cosmetics

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Review

A Review of Moisturizers; History, Preparation, Characterization and Applications

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Abstract: Moisturizers are one of the most widely used preparations in cosmetics and have been extensively used to soften the skin for consumers. Moisturizers work effectively in combating dry skin which may cause pain, tightness, itch, stinging, and/or tingling. The aim of this review is to evaluate published studies on the history, ingredients, preparation processes, characteristics, uses, and applications of moisturizers. Moisturizers bridge the gap between medicine and consumer goods by being used to make the skin more beautiful and healthy. In the future, in moisturizer therapy, the capacity to adapt specific agents to specific dermatological demands will be crucial. Cosmetically, moisturizers make the skin smooth by the mechanism of increasing the water content in the stratum corneum, hence exerting its most vital action, which is moisturizing action and maintaining a normal skin pH.

Keywords: moisturizers; emollients; cosmetics; dry skin; characterization

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1. Introduction

There is a growing body of literature that recognizes the importance of moisturizers. It is essential for a wide range of fields, such as cosmetics and pharmacy [1]. Moisturizers are very popular dermatological products prescribed due to their proven efficiency to prevent and treat various dermatological conditions [2,3]. The terms "moisturizer" and "emollient" are often used interchangeably despite occlusives and humectants being usually included in moisturizers with the purpose of increasing the water-binding capacity of the stratum corneum (SC) of the skin [4].

Moisturizers are widely used for both normal and dry skin [1]. Application of these preparations can increase the water content in the stratum corneum, hence exerting its most vital action, which is moisturizing action aside from maintaining a normal skin pH, and allowing the lipid bilayers in the skin to more easily normalize and re-establish their capacity to connect corneocytes together and allow for moisture retention in the intercellular spaces [1,5,6]. Subsequently, the hydration interrupts the dry skin cycle, making the skin surface smooth, soft, pliable and more extensible [1,6]. In addition, some other plausible actions exerted by moisturizers include anti-inflammatory action by blocking cyclooxygenase activity, antimitotic action, antipruritic action via downregulation of cytokines, photoprotective action, antimicrobial action and wound healing [6].

Moisturizers are seldom associated with health hazards compared to prescription topical drugs despite being applied on large surface areas of the body for a long duration.

To date, few studies have used observational data to indicate that various ingredients with different characteristics are used in the preparation of moisturizers [4]. Therefore, dermatologists should consider characteristics, such as aesthetic beauty, which influence patient adherence, in addition to predicted clinical efficacy. Irritation and allergenicity, which affect safety and tolerability, are also factors to consider when making moisturizer recommendations to prevent unnecessary discomfort [4]. Moisturizers are often associated with a variety of discomforts, such as burning sensations, tightness, stinging and itching. The most common side effect is skin irritation, which is described as subjective sensations or sensory reactions with or without indications of inflammation [2]. Therefore, the purpose of this review is to systematically review the published data for moisturizers, aiming to bring forth information on the history, ingredients, methods of preparation, characterization, uses and applications of moisturizers.

2. History of Moisturizer

Even though cosmetics have most certainly existed for much longer, the first evidence of cosmetics dates from about 6000 years ago in Ancient Egypt. Aloe, myrrh, and frankincense are common among Egyptians. Ancient Egyptians believed these products, particularly frankincense, had anti-aging properties and used them as anti-wrinkle creams [7]. Jain et al. (2009) also reported that men and women in Egypt used scented oils and ointments to clean and smooth their skin and mask body odor as early as 10,000 BC. Egyptian hygiene and wellbeing were inextricably linked to cosmetics. For protection against the hot sun and dry winds, oils and creams were used [8]. Egyptian customs were exported and utilized by Greeks and Roman [7,9].

Crocodile excrement, white lead and chalk were commonly used by ladies to enhance the appearance of their skin. They also made face masks out of starch and eggs, which were thought to tighten the skin, reduce wrinkles, and keep the face looking youthful [7]. The term "cosmetic" comes from the Greek word "kosmetos," which means "adornment" or "ornament." Ointments containing cypress, cedar, and incense resins were applied at night. Lead acetate (white lead) and cinnabar were used to treat the skin (Hg).

