2017).

1.4. Cosmetic products

Cosmetic products are an essential part of the personal care routine and are designed to cleanse, beautify, protect and enhance the appearance and health of the skin, hair, nails and other parts of the body. The regulatory agencies provide clear definitions on what a cosmetic product should be, in order to ensure the safety and efficacy of these products (Ferreira et al., 2022; Manayi & Saeidnia, 2014). There are however some differences between the several regulatory agencies. For instances, according to European Union Regulation 1223/2009, cosmetics are defined as ‘any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair and hair systems, nails, lips and external genital organs) or with the teeth and mucous membranes of the mouth, with a view exclusively or mainly to cleansing, perfuming, modifying, protecting, keeping in good condition or correcting body odors’ (Official Journal of the European Union, 2009). On the other hand, in the United States, the Federal Food, Drug and Cosmetic Act (FD&C Act), administered by the Food and Drug Administration (FDA), defines a cosmetic as ‘any product (except soap) intended to be applied to human skin for cleansing, beautifying, promoting attractiveness or altering appearance’. Notably, the American definition explicitly excludes soap, which is categorized separately (Food and Drug Administration, 2024).

Both definitions reflect the wide range of products available on the market, but at the same time, they also establish important criteria for ensuring the safety and quality of cosmetic products. These criteria report to strict requirements for labelling, ingredient testing and product notification, with the ultimate aim of protecting the health and well-being of consumers (López-Galindo et al., 2007; Ukleja, 2013).

1.5. Objectives

Moisturizers provide functional benefits to the skin and consumers are increasingly looking for cosmetic products that meet their needs. The main functions of these products are to smooth and soften the skin, increase its hydration and improve the skin's visual appearance. Advice on choosing these products often comes from pharmacists, as they are one of the most accessible healthcare providers and play a crucial role in managing and advising their clients on skincare and cosmetic products.

The cosmetics market has seen a remarkable evolution and expansion over time, demonstrating an increase in the consumption of cosmetics as these products are now an integral part of the population's daily routine.

Although the cosmetics market continues to grow exponentially, consumers are increasingly looking for ingredients derived from natural sources rather than synthetic chemicals in the formulations they use. The search for cosmetics that meet consumer expectations is increasingly focused on the demand for products that use environmentally friendly, safer and more sustainable materials. The recent COVID-19 pandemic has contributed to a change in the population's mindset, with an increase in concern for the environment and human health, driving the adoption of a more sustainable lifestyle, including with regard to cosmetic products.

Based on this background, this work aims to compare the ingredients traditionally used in moisturizers, with other ingredients retrieved from natural and sustainable sources, more specifically by products of plant origin. Within this scope, *vitis vinifera* will be discussed, given that Portugal is one of the main producers of viticulture. Furthermore, cosmetics aiming skin hydration produced with seaweed, will also be reviewed, given the country's extensive coastline. For each ingredient, the action mechanism will be described, together with existent studies that document their efficacy. Furthermore, commercially available products with these ingredients will be referred.

1.6. Methods

This literature review was conducted with the aim of synthesizing current knowledge on the subject in question, in order to provide a comprehensive overview of the most relevant and recent studies on the topic under analysis. The methodology adopted followed a systematic research process, involving consultation of several sources of information, such as PubMed, Science Direct, Google Scholar, among others. In addition, various scientific journals and legislation were consulted, resulting in 155 bibliographical references.

Inclusion criteria were defined to ensure the relevance and timeliness of the selected publications. The main criteria included the selection of studies published from 2015 to the present day, as well as the selection of articles published in Portuguese or English, with the exception of articles that are relevant to the area under study.

2. Traditional ingredients used in moisturizers

As mentioned above, moisturizing formulations can be classified into 3 classes (humectants, emollients and occlusives), in which their mechanism of action differs even though the aim is the same: to moisturize (Z. D. Draelos, 2018). In many cases, the ingredients used in moisturizing products are identical or similar to the substances that make up the *stratum corneum*. It is also common for moisturizing formulations to combine different types of ingredients in order to optimize their effectiveness (Spada et al., 2018). Among the components commonly used are polyalcohols, vegetable oils, among others, which will be discussed in greater detail in this section.

Glycerin, also known as glycerol, is a trihydroxy alcohol that is widely used in a wide variety of moisturizing formulations (Fluhr et al., 2008; Mawazi et al., 2022). Its extensive use stems from its miscibility with water, which makes it a highly hygroscopic substance. Studies indicate that pure glycerin has the capacity to absorb its own weight in water, in just 3 days (Fluhr et al., 2008). Due to its ability to diffuse into the *stratum corneum* and retain water on the skin's surface, glycerin is one of the most used ingredients in moisturizing products (Fluhr et al., 2008). In addition to its moisturizing properties, glycerin also contributes to the regeneration of the skin barrier, improving integrity, stability and mechanical properties, especially in the *stratum corneum* (Mawazi et al., 2022).

Panthenol is a colorless, transparent and odorless alcohol with viscous properties. Its optical isomer D is known as dexpanthenol, acts as a precursor to pantothenic acid (vitamin B5) (Bissett, 2009; Mawazi et al., 2022). Because it is water-soluble and hydroscopic, panthenol is used as a moisturizing agent in cosmetic products, often in combination with glycerol (Bissett, 2009). In addition to its moisturizing properties, panthenol has the ability to promote wound healing and stimulate fibroblast proliferation, contributing to skin regeneration (Mawazi et al., 2022).

Lanolin is an oily, yellow substance with fat-like characteristics that is extracted from the sebaceous glands of sheep (Johnson et al., 2023; Kang et al., 2022). Its composition is mostly made up of sterol esters, as well as acids and sterols (Mawazi et al., 2022). Due to its hydrophobic properties, lanolin is often used as an ingredient in cosmetic formulations because of its ability to retain the moisture present in the epidermis. This compound can retain twice its weight in water and can reduce TEWL by

20 - 30% (Johnson et al., 2023). In addition, lanolin is able to penetrate and incorporate itself into the lipid structure of the *stratum corneum*, thus providing a prolonged moisturizing effect (Mawazi et al., 2022). However, despite its moisturizing properties, lanolin has an unpleasant smell, is expensive and is a potential allergen, therefore lanolin derivatives or extracts are often preferred to the lanolin itself (Kang et al., 2022; Mawazi et al., 2022).

3. State of the art ingredients used in moisturizers

3.1. Hyaluronic acid

Hyaluronic acid is a glycosaminoglycan (GAG) made up of repeating disaccharide units (N-acetyl-D-glucosamine and D-glucuronic acid) that are linked by glycosidic bonds (Figure 8).

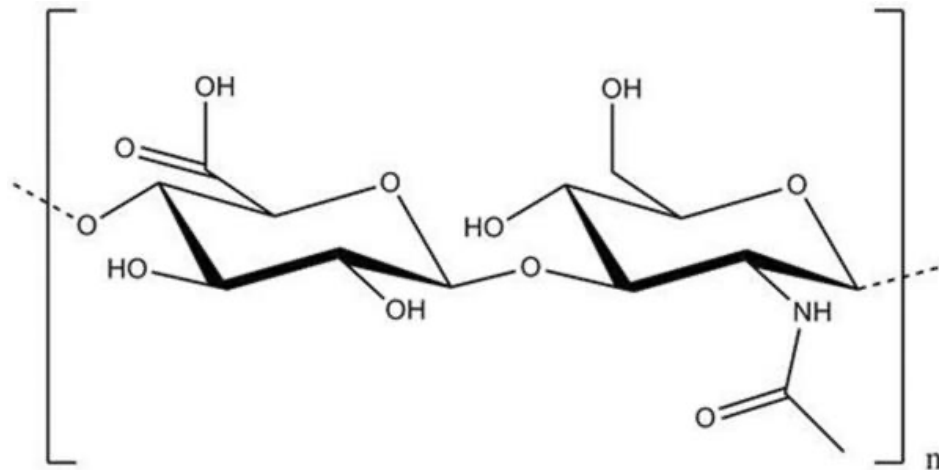


Figure 8 – Molecular structure of hyaluronic acid. Figure adapted from (Fakhari & Berkland, 2013).

The discovery of this important molecule was made by Karl Meyer and John Palmer, who isolated HA from the vitreous humour of the bovine eye (Juncan et al., 2021; Yasin et al., 2022). The name of this polysaccharide derives from the Greek word ‘*Hyalos*’, which means glass/vitreous, reflecting the origin of this molecule (Iaconisi et al., 2023). Since then, the presence of HA has been discovered in various tissues and fluids in vertebrate animals and humans (Juncan et al., 2021).

In the human body, the amount of HA is around 15 grams for a 70 kg adult, with the highest concentrations being present in the umbilical cord, synovial fluid, dermis, vitreous humour and brain (Table 3) (Abatangelo et al., 2020; Fallacara et al., 2018).

Table 3 – Examples of tissues and fluids containing HA. Adapted from (Chang et al., 2021).

Structure of the organism	Concentration ($\mu\text{g/g}$)
Umbilical cord	4100
Synovial fluid	1400-3600
Dermis	200
Vitreous humour	140-338
Brain	35-115

Each HA molecule can be regarded as a polysaccharide, formed by 20 to 200 repeated disaccharide sequences. The total number of repeated disaccharides can reach up to 10,000 (Juncan et al., 2021). This means that the HA polymer chain can reach a high molecular weight (105-107 Da) (Yasin et al., 2022). Due to this variability in the number of repeating units, HA can be categorized according to its molecular weight (Chang et al., 2021):

- ✓ Low molecular weight HA (LMW-HA): $1-25 \times 10^4$ Da;
- ✓ Medium molecular weight HA (MMW-HA): $25-10 \times 10^4$ Da;
- ✓ High molecular weight HA (HMW-HA): $> 1 \times 10^6$ Da;
- ✓ Very high-molecular weight HA (vHMW-HA): $> 6 \times 10^6$ Da.

Hyaluronic acid is widely produced by various cells in the human body and is involved in fundamental biological processes such as cell differentiation, embryological development and even wound healing (Juncan et al., 2021). Due to these peculiar characteristics, HA has been increasingly researched and used in various areas of medicine (Bravo et al., 2022).

3.1.1. Main uses

HA is a constituent that has been widely studied and used in various areas of medicine and cosmetics due to its biocompatibility, biodegradability and non-immunogenicity (Graça et al., 2020). Some of these areas are ophthalmology, arthrology, pneumology, rhinology, urology, oncology, nutrition, dermatology, among others, as seen in Figure 9 (Juncan et al., 2021).

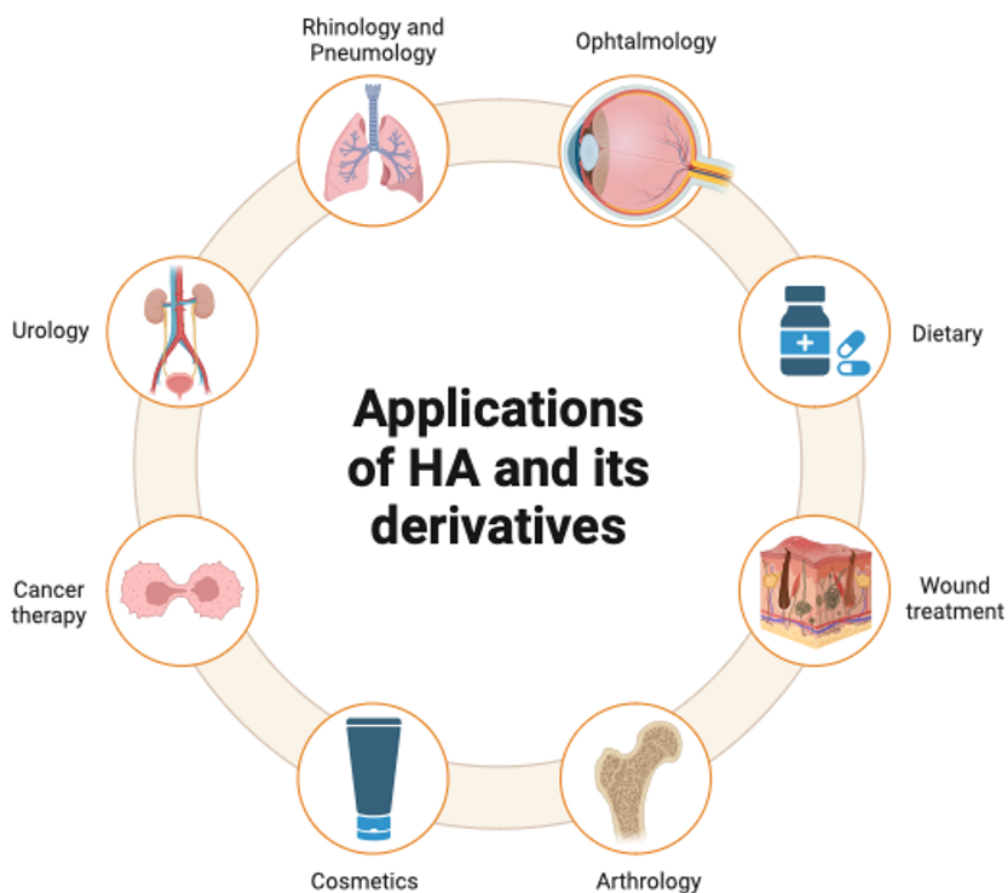


Figure 9 – Applications of HA and its derivatives. Adapted from (Fallacara et al., 2018).

One of the major uses of hyaluronic acid regards the treatment of osteoarthritis (OA). This compound is administered as an intra-articular injection to help increase the amount of HA within the synovial fluid, providing viscosity and elasticity within the joint space, thus helping to minimize joint pain (Huynh & Priefer, 2020; Y. S. Kim & Guilak, 2022).

In the field of ophthalmology, HA is an essential component in eye drops for the treatment of dry eye syndrome. Based on its viscoelastic properties, this molecule helps to lubricate the ocular surface, reducing friction during blinking and eye movements (Huynh & Priefer, 2020). In ophthalmic surgery, biomaterials such as hyaluronic acid are used to protect and lubricate the ocular tissues and minimize the loss of vitreous fluid (Harrer et al., 2021).

As previously detailed, HA displays an increasingly relevant role as a therapeutically agent in several diseases, however its use in cosmetics is also extremely

relevant (Juncan et al., 2021). As we get older, the amount of HA present in the skin decreases, which ultimately leads to skin dehydration, loss of firmness and presence of more wrinkles (Goberdhan et al., 2016). In this context, the administration of HA to the skin, can display a broad range of advantages, as described in Figure 10.

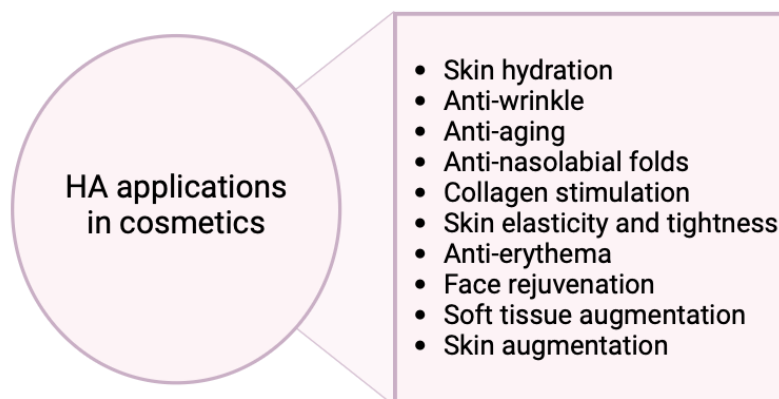


Figure 10 – HA applications in cosmetics. Adapted from (Bukhari et al., 2018).

3.1.2. Action mechanism

Hyaluronic acid is an essential component of the extracellular matrix that is responsible for providing structural support to the skin.

When this molecule reaches the dermis, it stimulates the production of collagen, which is an essential protein for skin structure and elasticity. Due to its hygroscopic characteristics, this polymer will help to retain water and will favor collagen synthesis by fibroblasts (Abatangelo et al., 2020; Becker et al., 2009).

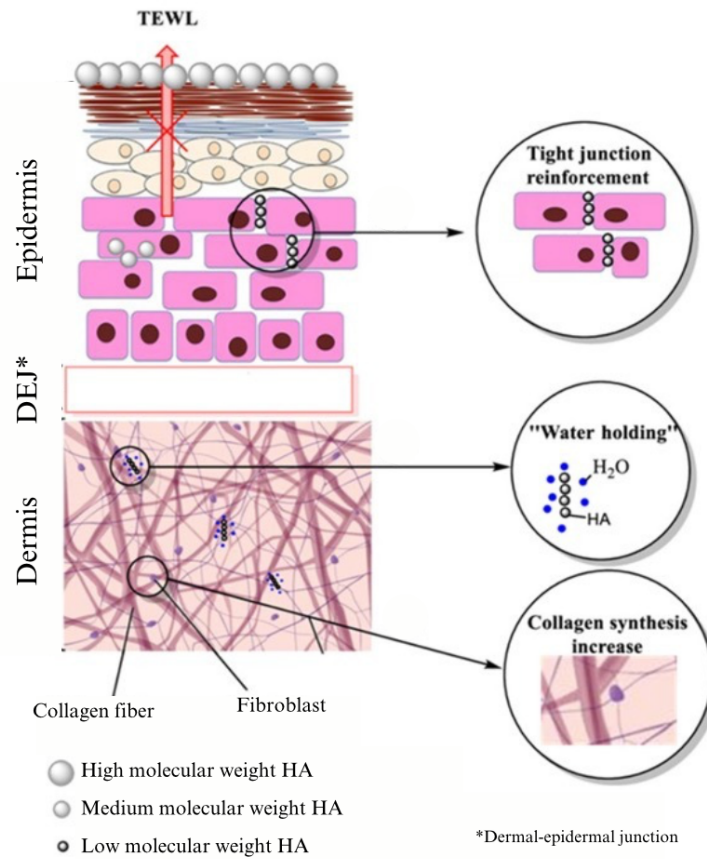


Figure 11 – HA action mechanisms. Adapted from (Juncan et al., 2021).

Depending on the molecular weight, HA used in topical formulations can present distinctive permeation characteristics, that ultimately impact the effect on the skin (Figure 11) (Juncan et al., 2021).

When considering HMW-HA, due to its large size, the degree of penetration is small, being the majority retained on the skin's surface. This type of HA will form a thin layer on the surface of the skin, acting as a barrier that attracts and retains water on the surface, thereby increasing the level of hydration and at the same time preventing TEWL (Juncan et al., 2021). It is important to note that hyaluronic acid is a highly hygroscopic molecule, capable of expanding 1000 times its volume in the presence of water (one HA molecule can bind to approximately 250 water molecules), making it easy to retain water in the upper layers of the epidermis (Becker et al., 2009; Yasin et al., 2022).

In turn, LMW-HA, has the ability to penetrate the skin. After topical administration, this molecule can be present in both the epidermis and dermis.

3.1.3. Clinical claims

Raab et al. carried out a clinical study to assess the tolerance and efficacy of topical application of HA in women with mild to moderate skin damage caused by sun exposure. The study lasted 12 weeks, with measurements taken at weeks 4, 8 and 12. The results showed that the use of a 1% HA formulation significantly improved skin integrity increased hydration in the SC and reduced TEWL. In addition, the reported tolerability was quite good, with a spontaneous increase in HA on the patients' skin as early as week 4. The main conclusions of this study pointed that the topical application of HA, in this target population, was effective both in stimulating the production of hyaluronic acid, several components of the skin's extracellular matrix and in improving skin hydration (Raab et al., 2017).

In a randomised and assessor-blinded study, the efficacy of a cream consisting of 1% hyaluronic acid and other bioactive compounds was evaluated and compared with a placebo. Measurements were taken 1, 8 and 24 hours after the cream was applied to the patients' forearms. The results showed that skin hydration after 24 hours was considerably higher in the area where the cream was applied, when compared to the placebo. In this way, it was possible to conclude that with just one application of the HA cream, the skin's hydration and barrier function improved (Milani & Sparavigna, 2017).

3.1.4. Hyaluronic Acid Products Market

In order to be used in cosmetic or pharmaceutical products, hyaluronic acid needs chemical modifications, since in its natural form it is rapidly degraded by the enzyme hyaluronidase, which breaks its chemical bonds, thereby reducing its biological activity. Modifications include adding new chemical groups to the HA molecule in order to reduce its hydrophilic nature, allowing it to be integrated with other hydrophobic components present in cosmetic formulations. In addition, it is also possible for HA to establish cross-links to form insoluble derivatives or hydrogels (Al-Halaseh et al., 2022). In this way, cosmetics can be based on hyaluronic acid in its hydrolysed form, or instead in a derivative of this compound, sodium hyaluronate (NaHA) (Fakhari & Berkland, 2013). Both HA and NaHA are incorporated into cosmetic products, and their concentrations varies between 0.2-1% and up to 2%, respectively (Ferkel et al., 2023).

In today's market, products made up of HA account for only 5%, while more than 95% of products contain sodium hyaluronate (Juncan et al., 2021). Pharmaceutical forms containing these ingredients include creams, lotions, serums, masks, among others (Juncan et al., 2021). Over the years, cosmetic brands have been creating new innovative products that combine hyaluronic acid with other active ingredients to reach a wider range of consumers (Yasin et al., 2022).

In 2022, the market for hyaluronic acid-based beauty products was valued at 2.1 billion dollars, with projections indicating that it could reach 4.0 billion dollars by the end of 2031. This growth is largely due to the increased prevalence of dermatological pathologies and the growing demand for more affordable and effective formulations in terms of skin hydration (Transparency Market Research, 2023).

Table 4 depicts examples of cosmetic products in which hyaluronic acid is the main ingredient responsible for skin hydration. These products were selected due to their economic revenue, according a report on the global hyaluronic acid beauty product market (Transparency Market Research, 2023).

Table 4 – Blockbuster skin hydration cosmetic products containing HA (Transparency Market Research, 2023).

Product	Brand	Dosage form	HA form
SkinCeuticals Hydrating B5	SkinCeuticals (EUA)	Serum	NaHa
Vicky Minéral 89	Vicky (France)	Serum	NaHA
L'Oréal Paris Hydra Filling Night Cream	L'Oréal Paris (France)	Cream	NaHA
Neutrogena Hydro Boost Cream	Neutrogena (EUA)	Cream	NaHA
Croma-Pharma Farewell Dry Skin	Croma-Pharma (Austria)	Serum	HMW-HA and LMW-HA
Biohyalux HA Hydro Intense Serum	Biohyalux (China)	Serum	Four different molecular weights of HA

3.2. Ceramides

Ceramides (CERs) belong to the class of sphingolipids, molecules that are made up of a fatty acid (FA) conjugated with sphingoid base (SB) via an amide bond (Figure 12) (Meckfessel & Brandt, 2014; Sajna et al., 2015).

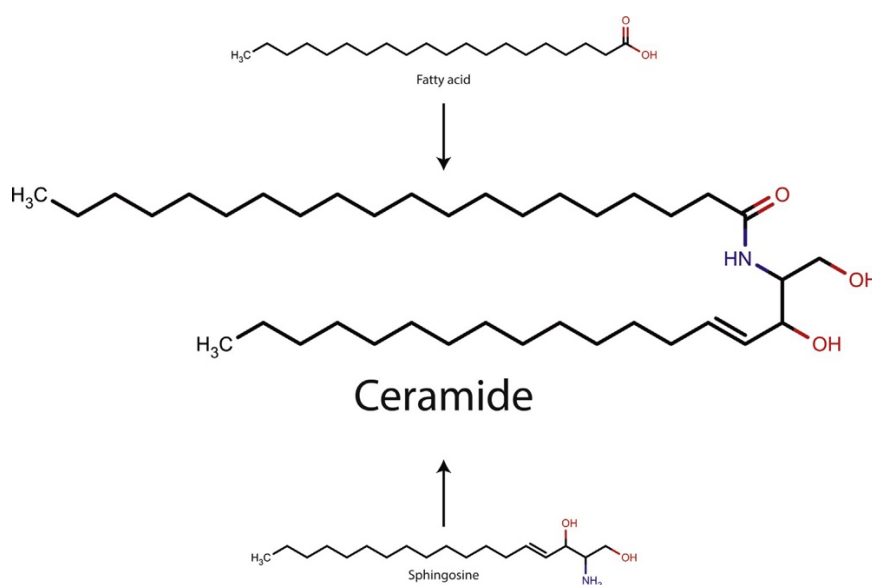


Figure 12 – Basic structure of ceramides. Adapted from (Meckfessel & Brandt, 2014).

The discovery of sphingolipids was made by a German doctor and biochemist called Johann Thudichum, who identified a type of lipid never seen before in the brain. Inspired by the mythological figure of the Sphinx, who guarded the entrance to the city of Thebes in Ancient Greece and allowed only those who answered her questions correctly to pass through, Thudichum decided to call these molecules sphingolipids (Uchida & Park, 2021). Ceramides play an important role in maintaining homeostasis in the human body and are one of the main constituents of the epidermis (Meckfessel & Brandt, 2014; Uchida & Park, 2021). These molecules, together with other lipids, form a highly ordered lamellar structure that is essential for maintaining the skin's barrier function and preventing TEWL (Meckfessel & Brandt, 2014; Sajna et al., 2015).

The chemical structure of CERs is extremely heterogeneous with nearly 340 species of CERs already identified in the *stratum corneum* (Meckfessel & Brandt, 2014). The main chemical differences of CERs rely on the combination of the fatty acids type,

together with the sphingoid bases. More specifically, the length of each fatty acid chain, as well as the sphingoid bases moieties (Meckfessel & Brandt, 2014). There are 4 classes of fatty acids and 5 classes of sphingoid bases. In order to differentiate each ceramide, the nomenclature ‘CER(XY)’ is used, with X describing the class of fatty acids and Y referring to the sphingoid base. For example, ceramide is made of 5 α -hydroxy fatty acid (A) and by sphingosine (S), being therefore represented by CER(AS).

Table 5 shows examples of both fatty acids and sphingoid bases that give rise to a ceramide molecule (Meckfessel & Brandt, 2014).

Table 5 – Nomenclature of the different classes of ceramides. Adapted from (Fujii, 2021).

	Non-hydroxy (N)	α-Hydroxy (A)	ω-Hydroxy (O)	Esterified ω-hydroxy (EO)
Dihydrosphingosine (DS)	NDS	ADS	ODS	EODS
Sphingosine (S)	NS (Ceramide 2)	AS (Ceramide 5)	OS	EOS (Ceramide 1)
Phytosphingosine (P)	NP (Ceramide 3)	AP (Ceramide 6)	OP	EOP
6-Hydroxy sphingosine (H)	NH	AH (Ceramide 7)	OH	EOH (Ceramide 4)
1,14-Sphingadiene (SD)	NSD	ASD	OSD	EOSD

Ceramide 5 is found practically in all human tissues, while ceramides composed of a esterified ω -hydroxy fatty acid (EO) or 6-hydroxy sphingosine (H) are found exclusively in the epidermis (Fujii, 2021).

Pseudo-ceramides (pCERs), that mimic endogenous CERs, have been synthesized. These are chemically and therapeutically similar molecules to CERs, with the advantage of having a lower production cost (Uchida et al., 2008).

3.2.1. Main uses

The quantity and organization of ceramides in the *stratum corneum* are key parameters to maintain a healthy-looking skin. A decrease in the ceramide content in the skin can be responsible for several skin disorders. Therefore, ceramides can be used as a therapeutic agent in numerous skin conditions such as atopic dermatitis, psoriasis, acne, ichthyosis and dry skin (Figure 13) (Kahraman et al., 2019).

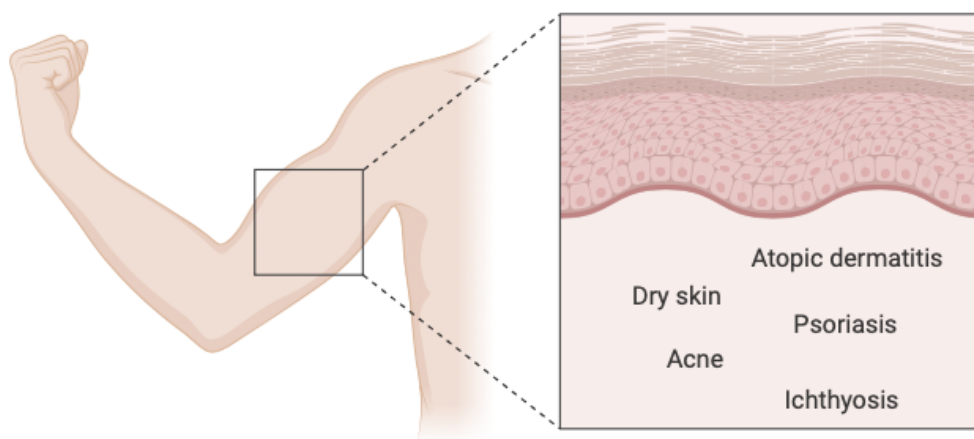


Figure 13 – Therapeutic applications of ceramides in skin disorders. Adapted from (Kahraman et al., 2019).

Atopic dermatitis (AD) is the most common inflammatory skin disease today, affecting approximately 20% of the population and directly impacting their quality of life (Weidinger et al., 2018). This condition is characterized by a decrease in *stratum corneum* lipids, in which ceramides are included, that compromises the normal functioning of the skin barrier. The use of formulations containing ceramides will help to replenish the lipids in the *stratum corneum*, prevent TEWL and ensuring a greater hydration (Kahraman et al., 2019).

Ichthyosis is a term that encompasses more than 50 types of disease, all characterized by generalized hyperkeratosis, dry skin and skin desquamation. Although these individuals have thick SC, there is usually an increase in TEWL. Ceramides can make a significant contribution to improving barrier function, increasing hydration and reducing skin desquamation (Vahlquist & Törmä, 2020).

3.2.2. Action mechanism

As mentioned above, ceramides make up around half of the intercellular lipids in the *stratum corneum* and are crucial molecules in both the lamellar structure of the skin and the integrity of the lipid barrier (Mijaljica et al., 2024). When there is a structural or proportional alteration in the ceramides present in the outermost layer of the epidermis, the skin's barrier function may be compromised.

The composition of ceramides in the skin can be influenced by various factors, such as exposure to ultraviolet radiation and ageing (Camilion et al., 2022; Mijaljica et al., 2024). These factors make the skin barrier more susceptible to contact with external agents such as chemicals, microorganisms and allergens that can reach the deeper layers of the skin, leading to an increase in TEWL and negatively affecting skin hydration (Masson, 2010). By re-establishing ceramide levels in the epidermis, with the help of exogenous CERs, the reconstitution of the lipid barrier integrity will be stimulated. This will promote an enhanced intercellular cohesion between corneocytes, which will ultimately lead to an expanded ability of the skin to retain water, reduce TEWL and increase skin hydration.

Ceramides also contribute to the reorganization of the lamellar structures of the *stratum corneum*, thus reinforcing the skin's barrier function and preventing the penetration of irritants and allergens (Feingold & Elias, 2014; Sahle et al., 2015; Tessema et al., 2017). Figure 14 shows how ceramide levels in the skin can affect skin hydration.

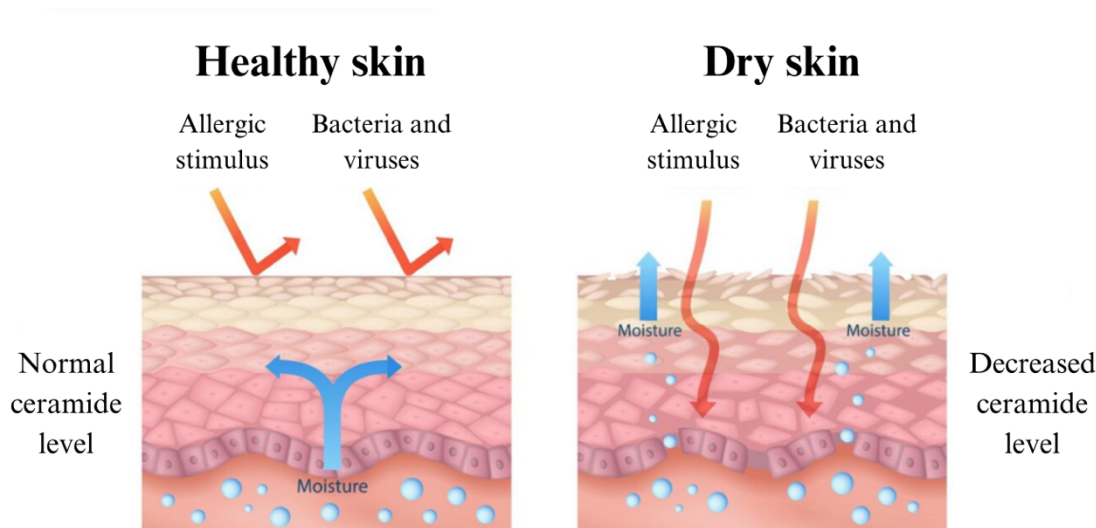


Figure 14 – Mechanism of action of ceramides in skin hydration. Adapted from Freepik.

The use of various subclasses of ceramides in moisturizing cosmetic products is based on the aforementioned properties (Kono et al., 2021; Mijaljica et al., 2024).