After the conquest of Carthage, figs (*Ficus carica L.*) became very common in Rome. In order to formulate facial cream, they were combined with banana (*Musa L.*), oats (*Avena L.*), and rose water. Galen is credited with inventing the *Frigus crepito*, a precursor to the present cold cream. It is used as a skin protector, comprising almond oil, rose water and beeswax [9]. Gels and salves were used to blanch skin in China, especially during the Shang Dynasty (1760BC). New fixings and techniques were developed and presented as skincare moved to Europe and the Middle East.

The first virus cream was made with rose oil and water, with beeswax liquefied into it. Scabs were treated with the mineral alum, and skin inflammation was treated with olive lead [7]. Creams, also known as topical formulations, have been a staple in cosmetics since ancient civilizations. Creams are cosmetic or pharmaceutical products based on the techniques applied. Unmedicated creams are widely used in a number of dermatological conditions. In ancient times, creams were simply made through the combination of two or more ingredients with water as a solvent [10]. Albert Kligman coined the term "cosmeceuticals" (a mixture of "cosmetics" and "pharmaceuticals") in 1984 to provide an expert description of products with both cosmetic and therapeutic value [11]. Newer approaches for cream formulation are being used as technology advances; hence, the cosmetics industry today is very different from the one described earlier [10,11].

Surprisingly, there is no agreement about what constitutes a moisturizer, despite having a deep history. The word is a neologism invented by Madison Avenue advertisers to promote the simplistic notion that they moisturize the skin [6]. The inclination to add oily materials to the skin is almost instinctive, and it can date back to the dawn of time [6]. Natural substances, such as honey, oils or lipids, and fiber have been used in topical treatments to heal wounds since the ancient Egyptians [12]. Moisturizers were once

thought to prevent transepidermal water loss (TEWL) by occlusion, preventing dryness, in addition to skin smoothness and elasticity maintenance [6,13].

The bricks and mortar model suggests that the stratum corneum (SC), while being a dead layer, functions as an active membrane [6]. Corneocytes are the bricks, with their tough cell membranes and keratin microfibrils, while the lipid layers between the cells are the mortar [14]. The loss of the predominant intercellular lipids that play a vital role in regulating skin humidity by forming bilayers, such as ceramides, cholesterol, and fatty acids, results in damage to the structure of the water barrier, resulting in dry skin [6,15]. When the moisture content of the skin falls below 10% and the SC loses its continuity, it is considered dry.

3. Ingredients

Emulsifiers, moisturizing agents, polymer/thickeners, sensory modifiers, and preservatives are among the ingredients used in commercially available moisturizers [16,17]. Humectants, occlusives, and emollients are the three main types of moisturizing ingredients (Table 1) [16].

In addition to such ingredients, advanced benefit ingredients including vitamins, antioxidants, lipids, or sunscreens are often included in the formulation of moisturizers [16].

Humectants draw and bind water due to their chemical nature, making them hygroscopic conditioning agents, that will most likely pull water from the deeper epidermis and dermis [16,18]. The presence of several hydroxy (−OH) functionalities allows them to be water-soluble in nature, besides having the capabilities to absorb and retain water in the molecules within the stratum corneum (SC), supplying moisture to the skin tissues and improving skin hydration [16,19]. They also have the ability to draw water from the dermis into the epidermis while also trapping water from the atmosphere. Humectants, when used without an occlusive agent, will only increase water loss from the injured skin surface in a low humidity environment [20–22]. This is because occlusive agents help to slow down the loss of moisture from the skin [22].

Humectants are not easily retained on the skin by wash-off items, such as cleansers even though they are important moisturizing ingredients in leave-on formulas. Despite that, they are still recommended to be used as leave-on products, especially humectants with a prolonged transepidermal water loss (TEWL) impact and the application should be at least twice a day or more based on skin dryness severity [23,24]. Ingredients that exhibit humectant properties are glycerin, lactic acid, panthenol, butylene glycol, propylene glycol, sodium pyrrolidone carboxylic acid (PCA) and urea [25].