3.2.3. Clinical claims

A double-blinded, 4-week randomized controlled trial (RCT) investigated the efficacy of a moisturizing cream composed of ceramides in the treatment of senile xerosis. Each patient used a ceramide moisturizer and a hydrophilic cream separately on each of their shins. During the first 24 hours, the cream was applied only once, after which it was applied twice a day for 28 days. Afterwards, the patients went 7 days without applying any type of cream. It was reported that the 7-day post-moisturizing efficacy on the side where the ceramide cream was applied increased skin hydration and decreased TEWL compared to the side where the other moisturizing cream was applied (Lueangarun et al., 2019).

Ishida et al. developed a 6-week study in which the target population regarded individuals with mild to severe atopic dermatitis who underwent a topical treatment with a synthetic engineered pseudoceramide. The patients applied the cream twice a day for four weeks and stopped for a week, in order to evaluate the results. After treatment, a significant reduction in AD symptoms was observed, thus reflecting a decrease in TEWL and an increase in the skin's water content (Ishida et al., 2020).

3.2.4. Ceramides Product Market

Ceramides have always been a mainstay in moisturizing the skin, but sometimes it's difficult to understand and identify their presence in cosmetic formulations.

Only the first ceramides that were discovered are labelled in the International Nomenclature of Cosmetic Ingredients (INCI), so all the other CERs that have been identified over time will appear under their chemical name on the ingredient labels of cosmetic products (Meckfessel & Brandt, 2014). For example, it is common to see the word 'ceramide' in the list of ingredients as ceramide AP or ceramide 6, but if the formulation contains phytosphingosine and sphingosine, their connection to the CERs will not be identified and it will be difficult for the consumer to identify the presence of these molecules.

Ingredients such as phytosphingosine and sphingosine, which are not ceramides but ceramide precursors that stimulate the skin to produce ceramides, often appear on labels. Pseudo-ceramides may also appear, the abbreviation of which usually has nothing to do with the word ceramides (ceramide R, PC104, PC-9S, among others) (A. R. Kim et al., 2019).

The concentration of ceramides in formulations can vary depending on the class of CERs used. According to suppliers, ceramide 2 and ceramide 5 concentrations are used up to 4% and 2% respectively (Burnett et al., 2020).

The market for ceramide-based skincare formulations is projected at \$424.7 million by the end of 2024. It is predicted that by 2034, the market will reach up to 739.4 million dollars. This increase reflects consumers' growing willingness to invest in high-quality cosmetics containing ingredients such as ceramides in order to achieve healthier and more hydrated skin. In response to this high demand, brands are constantly innovating and developing advanced skincare formulas that incorporate ceramides (Future Market Insights, 2024).

Table 6 shows examples of cosmetic formulations available on the market that contain ceramides. Key companies in the skincare market with ceramides were considered and the cosmetic formulations with highest revenue were selected (Baldwin et al., 2021; Del Rosso & Allison, 2019; Future Market Insights, 2024; Weber et al., 2012).

Table 6 – Blockbuster skin hydration cosmetic products containing ceramides (Future Market Insights, 2024).

Product	Brand	Dosage form	Types of CERs
CeraVe Facial Moisturising Lotion	CeraVe (USA)	Lotion	Ceramide NP, Ceramide AP and Ceramide EOP
La Roche-Posay Toleriane Sensitive Cream	La Roche-Posay (France)	Cream	Ceramide 3
Eucerin Advanced Repair Cream	Eucerin (Germany)	Cream	Ceramide NP
L'Oréal Paris Revitalift Filler	L'Oréal Paris (France)	Cream	Ceramide 5, Ceramide 3 and Ceramide R
Dr.Jart+ Ceramidin Liquid	Dr.Jart+ (South Korea)	Facial toner	Ceramide NP, Ceramide AP, Ceramide AS, Ceramide NS and Ceramide EOP
Holika Holika Good Cera	Holika Holika (South Korea)	Cream	Ceramide NP

South Korea has gained great prominence in the cosmetics market, ranking among the world's top 10 beauty markets by 2022 (International Trade Administration, 2023). Korean skincare products, known as “K-beauty”, have become increasingly popular due to their innovative natural ingredients and aesthetically appealing packaging (Nguyen et al., 2020). When it comes to moisturizing, K-beauty uses unconventional sources such as horse oil and starfish powder to extract moisturizing components, such as ceramides (Juhász et al., 2018; Lee et al., 2018). K-beauty's influence on social media has a strong impact on consumers' purchasing decisions, with its concept of Korean beauty, which promotes healthy, hydrated, even-toned, blemish-free and radiant skin (Nguyen et al., 2020).

4. New Trends In Moisturizing Ingredients: By Products Of Plant Origin

Nowadays, there is growing concern about the environmental impact of the ingredients used in cosmetics, which has stimulated the search for more sustainable alternatives (Martins & Marto, 2023; Sasounian et al., 2024). The careful choice of raw materials used in formulations reflects the public's awareness of more responsible and environmentally friendly practices when it comes to manufacturing cosmetic products, considering the associated environmental, social and economic impacts (Martins & Marto, 2023; Sasounian et al., 2024).

At the same time, consumer interest in cosmetics and personal care products that are safe and environmentally friendly has been growing globally. This increase in demand has encouraged cosmetic companies to develop more products that include natural ingredients, as well as expanding their sustainable and ecological product lines (Suphasomboon & Vassanadumrongdee, 2022).

The following chapters will describe moisturizing products that use industry by-products as a source of active ingredients for cosmetics. As referred in the introductory chapter, two examples were considered – *Vitis vinifera* and algae. Both raw materials display moisturizing properties and are extremely common in Portugal. The main uses, action mechanisms supporting skin hydration, clinical claims as well as examples of products already in the market with these ingredients will be addressed.

4.1. *Vitis vinifera* (L)

Vitis vinifera (L), also known as grapevine or vine, is a plant belonging to the genus *Vitis*, of the Vitaceae family. This species of vine is native to the Mediterranean region, extending as far south as Germany (Euro+Med PlantBase, 2017).

It is characterized as a climbing plant that can reach up to 35 meters, although it is usually kept between 1 and 3 meters due to the practice of pruning (Almargem, 2013).

This plant grows in temperate climates and is widely cultivated in Portugal, where its fruits, better known as *Vitis vinifera* (L), are generally used to produce wine, fresh grapes and dried grapes (Euro+Med PlantBase, 2017).

Grapes are among the most widely grown fruit crops in the world, with around half of their production destined for winemaking (Mildner-Szkudlarz et al., 2015). In 2022, global grape production reached approximately 71.3 million metric tonnes, of which 48% were wine grapes, 44% table grapes and 8% dried grapes (International Organisation of Vine and Wine, 2022).

In the same year, Portugal was the 10th largest wine producer in the world, with a vineyard area of 193,443 hectares (International Organisation of Vine and Wine, 2022).

Grapes have numerous health benefits due to their constitution, which includes various bioactive compounds such as proanthocyanidins, anthocyanins, flavonoids, phenolic acids and stilbenes (Serra et al., 2023). The concentrations of these phenolic compounds can vary depending on the morphological part of the plant in question, from the stem to the seeds (Goufo et al., 2020; Zhou et al., 2022).

Table 7 shows the different parts of the grape used in comparison with their polyphenol content.

Table 7 – Different chemical groups of polyphenols identified in different fruit parts. Adapted from (Nassiri-Asl & Hosseinzadeh, 2016).

Chemical groups of phenolic compounds	Products extracted from grapes					
	Stem	Seeds	Pomace	Raisins	Skin	Juice
Phenolic acids	✓	✓	✓	✓	✓	✓
Flavanols	✓		✓	✓	✓	✓
Flavonols	✓	✓	✓	✓	✓	✓
Anthocyanins	✓		✓	✓	✓	✓
Stilbenes	✓	✓	✓		✓	✓
Proanthocyanidins		✓	✓			

Vitis vinifera (L) are a rich source of phenolic compounds, mainly flavonoids, which are found mainly in the seeds and skin of the fruit (L. R. Silva & Queiroz, 2016; Zhou et al., 2022).

Within the phenolic compounds, the flavonoid class leads to the synthesis of various classes of metabolites, which according to their chemical structure at the level of the central ring, can be divided into flavonols, flavan-3-ol, proanthocyanidins and anthocyanins (Flamini et al., 2013).

In the skin of the fruit, the most abundant uncoloured phenolic compounds are the flavonol group, while in grape seeds the flavan-3-ol class stands out, such as catechin and polymers of procyanidins (L. R. Silva & Queiroz, 2016). In turn, anthocyanins are the main pigments in *Vitis vinifera (L)* that appear during the ripening of the fruit and are responsible for the colour of the wine. The main anthocyanins found in *Vitis vinifera (L)* are derived from cyanidin, peonidin, delphinidin and petunidin (L. R. Silva & Queiroz, 2016). In addition, stilbenes are also found in the seeds and skin of grapes, especially resveratrol in its trans form (3,5,4'-trihydroxystilbene) (Nassiri-Asl & Hosseinzadeh, 2009). This compound has beneficial effects on a range of diseases, including cardiovascular, inflammatory, neurodegenerative and metabolic disorders (Weiskirchen & Weiskirchen, 2016).

Figure 15 shows the phenolic compounds frequently found in *Vitis vinifera (L)* with their respective chemical structures.

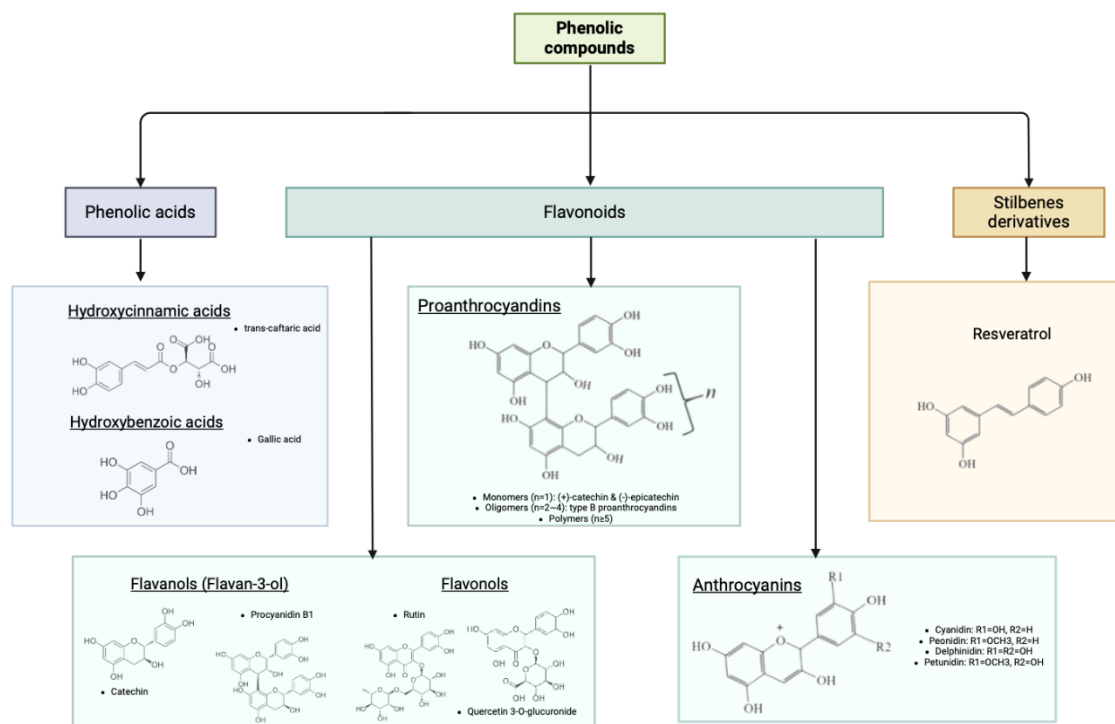


Figure 15 – Chemical structure of phenolic compounds. Adapted from (Zhou et al., 2022).

Currently, the phenolic compounds of this plant, which are essentially secondary metabolites, have attracted increasing attention due to their numerous health benefits, leading to growing interest in various areas, ranging from the food industry to the pharmaceutical and cosmetics industries (Leal et al., 2020; Sharafan et al., 2023).

4.1.1. Main uses

The most common use of *Vitis vinifera* (L) is in the food industry, and its uses include consumption as fresh fruit or as a raw material for other purposes. This fruit is widely used to produce wines, juices, dried fruit and also jams (Sharafan et al., 2023; Zhou et al., 2022). In addition, in the food industry, this plant can be used as a nutritional supplement or even as a food coloring (Sharafan et al., 2023).

The pharmaceutical industry is increasingly exploring the use of *Vitis vinifera* (L) as a key source of phenolic compounds with various applications. These phytochemicals and their derivatives have diverse properties, ranging from antioxidant, anti-inflammatory, cardioprotective, hepatoprotective, anti-obesity and even anti-cancer (Afnan et al., 2022; Sharafan et al., 2023).

Currently in the pharmaceutical sector, there are medicines based on the leaves of *Vitis vinifera* (L) authorised by the EMA for the treatment of symptoms and signs related to venous insufficiency (heavy legs, pain, tiredness and edema), for the symptomatic treatment of haemorrhoidal crises and capillary skin fragility (European Medicines Agency, 2017). *Vitis vinifera* (L) is also used as an active ingredient in the cosmetics industry in the form of emollients, humectants, emulsifiers, colour additives or fragrances (Sharafan et al., 2023).

Figure 16 shows the various applications of *Vitis vinifera* (L).

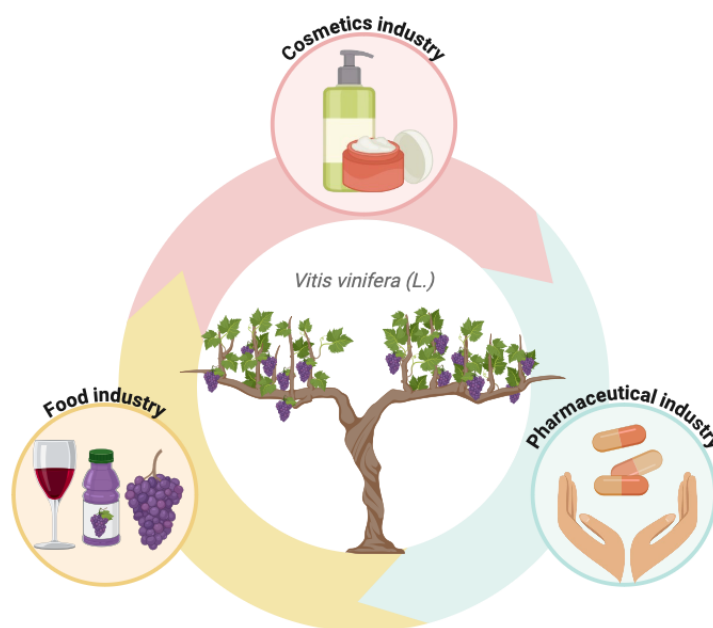


Figure 16 – Applications of *Vitis vinifera* (L). Adapted from (Sharafan et al., 2023).

Over the last few years, the demand in the cosmetics market for natural ingredients has been increasing. This is both a challenging as an attractive opportunity for the cosmetics market, in what concerns the sustainability of the formulations composition and production (Bom et al., 2019; Ribeiro et al., 2015; Statista, 2024).

In wine production, there are several components of the grape that are discarded, despite their significant amount of phenolic compounds with potential for application in skincare products and cosmetics (Serra et al., 2023). The incorporation of these bioactive compounds, through grape substrates, into cosmetic products has been shown to be effective in reducing the appearance of wrinkles, fine lines and age spots, as well as in improving skin elasticity and firmness, among other beneficial properties for skin health (Ky et al., 2014; Leal et al., 2020).

4.1.2. Action mechanism

The use of *Vitis vinifera* (L) and their derivatives in moisturizing cosmetic products is mainly due to their rich composition of bioactive compounds that interact with skin structures to improve water retention, promote the maintenance of the skin's barrier function and increase the expression of aquaporins, thus resulting in a significant improvement in skin hydration.

Antioxidants, such as resveratrol and flavonoids, play a fundamental role in protecting skin cells against extrinsic agents (i.e. ultraviolet radiation) that cause oxidative stress. These compounds inhibit or block the formation of free radicals, thus conserving collagen and elastic fibres and maintaining skin hydration (Nassiri-Asl & Hosseinzadeh, 2016; Zillich et al., 2015).

As well as being made up of phenolic compounds, *Vitis vinifera* (L) is also made up of fatty acids, and the composition of their seeds is rich in around 90% unsaturated fatty acids, mainly linoleic acid (65-70%) and oleic acid (20-40%) (Di Pietro Fernandes et al., 2023). As mentioned above, the *stratum corneum* is made up of intercellular lipids, such as linoleic acid, which is important in maintaining the skin's barrier function. When there is a decrease in this unsaturated fatty acid in the epidermis, the skin's barrier function may be compromised, thus contributing to TEWL and subsequently to skin dehydration (Martin et al., 2020; Vaughn et al., 2018). Therefore, the use of cosmetics based on grape seed oil will help to replenish the deficit in fatty acids in the epidermis, thus contributing to the normal functioning of the skin's barrier function (Martin et al., 2020).