Glycerin is the most extensively used humectant found in most moisturizers [5,18,22,26]. The increase in hydration varies from 1% to 25% or more, with the highest improvement seen between 20% and 40% depending on the chassis [16,27]. Glycerin has been shown to help in barrier regeneration, including stratum corneum integrity, stability, and mechanical properties, in addition to the hydrating properties on the skin surface [16,28]. Desmosomal degradation has also been shown to be aided by glycerin [16].

Panthenol is a viscous liquid that is colorless, clear and odorless. In tissue, it is converted to D-pantothenic acid (vitamin B5). Panthenol has the ability to facilitate wound healing and fibroblast proliferation in addition to its humectant properties [25]. Other commonly used alcohols with humectant properties include butylene glycol [29] and propylene glycol [30,31]. Propylene glycol has been regarded as a penetration enhancer that is occasionally used as a solvent and vehicle for compounds that are unstable or water-insoluble [31]. However, propylene glycol has been shown to be a sensitizing agent that contributes to irritation and contact dermatitis [25]. Propylene glycol is more irritating compared to butylene glycol [25].

Occlusive agents help maintain a moisturized state in the stratum corneum (SC) by avoiding excessive water loss from the skin's surface (Table 1) [16,18,22,26,32]. Although they are not 100% occlusive, they permit water transfer that is required for the normal functioning of the skin [16]. The increased water content has the effect of speeding up

barrier recovery [16,33]. Since most occlusive agents lack hydroxy functional groups in their chemical structure, they are unable to bind to water [16]. They can, however, efficiently seal moisture into skin as they can form uniform hydrophobic films [16]. Ingredients that exhibit occlusive properties include petrolatum, lanolin, mineral oils and silicone derivatives [25]. Petrolatum, also known as petroleum jelly, is the most popular occlusive [16,22,26,34]. Petrolatum is a semi-solid at room temperature, consisting of a highly refined mixture of short and long-chain alkanes, microcrystalline wax, and mineral oils. Petrolatum liquefies when applied to the skin and penetrates the SC, where it recrystallizes, creating a robust interstitial occlusive structure that results in a significant reduction of transepidermal water loss [16]. The hydrocarbon content in petrolatum is hydrogenated during the refining process to produce oxidation-resistant molecules, from liquid to solid waxes. This contributes to the long shelf life [35]. Nonetheless, the greasy texture poses a significant disadvantage for most occlusives and petrolatum [25]. On top of that, PAHs (polycyclic aromatic hydrocarbons) are a type of contaminant that can be contained in petrolatum; various studies have discovered that long-term exposure is associated with cancer, besides allergies and skin irritation [36].

Lanolin, a naturally occurring keratin conditioner, is made up mostly of sterol esters, but also acids and sterols [37–40]. It can compensate for several of the shortcomings of petrolatum with comparable efficacy that can be detected 14 days after the substance has been discontinued [37]. Its appeal stems from its ability to spread, as well as its melting point being near to skin temperature and its ability to absorb water [37]. Because of the role of these materials in skin biology, the sterol content is also significant [41,42].

Lanolin tends to penetrate and incorporate itself into the stratum corneum's lipid structure, which explains its long-lasting effects [37]. It is also known as wool alcohol and is not commonly used in the preparation of moisturizers due to its unpleasant odor, allergenic potential, and high cost [43,44]. Mineral oils (paraffinum liquidum) have a better texture, but they can only minimize TEWL by 30%. Silicone derivatives, such as cyclomethicone and dimethicone, have a less greasy feel, are hypoallergenic, and are commonly used in "oil-free" formulations [41,43,45]. The word "oil-free" means that the products contain neither vegetable nor mineral oils added [25].

Emollients are water-insoluble materials, such as oils and lipids that do not form an occlusive film [16,46]. The molecular weight of the substance may often distinguish an emollient from an occlusive [16,47,48]. They are often utilized because of their ability to smooth and soften skin and give it a silky texture [16,47]. They are mostly made up of lipids that are close to the skin's intercellular lipids, and they can possibly replenish the lipid matrix that is damaged [16,49]. By substituting the main lipid components, the moisturizers' combinations of ceramide, fatty acids and cholesterol can help fix lipid bilayers damaged by solvents, soaps and harsh dry or cold weather conditions [50]. Ingredients that exhibit emollient properties include cetylcaprylic/capric triglyceride, cetearyl or cetyl alcohol, or oils, such as soybean, sunflower seed and grapeseed oil [16]. The double bond numbers in a fatty acid and their distribution along the carbon chain are the most important characteristics [35]. The degree of unsaturation has a significant impact on handling ease. Unsaturated fatty acids are more readily oxidized compared to saturated fatty acids [35]. Consumer desires, relevant benefit and therapeutic use, as well as the ideal sensory experience, all influence the form and level of emollient [16].

Table 1. Common active ingredients present in moisturizers.

Emollients	Fatty emollients (Octyl stearate, jojoba oil, propylene glycol, castor oil, glyceryl stearate), dry emollients (Isopropyl palmitate, decyl oleate, isostearyl alcohol), protective emollients (Isopropyl isostearate, diisopropyl dilinoleate) and astringent emollients (octyl octanoate, cyclomethicone, isopropyl myristate, dimethicone)	[41,51–53]
Humectants	Alpha hydroxyl acids (Lactic acid and glycolic acid), glycerine (glycerol), sodium pyrrolidine carboxylic acid (PCA), allantoin, honey, panthenol, propylene glycol, butylene glycol, PEG, hyaluronic acid, aluminium lactate, sodium lactate, urea, gelatine and sorbitol	[6,50]
Occlusives	Hydrocarbons (Mineral oil, petrolatum, caprylic/capric triglyceride, paraffin, squalene), fatty alcohols (Stearyl alcohol, cetyl alcohol, lanolin), fatty acids (Stearic acid, lanolin acid), polyhydric alcohols (Propylene glycol), vegetable waxes (Candelilla, carnauba), phospholipids (Lecithin), sterols (Cholesterol) and wax esters (Lanolin, beeswax, stearyl stearate)	[41,51–53]
Exfoliants	Lactic acid, urea, malic acid	[50]

The amounts of occlusives, humectants and emollients in a moisturizer determine its effectiveness [16,54]. A decent moisturizer should provide a good balance of all three [16,38,55]. To replenish and preserve moisture, a combination of these ingredients in sufficient quantities is required in order to provide an atmosphere that allows for skin barrier repair [16,56]. Since the thickness can be controlled independently of effectiveness, this mixture can be created as a cream or lotion [16].

Emulsifiers are necessary for the stability of moisturizers. Moisturizers are generally formulated either as emulsions or kinetically stabilized colloidal suspensions of two immiscible liquids (Table 2) [16,57]. This means there is no discernible phase distinction and the in-use experience remains constant during the product's shelf life [16,58]. Emulsifiers may be anything from small monomeric surfactants to large polymeric fragments, surfactants, and aggregations of lamellar liquid crystal [16,59]. Emulsifiers have long carbon chains, similar to those found in skin lipids, which allows them to have skin benefits [16,60]. As a matter of fact, the closer the emulsifier's chemistry is to skin lipids, the more skin benefit it can provide [16]. Emulsifiers can be categorized into nonionic and ionic emulsifiers [35]. Depending on the surface-active component of the compound, the ionic groups are classified into anionic or cationic [35,61,62]. Long-chain fatty acids, such as stearic acid and palmitic acid, are an example of widely used anionic emulsifiers [35,63]. In the preparation of cream, the acids are often partially neutralized with cationic excipients, and their concentrations can vary from 1 to 10% [35,64]. The epidermal tissue also contains fatty acids with a chain length of 14 to 22 carbons [35,64]. Cholesterol which is another lipid bilayer component can be utilized as a nonionic emulsifier in moisturizers [31,35,65]. The hydrophilic activity of nonionic emulsifiers is primarily based on ether linkages and hydroxyl groups [35,66]. Nonionic emulsifiers generally result in less skin irritation compared with ionic emulsifiers [35]. Ingredients that are commonly used as emulsifiers include ethylene glycol monostearate, Laureth 4 and 9, nonoxinols and octoxinols [67]. However, there is a newer method for delivering active ingredients into the epidermis known as liposome dispersion which results in better action [6].

Polymers are another class of materials used to enhance moisturizer stability and alter thickness, texture, and sensory feel [16,68]. Synthetic polyacrylate-type polymers or natural polymers, such as starch may be used [16,69]. Depending on the emulsifier and polymer used, the appearance and texture of emulsions vary significantly, independent of their effectiveness [16].