On the other hand, the presence of polyphenols in *Vitis vinifera* (L) also plays an important role in hydrating the skin. As already mentioned, aquaporin-3 is a key protein responsible for transporting water and glycerol in the skin and is expressed in the plasma membrane of keratinocytes in the epidermis. Nakamura et al. revealed that the proanthocyanidins present in *Vitis vinifera* (L) are capable of increasing the expression of AQP3 in human keratinocytes, thus promoting hydration from the most superficial to the deepest layers of the skin (Fiorentini et al., 2015; Nakamura et al., 2020).

4.1.3. Clinical claims

Rafique et al. developed a study based on a topical water-in-oil W/O emulsion with 3% grape seed extract from *Vitis vinifera (L)* to evaluate the efficacy of this cream compared to a placebo. The study population regarded 20 healthy female patients aged between 28 and 58. The patients used the test solution for 12 weeks. Over these weeks, various skin parameters were analyzed: skin hydration, pH value, sebum content, average pore size, skin elasticity and roughness. The results revealed that there was an increase in skin hydration, elasticity and smoothness, as well as a decrease in pore size and roughness. The authors concluded that the cream containing grape extract could be a potential moisturizing and anti-ageing agent (Rafique & Shah, 2019).

A single-blinded randomised study was designed with the aim of evaluating the cutaneous effects of a water-in-oil (W/O) emulsion containing 2% Muscat hamburg grape seed extract, which is a red grape variety of *Vitis vinifera (L)*. The study compared the effect of the emulsion with a placebo. The study participants had to apply the corresponding product to each cheek twice a day for 8 weeks. The results showed that the emulsion reduced the skin's melanin content, sebum content and erythema, and that it increased skin elasticity. The authors concluded that the formulation possessed antioxidant properties, alongside with natural skin whitener properties (i.e. decreasing the melanin content), moisturizer (by increasing the moisture content of the skin) and as a potential anti-ageing agent (due to the increase in skin elasticity) (Sharif et al., 2015).

4.1.4. *Vitis vinifera (L)* - Derived Cosmetics in the Market

Vitis vinifera (L) extract is not published in any official pharmacopoeia, but there are monographs published by various organizations, such as the FDA and the European Medicines Agency's Committee on Herbal Medicinal Products (EMA-HMPC) (Sharafan et al., 2023).

According to the CosIng (Cosmetics Ingredients) database, there are various forms of raw materials derived from *Vitis vinifera (L)* that can be used in cosmetics with several purposes. In the field of skin hydration, *Vitis vinifera* seed extract, *Vitis vinifera* seed oil, *Vitis vinifera* fruit water, among others, can be used (European Commission, 2008).

In cosmetic formulations, the use of *Vitis vinifera (L)* grapes is generally used in low concentrations. In facial cleansers and masks, the grape extract content is used up to 2%, while in other formulations the concentration varies up to 1% (Fiume et al., 2014).

By 2022, the market for cosmetic products and food supplements based on grape skin extracts was estimated to have reached a value of 164.47 million dollars. Based on changing consumer preferences for products with a “clean” label, it is expected that this market could expand to 391.37 million dollars by 2033 (Future Market Insights, 2023).

Table 8 lists some of the brands that have developed cosmetics based on extracts from *Vitis vinifera (L)* grapes.

Table 8 – Examples of grape-based moisturizing products.

Product	Brand	Dosage form	Ingredients
Caudalie Vinosource-Hydra	Caudalie (France)	Cream	Grape water, grape seed oil, grape seed extract and grape juice
HydraVine Chardonnay Grape Mask	TheraVine (South Africa)	Face mask	Grape seed extract
Biolaven Day Face Cream	Biolaven (Poland)	Cream	Grape seed oil
Korres Body Smoothing Milk	Korres (Greece)	Body milk	Grape fruit extract
DieNikolai Grapeseed Oil Darling	DieNikolai (Austria)	Cream	Grape seed oil and grape skin extract
Dvine Grape Power Dynamic Day Cream	Dvine (Portugal)	Cream	Grape fruit water and grape seed oil

The Portuguese brand Dvine was created in 2017 by the pharmaceutical group Medinfar. Dvine uses grapes from the vineyards of the Douro Valley in northern Portugal to produce its skincare products. The brand is committed to deliver cosmetics with sustainability in mind, from its airless glass bottles to its cartons, which are made from sustainable forests. Currently, two skincare lines have been launched: the Light Harverst

line, which is dedicated to younger, brighter skin, and the Gold Harvest line, designed for a more mature skin with visible signs of ageing. The brand offers a variety of cosmetics, including cleansers, serums, eye care, day care and night care, essentially highlighting grapes and their active constituents in its formulations (*DVINE | Douro Beauty Essence*, n.d.).

4.2. Algae

Algae are aquatic photosynthetic organisms whose differences are based on their structure and size. This diverse group of organisms is able to grow in a wide variety of environments, from freshwater to seawater, deep oceans and even rocky shores. They can be multicellular, unicellular or colonial organisms, where currently more than 36,000 different types of species have been identified (Dini, 2023; M. Silva et al., 2024).

Macroalgae, or better known as seaweeds, are multicellular organisms rich in lipids and proteins that can measure from a few centimetres to a metre. Macroalgae are divided into three phyla according to their pigmentation: Chlorophyta (green algae), Rhodophyta (red algae) and Phaeophyta (brown algae) (Dini, 2023; M. Silva et al., 2024; Wang et al., 2015). Brown algae account for approximately 59% of all macroalgae cultivated in the world, followed by red algae with 40% and green algae with less than 1% (Wang et al., 2015).

Microalgae are simple unicellular or multicellular organisms rich in carbohydrates that grow easily in different environments. This group of organisms can be classified as prokaryotic or eukaryotic organisms and by their colour: Cyanophyta (blue-green prokaryotic algae), Chlorophyta (green eukaryotic algae), Rhodophyta (red eukaryotic algae), Chrysophyta (golden eukaryotic diatoms) and Pyrrophyta (brown eukaryotic dinoflagellates) (Dini, 2023; M. Silva et al., 2024). Figure 17 shows the different phyla of micro and macroalgae.

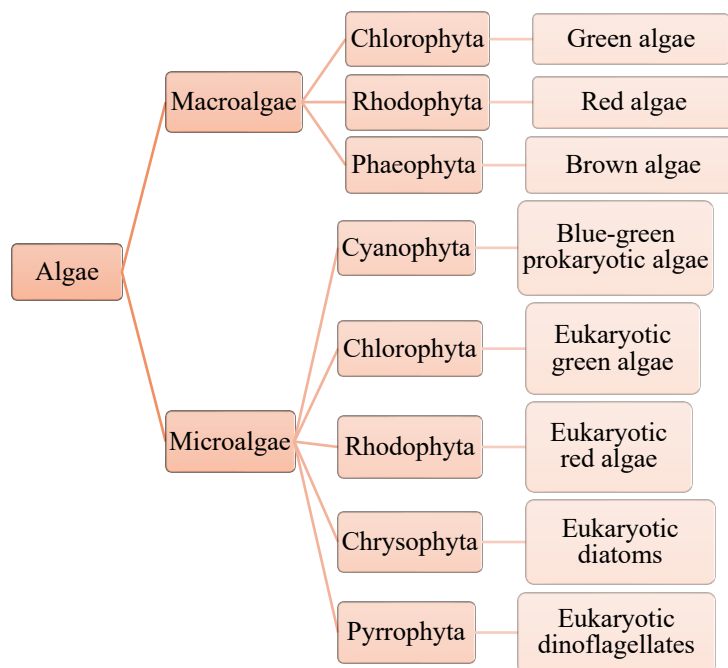


Figure 17 – Algae classifications. Adapted from (Dini, 2023).

Both macroalgae and microalgae have valuable potential due to their biologically active compounds. There is a huge diversity of natural bioactive compounds that are synthesized by algae, including antioxidants, pigments, carotenoids, protein-peptides and polysaccharides, as shown in Figure 18. The composition of algae metabolites can be influenced by intrinsic factors, such as the type and species, and by extrinsic factors, such as temperature and the composition of the aquatic environment (Aslam et al., 2021; Dini, 2023; Martínez-Ruiz et al., 2022).

Astaxanthin and lutein are two carotenoids that have aroused interest in the pharmaceutical world due to their natural antioxidant properties (Heo et al., 2010).

Beta-carotene, a carotenoid with antioxidant properties found in the microalga *Dunaliella salina*, and phycoerythrin, a red protein derived from red algae, are both used as colourants in the food and cosmetic industry (Hamouda & El-Naggar, 2021; Pourkarimi et al., 2020). Fucoxanthin, a carotenoid typically found in brown algae such as *Laminaria digitata*, has anti-inflammatory and antioxidant properties (Dini, 2023; Heo et al., 2010; Kelman et al., 2012).

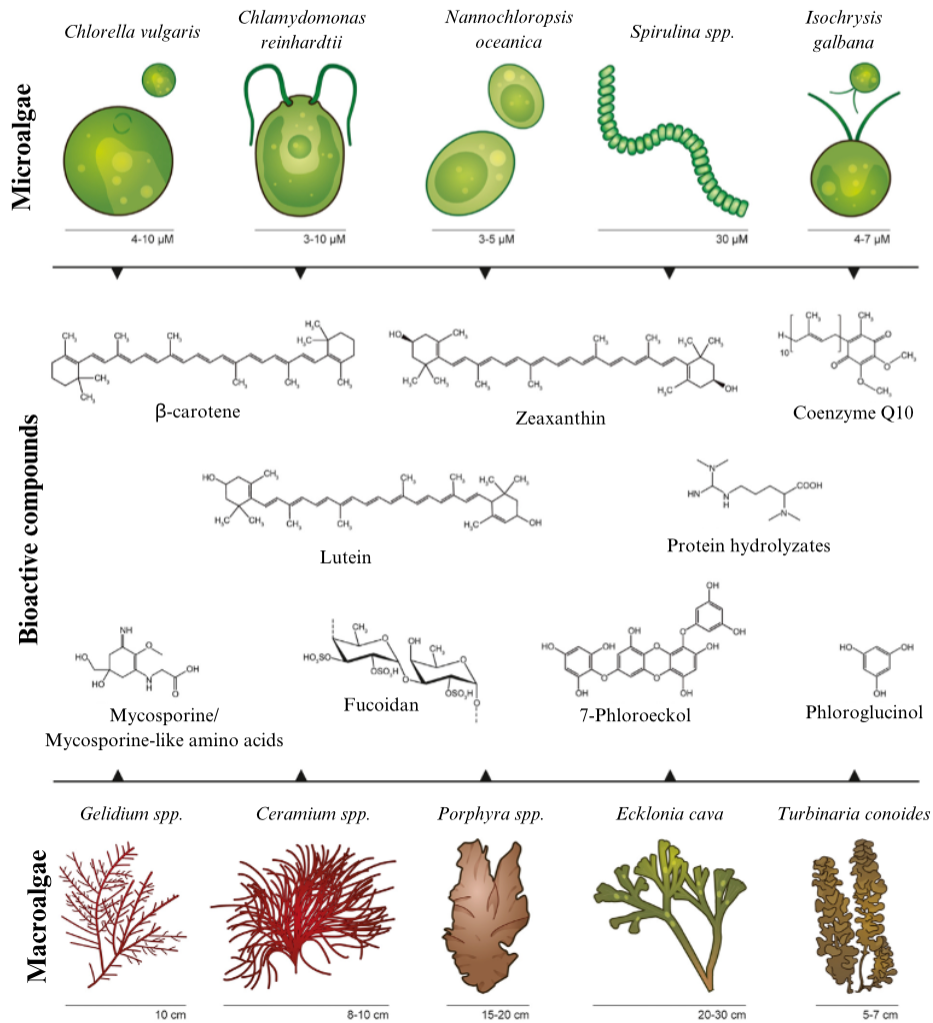


Figure 18 – Micro and macroalgae as mainstream bioactive compounds. Adapted from (Aslam et al., 2021).

4.2.1. Main uses

Algae exist naturally in the marine ecosystem, but they are also increasingly being cultivated continuously and artificially because they are considered an excellent natural resource. Algae species have been researched and explored, demonstrating a biodiversity of bioactive compounds with various biological applications and the potential to provide benefits in a wide variety of areas (Ariede et al., 2017; Aslam et al., 2021; Wang et al., 2015).

Algae are considered to be the most important biomass producers for many different applications. For example, they can be used for wastewater treatment, biofuels, food production, food additives and chemicals (Ariede et al., 2017; Wang et al., 2015).

Bioremediation by algae is a very effective strategy for avoiding the use of environmentally harmful chemicals in wastewater treatment (Alazaiza et al., 2022). Furthermore, the choice of algae as a source of biomass for the production of bioplastics is potentially replacing the synthesis of conventional bioplastics as a more sustainable alternative in the long term (Cheah et al., 2023). Figure 19 shows the various applications of algae biomass.

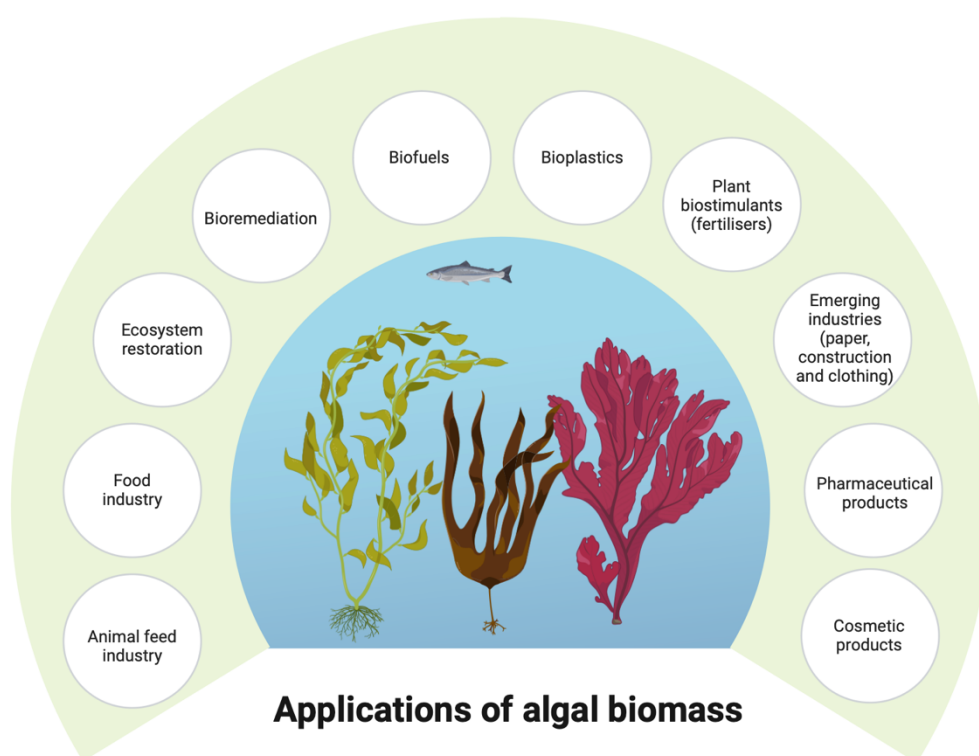


Figure 19 – Applications of algal biomass. Figure adapted from Comissão Europeia (2022).

In the pharmaceutical industry, algae have been widely used due to their antibacterial, antifungal, antiviral, antioxidant and anti-inflammatory properties (Aslam et al., 2021). Currently, microalgae are used to produce antibiotics, subunit vaccines, monoclonal antibodies, hepatotoxic and neurotoxic compounds, hormones, enzymes, among other pharmaceutical applications (Khavari et al., 2021).

Algae were introduced to the cosmetics field very early on due to their variety of secondary metabolites which are known for their beneficial effects on the skin (Ariede et al., 2017). Its derivatives can be used in three different ways: as additives that improve organoleptic properties, for stabilizing and preserving the formulation and also as compounds that perform an effective cosmetic function and activity (Michalak et al., 2020). They can be used as ingredients in lotions, soaps, shampoos, toothpastes, foams, gels, sun protection and hair products. On the other hand, they are often used as moisturizers, anti-ageing agents, skin whitening agents and also as anti-cellulite and slimming agents, as shown in Figure 20 (Dini, 2023; Michalak et al., 2020).