Water, is the most essential and commonly used raw material in the formulation of moisturizer cream as it is readily available and low cost [70,71]. Water is utilized as a solvent in skin creams to dissolve other ingredients; it must be free of contaminants and microbes [70,71]. Oil-in-water emulsions or water-in-oil emulsions are formulated depending on the amounts of water phase and oil phase used [70].

Niacinamide (Vitamin B3) is an inactive ingredient included in moisturizers that is the water-soluble physiologically active form of vitamin B3 used in many moisturizers and has a range of dermatological therapeutic benefits [16,72,73]. Niacinamide boosts ceramide production, decreases hyperpigmentation, has anti-inflammatory and antibacterial properties, and aids in anti-aging [16,74]. Flushing is a possible side effect of niacinamide-containing products. The offender ingredient is niacin, a form of vitamin B3 that can show up as a contaminant if raw material quality is not monitored properly [16,75].

Alpha hydroxy acids (AHAs), an additional ingredient in moisturizers, are commonly referred to as "fruit acids". They are a group of substances containing organic carboxylic compounds that include citric acid, glycolic acid, malic acid, lactic acid, and tartaric acid, all of which are naturally derived [16,76]. At different concentrations, AHAs have been used to improve desmosome resolution and induce desquamation, with beneficial effects on the epidermis and dermis [16,77]. AHAs are available at lower concentrations ranging from 5 to 10% that can be used on a daily basis to improve barrier function and improve the skin appearance related to wrinkling, sun damage and hyperpigmentation. Meanwhile, higher concentrations ranging from 20 to 70% are used as chemical peels [16]. Concerns have been raised about the efficacy of using AHA in everyday skincare items. Studies demonstrated an increased sensitivity to UV after using AHA-based products, prompting the recommendation of sun protection when using AHA-based products [37].

Peroxisome proliferator-activated receptors (PPARs) are transcription factors that are ligand-activated, having effects on skin barrier growth and maintenance, as well as increasing keratinocyte differentiation [16,78,79]. They increase epidermal thickness and synthesis of filaggrin, as well as the development of barrier-important lipids, such as ceramide and fatty acids, resulting in anti-aging benefits [16,78,80]. Unsaturated fatty acids that are naturally-occurring, such as conjugated linoleic acid (CLA), are examples of PPAR ligands [16]. When exposed to sunlight, such compounds oxidize quickly and lose efficiency [16].

Antioxidants, such as vitamins C (ascorbic acid) and E (α -tocopherol) are effective for protecting the skin from oxidative stress from the environment, such as UV rays and emissions [16,81]. However, when exposed to sunlight, they become unstable [16,82]. There are more stable types of these vitamins available, such as vitamin E acetate and magnesium ascorbyl phosphate [16,83,84]. However, inside the skin, these must be absorbed and transformed into the active form [16]. Since tartaric acid, citric acid, ethylenediaminetetraacetic acid, and its salts have minimal antioxidant activity, they serve as chelating agents, enhancing the effectiveness of antioxidants by reacting with heavy metal ions [6].

Hyaluronic acid (HA), a disaccharide polymer, is an essential part of the extracellular matrix, which helps keratinocytes proliferate, migrate, and heal wounds [16,85]. Due to its various hydroxyl moieties, HA is extremely hygroscopic and is frequently touted as a skincare wonder ingredient [16,86,87]. Because of its high molecular weight, topically-applied HA is unable to penetrate deeply enough into the skin to exert its biological effects [16].

Botanical substances are also used in the formulation of moisturizers [6,88,89]. However, the use of herbal extracts in moisturizers has not always been justified by clinical trials [90,91]. Instead, they could be added for marketing purposes to pique consumer interest in natural ingredients' alleged skin benefits. Aloe vera is the most well-known (*Aloe barbadensis* Miller leaf extract) [6]. The chemical compositions of different aloe species vary, and several investigations on the constituents do not specify the species studied [31,92]. Most of the customer's understanding of aloe's effectiveness is based on anecdotal evidence [31,93,94]. Burns and skin ulcers healing, as well as antibacterial and

anti-inflammatory properties, are all proposed benefits of aloe vera, but there is not sufficient evidence available to back up its usage [31,95]. Several studies on the effectiveness of aloe vera components have yielded contradictory findings, necessitating further clinical research with vehicle controls [31].