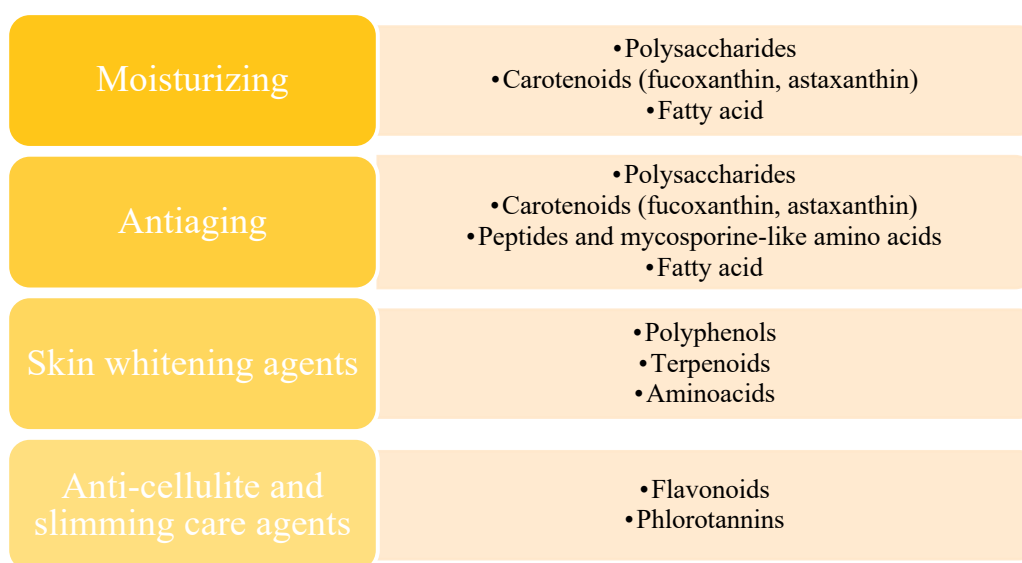


Figure 20 – Algae metabolites nutricosmetic potentialities. Adapted from (Dini, 2023).

4.2.2. Action mechanism

The polysaccharides found in algae are a key element in cosmetic products aiming skin hydration. These macromolecules are capable of storing water and establishing bonds with proteins, such as keratin, through hydrogen bonds, so that the degree of hydration of the outermost layer of the skin can be favored and maintained (Aslam et al., 2021).

Normally, polysaccharides extracted from algae, especially green seaweed, have a slower rate of moisture absorption compared to glycerin, a widely used humectant. However, despite this more gradual absorption, polysaccharides have a higher water

retention capacity, which results in longer hydration (Aslam et al., 2021; Zhang et al., 2022). The species *Ulva fasciata*, a green seaweed, is widely valued for its heteropolysaccharide content (Aslam et al., 2021). Sulphated polysaccharides obtained from red algae, particularly *Porphyra haitanensis*, are able to regulate the maturation of the keratinised envelope of the *stratum corneum* and improve the dermal-epidermal junction, which will promote better skin hydration (Aslam et al., 2021; Dini, 2023). In addition, alginates, from brown macroalgae, and agar, from red macroalgae, have a water retention capacity and contribute significantly to hydrate the skin (Dini, 2023).

Another relevant constituent present in algae with hydration properties regarding the lipids. The cosmetics sector has shown a growing interest in algae, particularly due to their high content of polyunsaturated fatty acids (PUFAs), phytosterols and carotenoids (De Luca et al., 2021).

The brown macroalga *Laminaria ochroleuca* stands out for its composition rich in unsaturated fatty acids, such as linoleic acid, oleic acid, linolenic acid and palmitoleic acid. As mentioned above, some of these compounds are often incorporated into emollient formulations, which play a fundamental role in maintaining the integrity of the skin barrier and reducing TEWL, thus contributing to skin hydration (Aslam et al., 2021; Dini, 2023).

The species *Cladophora glomerata*, which is a green microalgae, also has a profile rich in unsaturated fatty acids, which can be used in the production of oil-in-water emulsions, as well as sulphated polysaccharides which have moisturizing properties (Dini, 2023; Messyasz et al., 2018). Topical administration of carotenoids, such as astaxanthin, present in some species of microalgae, has been shown to be effective in improving skin hydration by regulating aquaporin levels (Ikarashi et al., 2020).

It has also been reported that certain species of red macroalgae, such as *Porphyra* and *Palmaria*, have high levels of arginine, an intermediate product of the urea cycle. This compound is part of the NMFs and plays a crucial role in the skin's natural moisturizing mechanism (Bedoux et al., 2014).

4.2.3. Clinical claims

Leelapornpisid et al. conducted a study to compare the moisturizing effect of a cream formulated with a green freshwater macroalgae (*Rhizoclonium hieroglyphicum* at

0.3%) with moisturizers already on the market, including glycerine (5%), propyleneglycol (5%) and hyaluronic acid (0.5%). Thirty individuals of both sexes aged between 30 and 60 took part. Skin hydration was measured before and after applying the creams at intervals of 15, 30 and 60 minutes for a short-term assessment and after 1 week of use, with twice daily applications, for a long-term assessment. The results indicated a significant increase in skin hydration, both in the short and long term, with the use of the algae extract cream compared to untreated skin. In turn, the long-term moisturizing effect of the macroalgae cream was similar to that of creams containing glycerin, propylene glycol and HA.

It is worth noting that over 80% of the participants expressed satisfaction with the macroalgae-based formulation, suggesting that this natural ingredient may be a more sustainable option for moisturizing the skin (Leelapornpisid et al., 2014; Murphy & Dow, 2021).

Choi et al. evaluated the moisturizing activity of 12 species of Korean algae using formulations containing 5% extract of each of the respective algae. This property was assessed using a corneometer probe, applying the cream to the participants' forearms and comparing it to a placebo (Choi et al., 2013). After 2 hours, the cream containing 10% *Laminaria japonica* extract showed a significant improvement in skin hydration compared to the placebo. The next measurement, taken 8 hours later, showed a reduction in TEWL with the same cream. The results indicated that *Laminaria japonica* extracts increased skin hydration over a period of 8 hours, with peak efficacy observed after two hours. The authors concluded that this brown seaweed has moisturizing properties, attributed to the humectants and hydrocolloids present in its composition, which makes it a promising ingredient in skin moisturizing formulations (Choi et al., 2013).

4.2.4. Algae-derived cosmetics already in the market

In the formulation of cosmetic products, seaweed can be used in its fresh state or in a fermented form. Furthermore, a single component of seaweed maybe used, or instead an extract of the plant. There are also example of cosmetic products in which specific species of seaweed or mixtures of several species are used, often together with extracts of other raw materials (i.e. terrestrial plants, medicinal herbs), as well as ingredients traditionally used in formulations. These combinations of algae species with other

components can be strategically used to promote a synergistic cosmetic effect of the components (Lopez-Hortas et al., 2021).

Algae perform different functions in cosmetic formulations, and can act as a moisturizing agent, excipient, thickener, colorant, preservative, additive, flavoring or even as a fragrance component (Morais et al., 2021).

The market for algae-based cosmetic products is estimated to reach a value of 1.10 billion dollars by 2031. In terms of volume, the market is expected to reach close to 87,000 tons in the same period (Meticulous Market Research, 2024).

In Europe, microalgae biomass has become increasingly relevant in the cosmetics sector, accounting for 24% of its use, which reflects the increased interest in the benefits that microalgae enhance in cosmetic and wellness formulations. With regard to macroalgae, 17 % of European companies use their production for cosmetic products (European Parliament, 2023).

Table 9 shows examples of moisturizing cosmetic products based on algae extracts alone or in combination with other species, as well as the type of formulation.

Table 9 – Examples of algae-based moisturizing products.

Product	Brand	Dosage form	Ingredients
Nuxe Crème Fraîche de Beauté	Nuxe (France)	Cream	Red algae extract
Lierac The Moisturizing Lotion	Lierac (France)	Lotion	Green and brown algae
SkinCeuticals Daily Moisture	SkinCeuticals (USA)	Cream	Red and brown algae extract
Crème de La Mer	La Mer (USA)	Cream	Brown algae extract
VOYA Renewal Eyes	VOYA (Ireland)	Eye mascara	Brown algae extract
BodyOcean Bio Regenerating Face Cream	BodyOcean (Portugal)	Cream	Red algae extract

BodyOcean is a Portuguese brand dedicated to the development and production of skincare products, using extracts of the wild red algae *Asparagopsis armata* as the

main ingredient. This algae is collected by hand by divers on the island of Faial in the Azores. After collection, they are subjected to an oven-drying process, which lasts an average of around 3 days. Currently, the brand only sells one product, an organic restorative face cream, available in 30 mL or 50 mL packs. According to BodyOcean, this cream promotes regeneration and hydration of the epidermis, resulting in smoother, brighter skin. It is important to note that 70% of the ingredients used are of organic origin, reflecting the brand's commitment to environmental sustainability and the socio-economic development of the regions involved in the production process (*BodyOcean – Wild & Organic Skincare*, n.d.).

4.8 Summing up

As mentioned in previous chapters, various ingredients with moisturizing and beneficial properties for the skin are incorporated into cosmetic product formulations. These include hyaluronic acid, ceramides, grape and algae extracts, which have gained prominence both in scientific studies and well as in the launch of new cosmetic products. Table 10 presents a comparative table summarizing the main characteristics of these ingredients, including their bioactivity, their role in moisturizing, scientific evidence proving their efficacy, as well as examples of cosmetic products available on the market.

Table 10 – Comparative analysis of the ingredients used in moisturizing cosmetic formulations that have been discussed throughout this work.

Ingredient being analyzed	Characteristics	Bioactivity	Role in skin hydration	Findings	Cosmetic products on the market
Acid Hyaluronic	Ubiquitous glycosaminoglycan in the human body; Molecule with a high-water retention capacity; Can be formed with different molecular weights (LMW, MMW, HMW, vHMW).	Cell regenerator; Anti-inflammatory; Moisturizing; Anti-wrinkle; Anti-aging; Collagen stimulation.	HMW-HA acts on the epidermis, forming a barrier that attracts and retains water, thus moisturizing and preventing TEWL; LMW-HA penetrates the skin right down to the dermis, retaining water and stimulating collagen production and deeper hydration.	A 1% HA formulation significantly improved the skin's constitution, increased hydration in the SC and reduced TEWL. In a randomized, blind study, the use of a cream with 1% HA and other bioactive compounds was shown to improve hydration and the skin's barrier function 24 hours after application.	L'Oréal Paris Hydra Filling Night Cream; Croma-Pharma Farewell Dry Skin; Biohyalux HA Hydro Intense Serum.
Ceramides	Sphingolipid naturally present in the <i>stratum corneum</i> ; An essential molecule for maintaining the skin's barrier integrity; Can be made up of different fatty acids and sphingoid bases giving rise to different types of ceramides.	Maintaining the skin's barrier function; Preventing TEWL; Moisturizing.	Ceramides help restore and maintain the integrity of the skin barrier, preventing TEWL, increasing the level of hydration and preventing irritants and allergens from entering the skin.	A randomized controlled trial revealed that the use of a moisturizing cream composed of ceramides increased skin hydration and decreased TEWL in elderly people with dry skin. In another study, a topical treatment with pCER was carried out on subjects with atopic dermatitis, which ultimately revealed that the application of the cream significantly reduced AD symptoms, decreased TEWL and increased skin water content.	CeraVe Facial Moisturising Lotion; Dr.Jart+ Ceramidin Liquid; Holika Holika Good Cera.
Grapes	Fruit produced by the <i>Vitis vinifera</i> (<i>L</i>) plant; It is one of the most cultivated fruit crops in the world; Rich source of phenolic compounds.	Antioxidant; Anti-inflammatory; Cardioprotective; Hepatoprotective; Anti-obesity; Anti-cancer; Moisturizing.	Grapes and their derivatives contain bioactive compounds (i.e resveratrol, flavonoids) that help retain water, maintain the skin's barrier function and increase the expression of aquaporins, thus promoting greater skin hydration.	A study was carried out in which an emulsion with 3% grapeseed extract was created which showed excellent results in increasing the skin's hydration, elasticity and smoothness, as well as a reduction in pore size and roughness. A cream with 2% Muscat hamburg grapeseed extract was shown to have antioxidant, natural skin whitening, moisturizing and anti-aging properties.	Caudalie Vinosource – Hydra; HydraVine Chardonnay Grape Mask; Dvine Grape Power Dynamic Day Cream.
Algae	Photosynthetic aquatic organisms; They can be divided into macroalgae and microalgae; They have an enormous diversity of biologically active compounds.	Antibacterial; Antifungal; Antiviral; Antioxidant; Anti-inflammatory; Moisturizing; Antiaging.	Some species of algae, such as <i>Ulva fasciata</i> , have polysaccharides that retain water and strengthen the skin barrier, promoting longer-lasting hydration. Other species, such as <i>Laminaria ochroleuca</i> , are rich in unsaturated fatty acids, which help to reduce water loss and preserve the skin's integrity.	A cream formulated with 0.3% freshwater green macroalgae (<i>Rhizoclonium hieroglyphicum</i>) showed an increase in skin hydration, both in the short and long term. The moisturizing activity of a formulation containing 12 species of Korean algae was evaluated, in which the brown alga <i>Laminaria japonica</i> stood out the most, managing to increase hydration and reduce TEWL.	Nuxe Crème Fraîche de Beauté; Lierac The Moisturizing Lotion; BodyOcean Bio Regenerating Face Cream.

5. Conclusions and Future Perspective

The choice of new, more environmentally friendly ingredients has been implemented by several cosmetics brands. The reuse of waste and the use of marine organisms are some examples of ways to obtain more profitable ingredients for the manufacture of cosmetic formulations.

Vitis vinifera (L) has been extensively exploited due to their beneficial properties for human health. The by-products derived from this fruit (i.e. stem, pomace, skin) are extremely rich in phenolic compounds, which makes their reuse essential to minimize the environmental impact they cause. On the other hand, algae are marine organisms that are an abundant source of biologically active compounds (i.e. lutein, beta-carotene), offering a more sustainable way of developing cosmetic formulations and at the same time reducing the impact on the environment.

The use of state-of-the-art ingredients, such as hyaluronic acid and ceramides, continues to be a strong source of composition for moisturizing cosmetic formulations. These components stand out both for their ease of production and for their diverse applications in the health sector and the cosmetics industry and are still widely known and scientifically studied.

The evolution of the cosmetics industry continues to be strongly driven by the influence of the media and the wide dissemination of scientific studies. These factors contribute to an exponential increase in the population's perception of the potential risks associated with chemical products, as well as the benefits of more sustainable constituents used in cosmetic formulations. There is growing consumer concern about the safety, efficacy and impact of the choice and correct use of products used in their skincare routine. Although the use of natural and ecological sources in cosmetics formulation offers several advantages, there are some challenges that must be taken into account, such as product accessibility due to high costs, the short shelf life of natural ingredients and the limitations imposed by the seasonality of these resources.

The cosmetics industry will continue to incorporate traditionally used ingredients into its formulations (i.e. lanolin, glycerin), which will continue to play a key role in the formulation of moisturizing products globally. On the other hand, more eco-friendly ingredients are gaining more and more ground in the cosmetics market, making them a promising and more profitable source in the cosmetics industry. In this monograph, it was

possible to overview the conventionally used ingredients for skin hydration as well as the latest generation of ingredients, together with new trends in the cosmetics sector: ingredients of natural origin. It is possible that new, more sustainable and eco-friendly ingredients could be the future of moisturizing cosmetics.

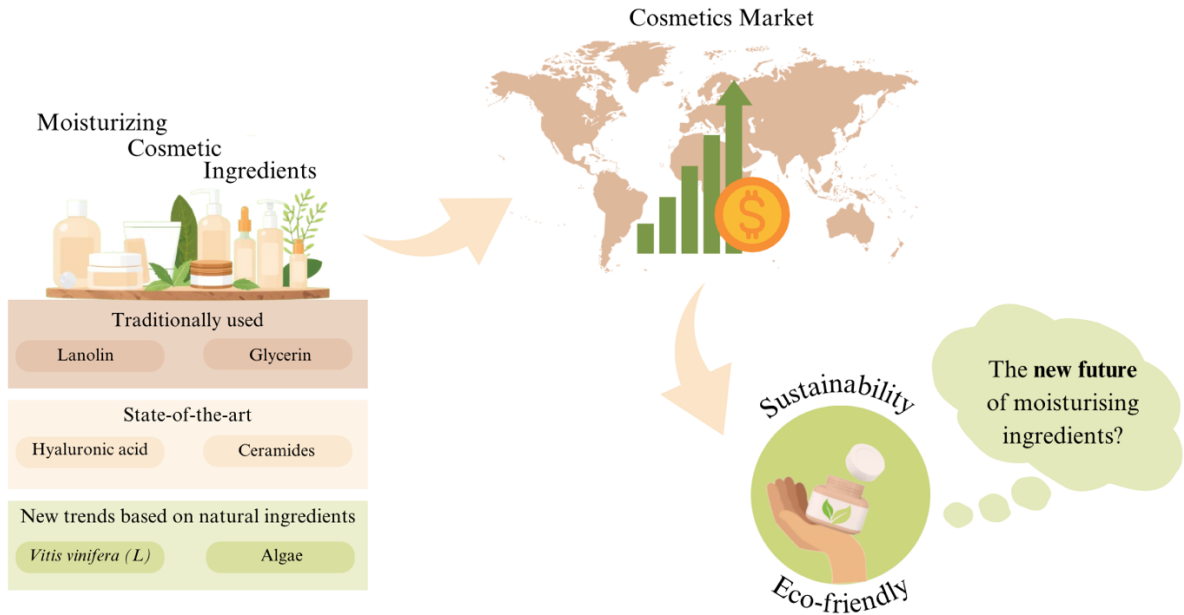


Figure 21 – Graphical abstract: Unravelling Skin Hydration – New Trends in Moisturizing Ingredients.

References

- Abatangelo, G., Vindigni, V., Avruscio, G., Pandis, L., & Brun, P. (2020). Hyaluronic Acid: Redefining Its Role. *Cells* 2020, Vol. 9, Page 1743, 9(7), 1743. <https://doi.org/10.3390/CELLS9071743>
- Afnan, Saleem, A., Akhtar, M. F., Sharif, A., Akhtar, B., Siddique, R., Ashraf, G. M., Alghamdi, B. S., & Alharthy, S. A. (2022). Anticancer, Cardio-Protective and Anti-Inflammatory Potential of Natural-Sources-Derived Phenolic Acids. *Molecules*, 27(21). <https://doi.org/10.3390/MOLECULES27217286>
- Alazaiza, M. Y. D., Albahnasawi, A., Ahmad, Z., Bashir, M. J. K., Al-Wahaibi, T., Abujazar, M. S. S., Abu Amr, S. S., & Nassani, D. E. (2022). Potential use of algae for the bioremediation of different types of wastewater and contaminants: Production of bioproducts and biofuel for green circular economy. *Journal of Environmental Management*, 324, 116415. <https://doi.org/10.1016/J.JENVMAN.2022.116415>
- Al-Halaseh, L. K., Al-Jawabri, N. A., Tarawneh, S. K., Al-Qdah, W. K., Abu-Hajleh, M. N., Al-Samydai, A. M., & Ahmed, M. A. (2022). A review of the cosmetic use and potentially therapeutic importance of hyaluronic acid ARTICLE INFO. *Journal of Applied Pharmaceutical Science*, 12(07), 34–041. <https://doi.org/10.7324/JAPS.2022.120703>
- Almargem. (2013). *Vitis Vinifera (L.)*. Retrieved September 26, 2024, from <http://almargem.org/biodiv/especie/vitis-vinifera/>
- A. L. Wagemaker, T., Rosado, C., P. Andrade, J., Fernandes, A. S., Rijo, P., Maia Campos, P., & Monteiro Rodrigues, L. (2013). Evaluation of the sensory properties of a cosmetic formulation containing green coffee oi. *Journal Biomedical and Biopharmaceutical Research*, 10(1), 101–108. <https://doi.org/10.19277/BBR.10.1.56>
- American Skin Association. (2020). *Healthy Skin*. Retrieved September 26, 2024, from <https://www.americanskin.org/resource/>
- Ariede, M. B., Candido, T. M., Jacome, A. L. M., Velasco, M. V. R., de Carvalho, J. C. M., & Baby, A. R. (2017). Cosmetic attributes of algae - A review. *Algal Research*, 25, 483–487. <https://doi.org/10.1016/J.ALGAL.2017.05.01>

Aslam, A., Bahadar, A., Liaquat, R., Saleem, M., Waqas, A., & Zwawi, M. (2021). Algae as an attractive source for cosmetics to counter environmental stress. *Science of The Total Environment*, 772, 144905. <https://doi.org/10.1016/J.SCITOTENV.2020.144905>

Baldwin, H., Alexis, A. F., Andriessen, A., Berson, D. S., Farris, P., Harper, J., Lain, E., Marchbein, S., Gold, L. S., & Tan, J. (2021). Evidence of barrier deficiency in rosacea and the importance of integrating OTC skincare products into treatment regimens. *Journal of Drugs in Dermatology*, 20(4), 384–392. <https://doi.org/10.36849/JDD.5861>

Barbieri, J. S., Wanat, K., & Seykora, J. (2014). Skin: Basic Structure and Function. *Pathobiology of Human Disease: A Dynamic Encyclopedia of Disease Mechanisms*, 1134–1144. <https://doi.org/10.1016/B978-0-12-386456-7.03501-2>

Barel, A. O., Paye, M., & Maibach, H. I. (2009). *Handbook of Cosmetic Science and Technology* (3rd ed.). Informa Healthcare USA, Inc.

Barnes, T. M., Mijaljica, D., Townley, J. P., Spada, F., & Harrison, I. P. (2021). Vehicles for drug delivery and cosmetic moisturizers: Review and comparison. *Pharmaceutics*, 13(12). <https://doi.org/10.3390/PHARMACEUTICS13122012>

Baroni, A., Buommino, E., De Gregorio, V., Ruocco, E., Ruocco, V., & Wolf, R. (2012). Structure and function of the epidermis related to barrier properties. *Clinics in Dermatology*, 30(3), 257–262. <https://doi.org/10.1016/J.CLINDERMATOL.2011.08.007>

Bäsler, K., Bergmann, S., Heisig, M., Naegel, A., Zorn-Kruppa, M., & Brandner, J. M. (2016). The role of tight junctions in skin barrier function and dermal absorption. *Journal of Controlled Release*, 242, 105–118. <https://doi.org/10.1016/J.JCONREL.2016.08.007>

Becker, L. C., Bergfeld, W. F., Belsito, D. V., Klaassen, C. D., Marks, J. G., Shank, R. C., Slaga, T. J., Snyder, P. W., & Andersen, F. A. (2009). Final report of the safety assessment of hyaluronic acid, potassium hyaluronate, and sodium hyaluronate. *International Journal of Toxicology*, 28(4 Suppl), 5–67. <https://doi.org/10.1177/1091581809337738>

Bedoux, G., Hardouin, K., Burlot, A. S., & Bourgougnon, N. (2014). Bioactive Components from Seaweeds: Cosmetic Applications and Future

- Development. *Advances in Botanical Research*, 71, 345–378. <https://doi.org/10.1016/B978-0-12-408062-1.00012-3>
- Bissett, D. L. (2009). Common cosmeceuticals. *Clinics in Dermatology*, 27(5), 435–445. <https://doi.org/10.1016/J.CLINDERMATOL.2009.05.006>
- BodyOcean – Wild & Organic Skincare. (n.d.). Retrieved October 16, 2024, from <https://bodyocean.pt>
- Bollag, W. B., Aitkens, L., White, J., & Hyndman, K. A. (2020). Aquaporin-3 in the epidermis: more than skin deep. *American Journal of Physiology - Cell Physiology*, 318(6), C1144. <https://doi.org/10.1152/AJPCCELL.00075.2020>
- Bom, S., Jorge, J., Ribeiro, H. M., & Marto, J. (2019). A step forward on sustainability in the cosmetics industry: A review. *Journal of Cleaner Production*, 225, 270–290. <https://doi.org/10.1016/J.JCLEPRO.2019.03.255>
- Bonté, F. (2011). Skin moisturization mechanisms: New data. *Annales Pharmaceutiques Françaises*, 69(3), 135–141. <https://doi.org/10.1016/J.PHARMA.2011.01.004>
- Bravo, B., Correia, P., Gonçalves Junior, J. E., Sant’Anna, B., & Kerob, D. (2022). Benefits of topical hyaluronic acid for skin quality and signs of skin aging: From literature review to clinical evidence. *Dermatologic Therapy*, 35(12). <https://doi.org/10.1111/DTH.15903>
- Brown, M., Williams, A., Chilcott, R. P., Brady, B., Lenn, J., Evans, C., Allen, L., McAuley, W. J., Beebeejaun, M., Haslinger, J., Beuttel, C., Vieira, R., Guidali, F., & Miranda, M. (2024). Topically Applied Therapies for the Treatment of Skin Disease: Past, Present, and Future. *Pharmacological Reviews*, 76(5), 689–790. <https://doi.org/10.1124/PHARMREV.123.000549>
- Brown, T. M., & Krishnamurthy, K. (2022). Histology, Dermis. *StatPearls*. <https://www.ncbi.nlm.nih.gov/books/NBK535346/>
- Bukhari, S. N. A., Roswandi, N. L., Waqas, M., Habib, H., Hussain, F., Khan, S., Sohail, M., Ramli, N. A., Thu, H. E., & Hussain, Z. (2018). Hyaluronic acid, a promising skin rejuvenating biomedicine: A review of recent updates and pre-clinical and clinical investigations on cosmetic and nutricosmetic effects. *International Journal of Biological Macromolecules*, 120, 1682–1695. <https://doi.org/10.1016/J.IJBIOMAC.2018.09.188>
- Burnett, C. L., Boyer, I. J., Bergfeld, W. F., Belsito, D. V., Hill, R. A., Klaassen, C. D., Liebler, D. C., Marks, J. G., Shank, R. C., Slaga, T. J., Snyder, P.

W., Gill, L. J., & Heldreth, B. (2020). Safety Assessment of Ceramides as Used in Cosmetics. *International Journal of Toxicology*, 39(3_suppl), 5S-25S. https://doi.org/10.1177/1091581820958692/ASSET/IMAGES/LARGE/10.1177_1091581820958692-FIG3.JPEG

Camilion, J. V., Khanna, S., Anasseri, S., Laney, C., & Mayrovitz, H. N. (2022). Physiological, Pathological, and Circadian Factors Impacting Skin Hydration. *Cureus*, 14(8). <https://doi.org/10.7759/CUREUS.27666>

Castro, M. L., Ferreira, J. P., Pintado, M., Ramos, O. L., Borges, S., & Baptista-Silva, S. (2023). Grape By-Products in Sustainable Cosmetics: Nanoencapsulation and Market Trends. *Applied Sciences* 2023, Vol. 13, Page 9168, 13(16), 9168. <https://doi.org/10.3390/APP13169168>

Chanda, A., & Singh, G. (2023). Skin. *Materials Horizons: From Nature to Nanomaterials*, 13–23. https://doi.org/10.1007/978-981-99-2225-3_2

Chang, W. H., Liu, P. Y., Lin, M. H., Lu, C. J., Chou, H. Y., Nian, C. Y., Jiang, Y. T., & Hsu, Y. H. H. (2021). Applications of Hyaluronic Acid in Ophthalmology and Contact Lenses. *Molecules*, 26(9). <https://doi.org/10.3390/MOLECULES26092485>

Cheah, W. Y., Er, A. C., Aiyub, K., Mohd Yasin, N. H., Ngan, S. L., Chew, K. W., Khoo, K. S., Ling, T. C., Juan, J. C., Ma, Z., & Show, P. L. (2023). Current status and perspectives of algae-based bioplastics: A reviewed potential for sustainability. *Algal Research*, 71, 103078. <https://doi.org/10.1016/J.ALGAL.2023.103078>

Choi, J.-S., Moon, W. S., Choi, J. N., Do, K. H., Moon, S. H., Cho, K. K., Han, C.-J., & Choi, I. S. (2013). Effects of seaweed *Laminaria japonica* extracts on skin moisturizing activity in vivo. *Journal of Cosmetic Science*, 64(3), 193–205.

Comissão Europeia. (2022). *COMUNICAÇÃO DA COMISSÃO AO PARLAMENTO EUROPEU, AO CONSELHO, AO COMITÉ ECONÓMICO E SOCIAL EUROPEU E AO COMITÉ DAS REGIÕES*. Retrieved September 26, 2024, from <https://eur-lex.europa.eu/legal-content/PT/TXT/HTML/?uri=CELEX%3A52022DC0592>

De Luca, M., Pappalardo, I., Limongi, A. R., Viviano, E., Radice, R. P., Todisco, S., Martelli, G., Infantino, V., & Vassallo, A. (2021). Lipids from

Microalgae for Cosmetic Applications. *Cosmetics 2021*, Vol. 8, Page 52, 8(2), 52. <https://doi.org/10.3390/COSMETICS8020052>

Di Pietro Fernandes, C., Santana, L. F., dos Santos, J. R., Fernandes, D. S., Hiane, P. A., Pott, A., Freitas, K. de C., Bogo, D., do Nascimento, V. A., Filiú, W. F. de O., Asato, M. A., & Guimarães, R. de C. A. (2023). Nutraceutical Potential of Grape (*Vitis vinifera* L.) Seed Oil in Oxidative Stress, Inflammation, Obesity and Metabolic Alterations. *Molecules 2023*, Vol. 28, Page 7811, 28(23), 7811. <https://doi.org/10.3390/MOLECULES28237811>

Del Rosso, J. Q., & Allison. (2019). Ceramide- and Keratolytic-containing Body Cleanser and Cream Application in Patients with Psoriasis: Outcomes from a Consumer Usage Study. *The Journal of Clinical and Aesthetic Dermatology*, 12(7), 18. <https://pubmed.ncbi.nlm.nih.gov/articles/PMC6715330/>

Dini, I. (2023). The Potential of Algae in the Nutricosmetic Sector. *Molecules*, 28(10). <https://doi.org/10.3390/MOLECULES28104032>

Draelos, Z. (2012). Aquaporins: An introduction to a key factor in the mechanism of skin hydration. *Journal of Clinical and Aesthetic Dermatology*, 5(7), 53. https://www.researchgate.net/publication/229154144_Aquaporins_An_introduction_to_a_key_factor_in_the_mechanism_of_skin_hydration

Draelos, Z. D. (2013). Cosmetic therapy. *Comprehensive Dermatologic Drug Therapy: Expert Consult - Online and Print*, 604-612.e1. <https://doi.org/10.1016/B978-1-4377-2003-7.00052-2>

Draelos, Z. D. (2018). The science behind skin care: Moisturizers. *Journal of Cosmetic Dermatology*, 17(2), 138–144. <https://doi.org/10.1111/JOCD.12490>

DVINE | Douro Beauty Essence. (n.d.). Retrieved October 17, 2024, from <https://dvineskin.com/>

Euro+Med PlantBase. (2017). *Vitis vinifera*. Retrieved September 26, 2024, from https://euoplusmed.org/cdm_dataportal/taxon/4403205a-0728-4fde-a9bc-9fead4abe334

European Commission. (2008). *CosIng - Cosmetics ingredients*. Retrieved September 26, 2024, from <https://ec.europa.eu/growth/tools-databases/cosing/>

European Medicines Agency. (2017). *Grapevine leaf, Vitis vinifera L., folium*. Retrieved September 26, 2024, from

https://www.ema.europa.eu/en/documents/herbal-summary/grapevine-leaf-summary-public_en.pdf

European Parliament. (2023). *The future of the EU algae sector*. Retrieved September 26, 2024, from [https://www.europarl.europa.eu/RegData/etudes/STUD/2023/733114/IPOL_STU\(2023\)733114_EN.pdf](https://www.europarl.europa.eu/RegData/etudes/STUD/2023/733114/IPOL_STU(2023)733114_EN.pdf)

Fabbro, S. K., Mostow, E. N., Helms, S. E., Kasmer, R., & Brodell, R. T. (2014). The pharmacist role in dermatologic care. *Currents in Pharmacy Teaching and Learning*, 6(1), 92–105. <https://doi.org/10.1016/J.CPTL.2013.09.008>

Fakhari, A., & Berkland, C. (2013). Applications and Emerging Trends of Hyaluronic Acid in Tissue Engineering, as a Dermal Filler, and in Osteoarthritis Treatment. *Acta Biomaterialia*, 9(7), 7081. <https://doi.org/10.1016/J.ACTBIO.2013.03.005>

Fallacara, A., Baldini, E., Manfredini, S., & Vertuani, S. (2018). Hyaluronic Acid in the Third Millennium. *Polymers*, 10(7). <https://doi.org/10.3390/POLYM10070701>

Feingold, K. R., & Elias, P. M. (2014). Role of lipids in the formation and maintenance of the cutaneous permeability barrier. *Biochimica et Biophysica Acta (BBA) - Molecular and Cell Biology of Lipids*, 1841(3), 280–294. <https://doi.org/10.1016/J.BBALIP.2013.11.007>

Ferkel, E., Manjoo, A., Martins, D., Bhandari, M., Sethi, P., & Nicholls, M. (2023). Intra-articular Hyaluronic Acid Treatments for Knee Osteoarthritis: A Systematic Review of Product Properties. *Cartilage*, 14(4), 424. <https://doi.org/10.1177/19476035231154530>