Allantoin is a compound that can be found in comfrey roots. It is a synthetic derivative called aluminum dihydroxy allantoinate [96,97]. It has been promoted as a moisturizer and keratolytic [6,98]. However, there is not sufficient evidence available to back up its usage. Oatmeal (*Avena sativa*) baths for calming rashes have been used by nurses for decades [6]. Meanwhile, the husk of oats can also be used as an exfoliant [37].

Bioflavonoids or plant-derived polyphenols, due to their antioxidant properties, are becoming more common in topical products [99]. Vitamin E, ascorbic acid, ubiquinol, and uric acid are all antioxidants found in normal skin. Their levels in the skin are affected by oxidative stress, and topical antioxidant therapy has been suggested to be beneficial to the skin. For instance, red tomato (*Lycopersicum esculentum*) contains an open-chain, unsaturated carotenoid that possesses protective effects against UV rays [31]. However, it remains to be proven how effective they are for reducing oxidative stress in the skin [6].

Fragrances and coloring agents are used more for their aesthetic value than for their moisturizing properties (Table 2) [6,12,100]. Such ingredients include benzoin resin, cinnamates, cinnamic acid and menthol. Coloring agents produce subtle hues and other optical effects, resulting in greater acceptance, though they can sometimes cause irritant dermatitis [6]. Certain moisturizers have fragrance ingredients incorporated in the form of masking agents, preventing the brain from perceiving their odor, even though they are advertised as "fragrance-free" or "unscented" [101,102]. Many unlisted fragrance ingredients are irritants that can cause allergies, extreme headaches, and asthma symptoms [36,103]. Perfumes can aggravate asthma in children and even lead to its development. It is the second most common source of allergy symptoms in patients [36].

Preservatives are used to kill or inhibit microorganism growth that is accidentally introduced during manufacturing or use [104]. Pathogens and nonpathogens are also possible contaminants [105–107]. The ideal preservative should have a wide spectrum of activity, be stable in the product, safe to use and have no effect on the product's physical properties [108]. Since no single preservative can satisfy all of these criteria, a mixture of substances is commonly used [4]. Ingredients that are widely used as preservatives in moisturizers include parabens (methyl-, propyl-, ethyl- and butyl-paraben) and phenoxyethanol [6].

Previous research has suggested that parabens can pose serious health risks, especially to humans (Table 3). As a result, there is an increasing market for preservative-free cosmetics [109,110]. Natural compounds, such as plant extracts or essential oils, may be used to replace parabens and address the issue of microbial purity in cosmetics [109]. Parabens are a form of preservative that easily penetrates the skin and is suspected of interfering with hormone function, resulting in endocrine disruption [36,111]. They interrupt male reproductive functions besides having the ability to mimic estrogens, the female sex hormones [36,112].

According to several studies, when methylparaben is applied to the skin, it will interact with other chemicals, causing skin aging and damage to DNA [36,113]. However, when consumed, parabens in food are metabolized, making them less estrogenic [114]. Meanwhile, parabens in cosmetics are applied directly to the skin and absorbed into the body. They then bypass the metabolic process, entering the bloodstream and body organs intact [111,115]. They have been linked to cancer and neurotoxicity among other health issues [36].

In order to resist contamination and microbial growth, products without preservatives added have to depend on low water activity, such as high alcohol concentration, low pH, and/or other agents that are not considered preservatives, such as essential oils [31,116]. However, other types of inconveniences can result from such formulations, such as insufficient preservation, poor cosmetic properties, or the risk of other adverse reactions [31,117].

When an allergy reaction is suspected, substances, such as ethylhexylglycerin and caprylyl glycol are normally used to replace preservatives (Table 3) [31].