Ferreira, M., Matos, A., Couras, A., Marto, J., & Ribeiro, H. (2022). Overview of Cosmetic Regulatory Frameworks around the World. *Cosmetics 2022*, Vol. 9, Page 72, 9(4), 72. <https://doi.org/10.3390/COSMETICS9040072>

Fiorentini, D., Zambonin, L., Vieceli Dalla Sega, F., & Hrelia, S. (2015). Polyphenols as Modulators of Aquaporin Family in Health and Disease. *Oxidative Medicine and Cellular Longevity*, 2015. <https://doi.org/10.1155/2015/196914>

Fiume, M. M., Bergfeld, W. F., Belsito, D. V., Hill, R. A., Klaassen, C. D., Liebler, D. C., Marks, J. G., Shank, R. C., Slaga, T. J., Snyder, P. W., Andersen, F. A., & Gill, L. J. (2014). Safety assessment of vitis vinifera (grape)-derived

ingredients as used in cosmetics. *International Journal of Toxicology*, 33(6), 48S-83S.

https://doi.org/10.1177/1091581814545247/ASSET/IMAGES/LARGE/10.1177_1091581814545247-FIG2.JPEG

Flamini, R., Mattivi, F., De Rosso, M., Arapitsas, P., & Bavaresco, L. (2013). Advanced Knowledge of Three Important Classes of Grape Phenolics: Anthocyanins, Stilbenes and Flavonols. *International Journal of Molecular Sciences* 2013, Vol. 14, Pages 19651-19669, 14(10), 19651–19669. <https://doi.org/10.3390/IJMS141019651>

Fluhr, J. W., Darlenski, R., & Surber, C. (2008). Glycerol and the skin: holistic approach to its origin and functions. *British Journal of Dermatology*, 159(1), 23–34. <https://doi.org/10.1111/J.1365-2133.2008.08643>. Food and Drug Administration. (2024). *Is It a Cosmetic, a Drug, or Both? (Or Is It Soap?)*. Retrieved October 13, 2024, from <https://www.fda.gov/cosmetics/cosmetics-laws-regulations/it-cosmetic-drug-or-both-or-it-soap>

Freeman, S. C., & Sonthalia, S. (2023). Histology, Keratohyalin Granules. *StatPearls*. <https://www.ncbi.nlm.nih.gov/books/NBK537049/>

Fujii, M. (2021). The Pathogenic and Therapeutic Implications of Ceramide Abnormalities in Atopic Dermatitis. *Cells*, 10(9). <https://doi.org/10.3390/CELLS10092386>

Future Market Insights. (2023). *Global Grape Skin Extract Market Snapshot (2023 to 2033)*. Retrieved October 19, 2024 <https://www.futuremarketinsights.com/reports/grape-skin-extract-market>

Future Market Insights. (2024). *Ceramide Skincare Market*. Retrieved October 19, 2024, from <https://www.futuremarketinsights.com/reports/ceramide-skincare-market>

Gilaberte, Y., Prieto-Torres, L., Pastushenko, I., & Juarranz, Á. (2016). Anatomy and Function of the Skin. *Nanoscience in Dermatology*, 1–14. <https://doi.org/10.1016/B978-0-12-802926-8.00001-X>

Goberdhan, L., Makino, E., Fleck, T., & Mehta, R. (2016). Immediate and long-term effects of a topical serum with five forms of hyaluronic acid on facial wrinkles and intrinsic skin moisture content. *Journal of the American Academy of Dermatology*, 74(5). <https://doi.org/https://doi.org/10.1016/j.jaad.2016.02.072>

Goufo, P., Singh, R. K., & Cortez, I. (2020). A Reference List of Phenolic Compounds (Including Stilbenes) in Grapevine (*Vitis vinifera* L.) Roots, Woods, Canes, Stems, and Leaves. *Antioxidants*, 9(5). <https://doi.org/10.3390/ANTIOX9050398>

Graça, M. F. P., Miguel, S. P., Cabral, C. S. D., & Correia, I. J. (2020). Hyaluronic acid—Based wound dressings: A review. *Carbohydrate Polymers*, 241, 116364. <https://doi.org/10.1016/J.CARBPOL.2020.116364>

Hamouda, R. A., & El-Naggar, N. E. A. (2021). Cyanobacteria-based microbial cell factories for production of industrial products. *Microbial Cell Factories Engineering for Production of Biomolecules*, 277–302. <https://doi.org/10.1016/B978-0-12-821477-0.00007-6>Hara-Chikuma, M., & Verkman, A. S. (2008). Roles of Aquaporin-3 in the Epidermis. *Journal of Investigative Dermatology*, 128(9), 2145–2151. <https://doi.org/10.1038/JID.2008.70>

Harrer, D., Sanchez Armengol, E., Friedl, J. D., Jalil, A., Jelkmann, M., Leichner, C., & Laffleur, F. (2021). Is hyaluronic acid the perfect excipient for the pharmaceutical need? *International Journal of Pharmaceutics*, 601, 120589. <https://doi.org/10.1016/J.IJPHARM.2021.120589>

Harvey, J., Shariff, Z., Anderson, C., Boyd, M. J., Ridd, M. J., Santer, M., Thomas, K. S., Maidment, I., & Leighton, P. (2024). Original research: How can community pharmacists be supported to manage skin conditions? A multistage stakeholder research prioritisation exercise. *BMJ Open*, 14(1), 71863. <https://doi.org/10.1136/BMJOPEN-2023-071863>

Heo, S. J., Yoon, W. J., Kim, K. N., Ahn, G. N., Kang, S. M., Kang, D. H., affan, A., Oh, C., Jung, W. K., & Jeon, Y. J. (2010). Evaluation of anti-inflammatory effect of fucoxanthin isolated from brown algae in lipopolysaccharide-stimulated RAW 264.7 macrophages. *Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association*, 48(8–9), 2045–2051. <https://doi.org/10.1016/J.FCT.2010.05.003>

Huynh, A., & Priefer, R. (2020). Hyaluronic acid applications in ophthalmology, rheumatology, and dermatology. *Carbohydrate Research*, 489, 107950. <https://doi.org/10.1016/J.CARRES.2020.107950>

Iaconisi, G. N., Lunetti, P., Gallo, N., Cappello, A. R., Fiermonte, G., Dolce, V., & Capobianco, L. (2023). Hyaluronic Acid: A Powerful Biomolecule with Wide-Ranging Applications—A Comprehensive Review. *International Journal of Molecular Sciences*, *24*(12), 24. <https://doi.org/10.3390/IJMS241210296>

Ikarashi, N., Kon, R., Nagoya, C., Ishikura, A., Sugiyama, Y., Takahashi, J., & Sugiyama, K. (2020). Effect of Astaxanthin on the Expression and Activity of Aquaporin-3 in Skin in an In-Vitro Study. *Life*, *10*(9), 1–8. <https://doi.org/10.3390/LIFE10090193>

Institute for Quality and Efficiency in Health Care. (2022). *In brief: How does skin work?* Retrieved September 26, 2024, from [https://www.ncbi.nlm.nih.gov/books/NBK279255/International Organisation of Vine and Wine](https://www.ncbi.nlm.nih.gov/books/NBK279255/International%20Organisation%20of%20Vine%20and%20Wine). (2022). *World Statistics*. Retrieved September 26, 2024, from <https://www.oiv.int/what-we-do/global-report?oiv>

International Trade Administration. (2023). *South Korea Organic Beauty Market*. Retrieved October 25, 2024, from <https://www.trade.gov/market-intelligence/south-korea-organic-beauty-market>

Ishida, K., Takahashi, A., Bito, K., Draelos, Z., & Imokawa, G. (2020). Treatment with Synthetic Pseudoceramide Improves Atopic Skin, Switching the Ceramide Profile to a Healthy Skin Phenotype. *Journal of Investigative Dermatology*, *140*, 1762-1770.e8. <https://doi.org/10.1016/j.jid.2020.01.014>

Jepps, O. G., Dancik, Y., Anissimov, Y. G., & Roberts, M. S. (2013). Modeling the human skin barrier — Towards a better understanding of dermal absorption. *Advanced Drug Delivery Reviews*, *65*(2), 152–168. <https://doi.org/10.1016/J.ADDR.2012.04.003>

Johnson, H., Norman, T., Adler, B. L., & Yu, J. De. (2023). Lanolin: The 2023 American Contact Dermatitis Society Allergen of the Year. *Cutis*, *112*(2), 78–81. <https://doi.org/10.12788/CUTIS.0825>

Juhász, M. L. W., Levin, M. K., & Marmur, E. S. (2018). The use of natural ingredients in innovative Korean cosmeceuticals. In *Journal of Cosmetic Dermatology* (Vol. 17, Issue 3, pp. 305–312). Blackwell Publishing Ltd. <https://doi.org/10.1111/jocd.12492>

Juncan, A. M., Moisă, D. G., Santini, A., Morgovan, C., Rus, L. L., Vonica-țincu, A. L., & Loghin, F. (2021). Advantages of Hyaluronic Acid and Its

Combination with Other Bioactive Ingredients in Cosmeceuticals. *Molecules*, 26(15). <https://doi.org/10.3390/MOLECULES26154429>

Kahraman, E., Kaykın, M., Bektay, H. Ş., & Güngör, S. (2019). Recent Advances on Topical Application of Ceramides to Restore Barrier Function of Skin. *Cosmetics* 2019, Vol. 6, Page 52, 6(3), 52. <https://doi.org/10.3390/COSMETICS6030052>

Kang, S. Y., Um, J. Y., Chung, B. Y., Lee, S. Y., Park, J. S., Kim, J. C., Park, C. W., & Kim, H. O. (2022). Moisturizer in Patients with Inflammatory Skin Diseases. *Medicina* 2022, Vol. 58, Page 888, 58(7), 888. <https://doi.org/10.3390/MEDICINA58070888>

Kelman, D., Posner, E. K., McDermid, K. J., Tabandera, N. K., Wright, P. R., & Wright, A. D. (2012). Antioxidant Activity of Hawaiian Marine Algae. *Marine Drugs*, 10(2), 403. <https://doi.org/10.3390/MD10020403>

Khavari, F., Saidijam, M., Taheri, M., & Nouri, F. (2021). Microalgae: therapeutic potentials and applications. *Molecular Biology Reports*, 48(5), 4757. <https://doi.org/10.1007/S11033-021-06422-W>

Kim, A. R., Lee, N. H., Park, Y. M., & Park, S. N. (2019). Preparation and characterization of novel pseudo ceramide liposomes for the transdermal delivery of baicalein. *Journal of Drug Delivery Science and Technology*, 52, 150–156. <https://doi.org/10.1016/J.JDDST.2019.04.009>

Kim, Y. S., & Guilak, F. (2022). Engineering Hyaluronic Acid for the Development of New Treatment Strategies for Osteoarthritis. *International Journal of Molecular Sciences*, 23(15). <https://doi.org/10.3390/IJMS23158662>

Kono, T., Miyachi, Y., & Kawashima, M. (2021). Clinical significance of the water retention and barrier function-improving capabilities of ceramide-containing formulations: A qualitative review. *The Journal of Dermatology*, 48(12), 1807–1816. <https://doi.org/10.1111/1346-8138.16175>

Ky, I., Lorrain, B., Kolbas, N., Crozier, A., & Teissedre, P. L. (2014). Wine by-Products: Phenolic Characterization and Antioxidant Activity Evaluation of Grapes and Grape Pomaces from Six Different French Grape Varieties. *Molecules*, 19(1), 482. <https://doi.org/10.3390/MOLECULES19010482>

Leal, C., Gouvinhas, I., Santos, R. A., Rosa, E., Silva, A. M., Saavedra, M. J., & Barros, A. I. R. N. A. (2020). Potential application of grape (*Vitis vinifera* L.)

stem extracts in the cosmetic and pharmaceutical industries: Valorization of a by-product. *Industrial Crops and Products*, 154, 112675. <https://doi.org/10.1016/J.INDCROP.2020.112675>

Lee, C., Eom, Y. A., Yang, H., Jang, M., Jung, S. U., Park, Y. O., Lee, S. E., & Jung, H. (2018). Skin Barrier Restoration and Moisturization Using Horse Oil-Loaded Dissolving Microneedle Patches. *Skin Pharmacology and Physiology*, 31(3), 163–171. <https://doi.org/10.1159/000487401>

Leelapornpisid, P., Mungmai, L., Sirithunyalug, B., Jiranusornkul, S., & Peerapornpisal, Y. (2014). A Novel Moisturizer Extracted from Freshwater Macroalga [*Rhizoclonium hieroglyphicum* (C.Agardh) Kützing] for Skin Care Cosmetic. *J. Sci*, 41(5), 1195–1207. <http://epg.science.cmu.ac.th/ejournal/>

Lodén, M. (2016). Treatments Improving Skin Barrier Function. *Current Problems in Dermatology*, 49, 112–122. <https://doi.org/10.1159/000441586>

López-Galindo, A., Viseras, C., & Cerezo, P. (2007). Compositional, technical and safety specifications of clays to be used as pharmaceutical and cosmetic products. *Applied Clay Science*, 36(1–3), 51–63. <https://doi.org/10.1016/J.CLAY.2006.06.016>

Lopez-Hortas, L., Florez-Fernandez, N., Torres, M. D., Ferreira-Anta, T., Casas, M. P., Balboa, E. M., Falque, E., & Domínguez, H. (2021). Applying Seaweed Compounds in Cosmetics, Cosmeceuticals and Nutricosmetics. *Marine Drugs 2021, Vol. 19, Page 552*, 19(10), 552. <https://doi.org/10.3390/MD19100552>

Lueangarun, S., Tragulplaingam, P., Sugkraroek, S., & Tempark, T. (2019). The 24-hr, 28-day, and 7-day post-moisturizing efficacy of ceramides 1, 3, 6-II containing moisturizing cream compared with hydrophilic cream on skin dryness and barrier disruption in senile xerosis treatment. *Dermatologic Therapy*, 32(6), e13090. <https://doi.org/10.1111/DTH.13090>

Manayi, A., & Saeidnia, S. (2014). Cosmetics and Personal Care Products. *Encyclopedia of Toxicology: Third Edition*, 1043–1049. <https://doi.org/10.1016/B978-0-12-386454-3.00979-9>

Martin, M. E., Grao-Cruces, E., Millan-Linares, M. C., & Montserrat-De la Paz, S. (2020). Grape (*Vitis vinifera* L.) Seed Oil: A Functional Food from the Winemaking Industry. *Foods*, 9(10). <https://doi.org/10.3390/FOODS9101360>

Martínez-Ruiz, M., Martínez-González, C. A., Kim, D. H., Santiesteban-Romero, B., Reyes-Pardo, H., Villaseñor-Zepeda, K. R., Meléndez-Sánchez, E. R.,

Ramírez-Gamboa, D., Díaz-Zamorano, A. L., Sosa-Hernández, J. E., Coronado-Apodaca, K. G., Gámez-Méndez, A. M., Iqbal, H. M. N., & Parra-Saldivar, R. (2022). Microalgae Bioactive Compounds to Topical Applications Products—A Review. *Molecules*, 27(11). <https://doi.org/10.3390/MOLECULES27113512>

Martins, A. M., & Marto, J. M. (2023). A sustainable life cycle for cosmetics: From design and development to post-use phase. In *Sustainable Chemistry and Pharmacy* (Vol. 35). Elsevier B.V. <https://doi.org/10.1016/j.scp.2023.101178>

Masson, F. (2010). Acide hyaluronique et hydratation cutanée. *Annales de Dermatologie et de Vénéréologie*, 137(SUPPL. 1), S23–S25. [https://doi.org/10.1016/S0151-9638\(10\)70005-3](https://doi.org/10.1016/S0151-9638(10)70005-3)

Mawazi, S. M., Ann, J., Othman, N., Khan, J., Alolayan, S. O., Al Thagfan, S. S., & Kaleemullah, M. (2022). A Review of Moisturizers; History, Preparation, Characterization and Applications. *Cosmetics 2022, Vol. 9, Page 61*, 9(3), 61. <https://doi.org/10.3390/COSMETICS9030061>

Meckfessel, M. H., & Brandt, S. (2014). The structure, function, and importance of ceramides in skin and their use as therapeutic agents in skin-care products. *Journal of the American Academy of Dermatology*, 71(1), 177–184. <https://doi.org/10.1016/j.jaad.2014.01.891>

Messyasz, B., Michalak, I., Łęska, B., Schroeder, G., Górka, B., Korzeniowska, K., Lipok, J., Wieczorek, P., Rój, E., Wilk, R., Dobrzyńska-Inger, A., Górecki, H., & Chojnacka, K. (2018). Valuable natural products from marine and freshwater macroalgae obtained from supercritical fluid extracts. *Journal of Applied Phycology*, 30(1), 591. <https://doi.org/10.1007/S10811-017-1257-5>