Sunscreens are also included in moisturizer formulations due to media coverage provided on carcinogenicity and the accelerated skin-aging effects of sunlight [118,119]. The utilization of sunscreen products has increasingly widened not only in sunscreens but also in other cosmetics, such as moisturizers, where they can cause photocontact and contact allergic reactions [119–121]. Certain antioxidants, such as retinol palmitate, tocopherol (vitamin E) acetate and ascorbic acid (vitamin C), are utilized more specifically in sunscreen and moisturizing products to avoid aging [118,122]. However, in such preparations, they are uncommon causes of allergic contact dermatitis (Table 3) [118,123,124]. However, the low incidence of confirmed cases of allergic reactions may be due to a lack of recognition of a contact allergy or photoallergy to sunscreen products, as a differential diagnosis of a primary sun intolerance is not always evident [118]. Highly toxic para-aminobenzoic acid agents have been substituted by compounds, such as titanium dioxide, cinnamates and zinc oxide [6].

Table 2. Common Inactive Ingredients.

Thickeners	Carbomer, sorbitol, oleic acid, xanthan gum, isostearic acid, stearic acid and glyceryl stearate	[48]
Buffers	NaOH, TEA, maleic acid and citric acid	
Solvent	Water	
Preservatives	Potassium sorbate, rice bran oil, phenoxyethanol, disodium EDTA, propylparaben, methylparaben and vitamin C (L-Ascorbic Acid)	[4,48]
Lipids	γ-linoleic acid	[50,125]
Fragrance	Hazelnut fragrance	[50]
Colorants	TiO2	[50,126]
Emulsifiers	Cetearyl alcohol, sorbitan monolaurate and cetyl alcohol	[50,127]

Table 3. Adverse effects of moisturizers.

Adverse Effect	Plausible Causes	References
Cosmetic acne	Water in oil preparations that contains occlusive oils	[51,128]
Irritant reactions	Propylene glycol, solvents, proteins in vegetable oils, urea, hydroxyl acids	
Allergic contact dermatitis	Preservatives, propylene glycol, fragrances, sunscreens, lanolin, vitamin E, Kathon CG, herbal products (Aloe), chamomile oil, olive oil, tea tree oil	
Subjective irritation	Humectants (urea, lactic acid, PCA), preservatives (sorbic acid, benzoic acid)	
Photosensitivity eruptions and photomelanosis	Sunscreens, fragrances, hydroxyl acids, preservatives	
Occlusive folliculitis	Mineral oils, petrolatum	
Contact urticaria	Fragrances, balsam of peru, preservatives (sorbic acid)	
Poisoning in burn patients	Propylene glycol	
Intoxication	Salicylic acid	

4. Methods of Preparation

Moisturizers can be categorized into oil in water (o/w) moisturizers and water in oil (w/o) moisturizers based on the nature of the dispersed phase [129]. Compared to

ointments, water in oil (*w*/*o*) is less greasy and has better spreadability, while oil in water (*o*/*w*) readily rubs into the skin and is easily removed by water (Table 4) [130].

Table 4. Different dispensing formulations of moisturizers.

Class	Ointments	Lotions	Gel	Creams	References
Phase	Oil in water (*o*/*w*) or water in oil (*w*/*o*)	Oil in water	hydrophilic or hydrophobic	Oil in water (*o*/*w*) or water in oil (*w*/*o*)	[130,131]
Composition	*o*/*w* formulation consists of liquid and solid polyethylene glycol mixtures *w*/*o* formulation consists of water-insoluble hydrocarbons (hard, soft, liquid paraffin), vegetable oil, animal fats, waxes, polyalkylsiloxanes and synthetic glycerides	Water, propylene glycol and mineral oil	Hydrophilic gel (hydrogel): Water, glycerol/propylene glycol gelled with suitable agents, such as tragacanth, starch, cellulose derivatives, magnesium aluminium silicates and carboxyvinyl polymers Hydrophobic gel (oleogel): Liquid paraffin with polyethylene or fatty oils gelled with aluminium, colloidal silica or zinc soaps	*o*/*w* formulation consists of emulsifying agents, such as sodium or triethanolamine soaps, polysorbates and sulfated fatty alcohols combined, if necessary, with *w*/*o* emulsifying agents *w*/*o* formulation consists of an emulsifier, such as wool fat, monoglycerides and sorbitan esters	[1,6]
Preparation	Mostly 20% water and 80% oil and hence insufficient water for separation into the second phase at room temperature	For better spreadability, oil in water is prepared with emulsifiers. Typically comprises of aqueous vehicle, >50% water and volatiles	Contains liquid phase within a three-dimensional polymeric matrix that is cross-linked physically or chemically using appropriate gelling agents	Preparation of *o*/*w* creams at elevated temperatures and subsequently cooled down to room temperature to allow the internal phase to solidify oil (50%) and water (50%)	[1,6,132]
Usage	Beneficial when a high degree of occlusion is needed. In intertriginous and moisture-bearing regions, this product should not be used	After-shave lotions, moisturizers for the face (daytime), body and hairy parts	Since it is easily absorbed and noncomedogenic, it can be used in intertriginous areas and has a high acceptability on the face	When occlusion is not needed. Moisturizers that can be used at night. Hands, non-hairy bits, and face (at night)	[1,6]
Features	Greasy, glossy look when applied. Develops a protective layer on the skin, which is particularly useful when the humidity is low (60%)	Nongreasy, thinner which easily cover larger area	Easily absorbed, smooth finishing, noncomedogenic and non-oily	Viscous, opaque, non-greasy to mildly greasy	[1,6,132]