Meticulous Market Research. (2024). *Global Algae Products Market for Cosmetics by Type (Hydrocolloids, Lipids, Carotenoids), Source (Seaweed, Microalgae {Chlorella, Spirulina}), Form (Dry, Liquid), Application (Skin Care {Moisturizers}, Hair Care Products), and Geography - Forecast to 2031*. Retrieved September 26, 2024, from [https://www.researchandmarkets.com/report/algae-products?utm_source=BW&utm_medium=PressRelease&utm_code=prhplf&utm_campaign=1959519+-+%241.1+Billion+Algae+Products+\(Hydrocolloids%2C+Lipids%2C+Carotenoids\)+Markets+-](https://www.researchandmarkets.com/report/algae-products?utm_source=BW&utm_medium=PressRelease&utm_code=prhplf&utm_campaign=1959519+-+%241.1+Billion+Algae+Products+(Hydrocolloids%2C+Lipids%2C+Carotenoids)+Markets+-)

+Global+Forecast+to+2031%3A+Increasing+Consumer+Preference+for+Cruelty-Free+and+Vegan+Cosmetics+Driving+Demand+&utm_exec=chdomspi

Meza, C. (2018). *Layers of the Skin*. Retrieved September 26, 2024, from <https://medium.com/@cindymeza/layers-of-the-skin-fa974368418>

Michalak, I., Dmytryk, A., & Chojnacka, K. (2020). Algae Cosmetics. *Encyclopedia of Marine Biotechnology*, 65–85. <https://doi.org/10.1002/9781119143802.CH3>

Mijaljica, D., Townley, J. P., Hondros, A., Hewson, C., Harrison, I. P., & Spada, F. (2024). Considering Phytosphingosine-Based Ceramide Formulations for Atopic Skin Care. *Dermato 2024, Vol. 4, Pages 5-22*, 4(1), 5–22. <https://doi.org/10.3390/DERMATO4010002>

Milani, M., & Sparavigna, A. (2017). The 24-hour skin hydration and barrier function effects of a hyaluronic 1%, glycerin 5%, and Centella asiatica stem cells extract moisturizing fluid: an intra-subject, randomized, assessor-blinded study. *Clinical, Cosmetic and Investigational Dermatology*, 10, 311. <https://doi.org/10.2147/CCID.S144180>

Mildner-Szkudlarz, S., Siger, A., Szwengiel, A., & Bajerska, J. (2015). Natural compounds from grape by-products enhance nutritive value and reduce formation of CML in model muffins. *Food Chemistry*, 172, 78–85. <https://doi.org/10.1016/J.FOODCHEM.2014.09.036>

Morais, T., Cotas, J., Pacheco, D., & Pereira, L. (2021). Seaweeds Compounds: An Ecosustainable Source of Cosmetic Ingredients? *Cosmetics 2021, Vol. 8, Page 8*, 8(1), 8. <https://doi.org/10.3390/COSMETICS8010008>

Murphy, M. J., & Dow, A. A. (2021). Clinical Studies of the Safety and Efficacy of Macroalgae Extracts in Cosmeceuticals. *The Journal of Clinical and Aesthetic Dermatology*, 14(10), 37. [/pmc/articles/PMC8711622/](https://pubmed.ncbi.nlm.nih.gov/articles/PMC8711622/)

Nakamura, Y., Tsuchiya, T., Hara-Chikuma, M., Yasui, M., & Fukui, Y. (2020). Identification of compounds in red wine that effectively upregulate aquaporin-3 as a potential mechanism of enhancement of skin moisturizing. *Biochemistry and Biophysics Reports*, 24, 100864. <https://doi.org/10.1016/J.BBREP.2020.100864>

Nassiri-Asl, M., & Hosseinzadeh, H. (2009). Review of the pharmacological effects of *Vitis vinifera* (Grape) and its bioactive compounds. *Phytotherapy Research : PTR*, 23(9), 1197–1204. <https://doi.org/10.1002/PTR.2761>

Nassiri-Asl, M., & Hosseinzadeh, H. (2016). Review of the Pharmacological Effects of *Vitis vinifera* (Grape) and its Bioactive Constituents: An Update. *Phytotherapy Research : PTR*, 30(9), 1392–1403. <https://doi.org/10.1002/PTR.5644>

Nguyen, J. K., Masub, N., & Jagdeo, J. (2020). Bioactive ingredients in Korean cosmeceuticals: Trends and research evidence. In *Journal of Cosmetic Dermatology* (Vol. 19, Issue 7, pp. 1555–1569). Blackwell Publishing Ltd. <https://doi.org/10.1111/jocd.13344>

Nunes, M. A., Rodrigues, F., & Oliveira, M. B. P. P. (2017). Grape Processing By-Products as Active Ingredients for Cosmetic Proposes. *Handbook of Grape Processing By-Products: Sustainable Solutions*, 267–292. <https://doi.org/10.1016/B978-0-12-809870-7.00011-9>

Official Journal of the European Union. (2009). *REGULATION (EC) No 1223/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 30 November 2009 on cosmetic products*. <https://eur-lex.europa.eu/eli/reg/2009/1223/oj>

Olatunji, O., & Das, D. B. (2015). Drug Delivery Using Microneedles. *Reference Module in Biomedical Sciences*. <https://doi.org/10.1016/B978-0-12-801238-3.04255-0>

OpenStax. (2012). *Anatomy and Physiology*. Retrieved September 26, 2024, from <https://openstax.org/books/anatomy-and-physiology/pages/preface>

Pourkarimi, S., Hallajisani, A., Nouralishahi, A., Alizadehdakhel, A., & Golzary, A. (2020). Factors affecting production of beta-carotene from *Dunaliella salina* microalgae. *Biocatalysis and Agricultural Biotechnology*, 29, 101771. <https://doi.org/10.1016/J.BCAB.2020.101771>

Purnamawati, S., Indrastuti, N., Danarti, R., & Saefudin, T. (2017). The Role of Moisturizers in Addressing Various Kinds of Dermatitis: A Review. *Clinical Medicine & Research*, 15(3–4), 75. <https://doi.org/10.3121/CMR.2017.1363>

Raab, S., Yatskayer, M., Lynch, S., Manco, M., & Oresajo, C. (2017). Clinical Evaluation of a Multi-Modal Facial Serum That Addresses Hyaluronic Acid Levels in Skin - JDDonline - Journal of Drugs in Dermatology. *Journal of Drugs in Dermatology*, 16(9). <https://jddonline.com/articles/clinical-evaluation-of-a-multi-modal-facial-serum-that-addresses-hyaluronic-acid-levels-in-skin-S1545961617P0884X/>

- Rafique, M., & Shah, S. N. H. (2019). Anti-Ageing Potential of a Cream (W/O Emulsion) Containing Grape Seed Extract (GSE): Formulation and in vivo Evaluation of Effectiveness Using Non-Invasive Biophysical Technique. *Journal of Clinical & Experimental Dermatology Research*, 10(4), 1–9. <https://doi.org/10.35248/2155-9554.19.10.500>
- Rajkumar, J., Chandan, N., Lio, P., & Shi, V. (2023). The Skin Barrier and Moisturization: Function, Disruption, and Mechanisms of Repair. *Skin Pharmacology and Physiology*, 36(4), 174–185. <https://doi.org/10.1159/000534136>
- Rawlings, A. V., & Harding, C. R. (2004). Moisturization and skin barrier function. *Dermatologic Therapy*, 17(1), 43–48. <https://doi.org/10.1111/J.1396-0296.2004.04S1005.X>
- Ribeiro, A. S., Estanqueiro, M., Oliveira, M. B., & Lobo, J. M. S. (2015). Main Benefits and Applicability of Plant Extracts in Skin Care Products. *Cosmetics 2015*, Vol. 2, Pages 48-65, 2(2), 48–65. <https://doi.org/10.3390/COSMETICS2020048>
- Sahle, F. F., Gebre-Mariam, T., Dobner, B., Wohlrab, J., & Neubert, R. H. H. (2015). Skin Diseases Associated with the Depletion of Stratum Corneum Lipids and Stratum Corneum Lipid Substitution Therapy. *Skin Pharmacology and Physiology*, 28(1), 42–55. <https://doi.org/10.1159/000360009>
- Sajna, K. V., Gottumukkala, L. D., Sukumaran, R. K., & Pandey, A. (2015). White Biotechnology in Cosmetics. *Industrial Biorefineries and White Biotechnology*, 607–652. <https://doi.org/10.1016/B978-0-444-63453-5.00020-3>
- Seeley, R. R., Tate, P., & Stephens, T. D. (2011). *Anatomia & Fisiologia* (8th ed.). Lusociência.
- Sasounian, R., Martinez, R. M., Lopes, A. M., Giarolla, J., Rosado, C., Magalhães, W. V., Velasco, M. V. R., & Baby, A. R. (2024). Innovative Approaches to an Eco-Friendly Cosmetic Industry: A Review of Sustainable Ingredients. *Clean Technologies 2024*, Vol. 6, Pages 176-198, 6(1), 176–198. <https://doi.org/10.3390/CLEANTECHNOL6010011>
- Serra, M., Casas, A., Teixeira, J. A., & Barros, A. N. (2023). Revealing the Beauty Potential of Grape Stems: Harnessing Phenolic Compounds for Cosmetics. *International Journal of Molecular Sciences*, 24(14). <https://doi.org/10.3390/IJMS241411751>

Sharafan, M., Malinowska, M. A., Ekiert, H., Kwaśniak, B., Sikora, E., & Szopa, A. (2023). *Vitis vinifera* (Vine Grape) as a Valuable Cosmetic Raw Material. *Pharmaceutics*, 15(5). <https://doi.org/10.3390/PHARMACEUTICS15051372>

Sharif, A., Akhtar, N., Khan, M. S., Mena, A., Mena, B., Khan, B. A., & Mena, F. (2015). Formulation and evaluation on human skin of a water-in-oil emulsion containing Muscat hamburg black grape seed extract. *International Journal of Cosmetic Science*, 37(2), 253–258. <https://doi.org/10.1111/ICS.12184>

Silva, L. R., & Queiroz, M. (2016). Bioactive compounds of red grapes from Dão region (Portugal): Evaluation of phenolic and organic profile. *Asian Pacific Journal of Tropical Biomedicine*, 6(4), 315–321. <https://doi.org/10.1016/J.APJT.2015.12.015>

Silva, M., Avni, D., Varela, J., & Barreira, L. (2024). The Ocean's Pharmacy: Health Discoveries in Marine Algae. *Molecules*, 29(8), 1900. <https://doi.org/10.3390/MOLECULES29081900/S1>

Sociedade Portuguesa de Dermatologia e Venereologia. (n.d.). *A pele*. Retrieved October 13, 2024, from https://www.spdv.pt/_a_pele

Spada, F., Barnes, T. M., & Greive, K. A. (2018). Skin hydration is significantly increased by a cream formulated to mimic the skin's own natural moisturizing systems. *Clinical, Cosmetic and Investigational Dermatology*, 11, 491–497. <https://doi.org/10.2147/CCID.S177697>

Statista. (2024). *Revenue of the natural personal care market worldwide from 2019 to 2029*. Retrieved September 26, 2024, from <https://www.statista.com/forecasts/1468810/revenue-of-the-natural-personal-care-market-worldwide>

Suphasomboon, T., & Vassanadumrongdee, S. (2022). Toward sustainable consumption of green cosmetics and personal care products: The role of perceived value and ethical concern. *Sustainable Production and Consumption*, 33, 230–243. <https://doi.org/10.1016/J.SPC.2022.07.004>

Tessema, E. N., Gebre-Mariam, T., Neubert, R. H. H., & Wohlrab, J. (2017). Potential Applications of Phyto-Derived Ceramides in Improving Epidermal Barrier Function. *Skin Pharmacology and Physiology*, 30(3), 115–138. <https://doi.org/10.1159/000464337>

Tortora, G. J., & Derrickson, B. (2016). *Princípios de Anatomia e Fisiologia* (14th ed.). Guanabara Koogan.

Transparency Market Research. (2023). *Hyaluronic Acid Beauty Products Market*. Retrieved October 18, 2024, from <https://www.transparencymarketresearch.com/hyaluronic-acid-beauty-products-market.html>

Uchida, Y., Holleran, W. M., & Elias, P. M. (2008). On the effects of topical synthetic pseudoceramides: comparison of possible keratinocyte toxicities provoked by the pseudoceramides, PC104 and BIO391, and natural ceramides. *Journal of Dermatological Science*, 51(1), 37. <https://doi.org/10.1016/J.JDERMSCI.2008.02.007>

Uchida, Y., & Park, K. (2021). Ceramides in Skin Health and Disease: An Update. *American Journal of Clinical Dermatology*, 22(6), 853–866. <https://doi.org/10.1007/S40257-021-00619-2>

Ukleja, A. (2013). | 201 Protection of human health in cosmetics law. https://www.researchgate.net/publication/257537430_Protection_of_human_health_in_cosmetics_law

Vahlquist, A., & Törmä, H. (2020). Ichthyosis: A Road Model for Skin Research. *Acta Dermato-Venereologica*, 100(7), 197–206. <https://doi.org/10.2340/00015555-3433>

Vaughn, A. R., Clark, A. K., Sivamani, R. K., & Shi, V. Y. (2018). Natural Oils for Skin-Barrier Repair: Ancient Compounds Now Backed by Modern Science. *American Journal of Clinical Dermatology*, 19(1), 103–117. <https://doi.org/10.1007/S40257-017-0301-1/METRICS>

Wang, H. M. D., Chen, C. C., Huynh, P., & Chang, J. S. (2015). Exploring the potential of using algae in cosmetics. *Bioresource Technology*, 184, 355–362. <https://doi.org/10.1016/J.BIORTECH.2014.12.001>

Weidinger, S., Beck, L. A., Bieber, T., Kabashima, K., & Irvine, A. D. (2018). Atopic dermatitis. *Nature Reviews. Disease Primers*, 4(1). <https://doi.org/10.1038/S41572-018-0001-Z>

Weiskirchen, S., & Weiskirchen, R. (2016). Resveratrol: How Much Wine Do You Have to Drink to Stay Healthy? *Advances in Nutrition*, 7(4), 706. <https://doi.org/10.3945/AN.115.011627>

Voegeli, D. (2007). The role of emollients in the care of patients with dry skin. *Nursing Standard (Royal College of Nursing (Great Britain) : 1987)*, 22(7). <https://doi.org/10.7748/NS2007.10.22.7.62.C4626>

Woo, S. H., Lumpkin, E. A., & Patapoutian, A. (2015). Merkel cells and neurons keep in touch. *Trends in Cell Biology*, 25(2), 74. <https://doi.org/10.1016/J.TCB.2014.10.003>

World Statistics | OIV. (n.d.). Retrieved September 26, 2024, from <https://www.oiv.int/what-we-do/global-report?oiv>

Weber, T. M., Kausch, M., Eng, D., Rippke, F., Schoelermann, A. M., & Filbry, A. W. (2012). Treatment of Xerosis with a Topical Formulation Containing Glyceryl Glucoside, Natural Moisturizing Factors, and Ceramide. *The Journal of Clinical and Aesthetic Dermatology*, 5(8).

Yasin, A., Ren, Y., Li, J., Sheng, Y., Cao, C., & Zhang, K. (2022). Advances in Hyaluronic Acid for Biomedical Applications. *Frontiers in Bioengineering and Biotechnology*, 10. <https://doi.org/10.3389/FBIOE.2022.910290>

Yousef, H., Alhaji, M., Fakoya, A. O., & Sharma, S. (2024). Anatomy, Skin (Integument), Epidermis. *StatPearls*. <https://www.ncbi.nlm.nih.gov/books/NBK470464/>

Zhang, T., Guo, Q., Xin, Y., & Liu, Y. (2022). Comprehensive review in moisture retention mechanism of polysaccharides from algae, plants, bacteria and fungus. *Arabian Journal of Chemistry*, 15(10), 104163. <https://doi.org/10.1016/J.ARABJC.2022.104163>

Zhou, D. D., Li, J., Xiong, R. G., Saimaiti, A., Huang, S. Y., Wu, S. X., Yang, Z. J., Shang, A., Zhao, C. N., Gan, R. Y., & Li, H. Bin. (2022). Bioactive Compounds, Health Benefits and Food Applications of Grape. *Foods*, 11(18). <https://doi.org/10.3390/FOODS11182755>

Zillich, O. V., Schweiggert-Weisz, U., Eisner, P., & Kerscher, M. (2015). Polyphenols as active ingredients for cosmetic products. *International Journal of Cosmetic Science*, 37(5), 455–464. <https://doi.org/10.1111/ICS.12218>