4.1. Preparation of Oil in Water (o/w) Moisturizer

The emulsifier and oil-soluble components are combined in a beaker and melted at 75 °C in a water bath. Water, water-soluble materials and preservatives are melted at 75 °C in another beaker. The oil phase is placed in a mortar and pestle after heating, and the water phase is gradually added and triturated until a clicking sound is heard. Finally, perfuming agents and/or preservatives are added as the temperature cools down. The amount of water in this preparation will be greater than the amount of oil [70].

4.2. Preparation of Water in Oil (w/o) Moisturizer

The emulsifier and oil soluble components are melted together at 75 °C in one beaker. Water and water-soluble materials are taken to another beaker and melted at 75 °C. The water phase is placed in a mortar and pestle after melting, and the oil phase is gradually added and triturated until a clicking sound can be heard. The perfuming agent is added

after the cream has cooled to the desired temperature. This preparation would have a lower amount of water phase and a higher amount of oil phase [70].

Depending on the dispensing medium, moisturizers come in a variety of formulations. A cosmetic emulsion is the most common delivery method. The emulsification method incorporates several steps that contain the active ingredients (Table 4) [6].

5. Characterization

5.1. Determination of pH

At room temperature, the pH of the cream can be determined using a standard digital pH meter by diluting an appropriate quantity of the formulation with a suitable solvent in a beaker [70]. However, it is advisable to calibrate the pH meter before use with a standard buffer solution at pH 4 and pH 7 [133,134]. Meanwhile, according to Maha et al. (2018), the pH of a topical preparation should be between 4.5 to 6.5, which corresponds to the pH of the skin. The pH should not be too acidic, as this can irritate the skin, nor should it be too alkaline [135].

5.2. Organoleptic Properties/Physical Appearance

Involves grading of its texture and color [70]. To be more precise, the clarity, smell, texture, and foreign particles present were evaluated. The grittiness and stickiness were determined by rubbing them between two fingers [136]. Esoje et al. (2016) suggested that this test was to be conducted randomly, at different temperatures and storage duration to observe for any changes [137].

5.3. Centrifugation Test

It is conducted to assess the chemical and physical stability of the formulation under the influence of centrifugal force [138,139]. Five to ten grams of sample were centrifuged at 3000 rpm for 30 min at room temperature. The formulation was examined for phase separation after the centrifugation process, which is an indicator of formulation instability [109,138,139]. Meanwhile, Fernandes et al. (2018) evaluated both organoleptic (look, color, feel, thickness) and physical (phase separation and creaming) properties. Phase separation is denoted by the presence of caking, coalescence, and flocculation [140].

5.4. Mechanical Vibration Test

This test assesses the formulation's stability when subjected to mechanical vibration, which can result in phase separation and indicate instability. Five grams of sample were vibrated for 10 s on a vortex shaker (Haidalph) [109].

5.5. Spreadability

Spreadability is a term used to describe the area a topical application spreads after being applied to the skin of the affected areas, with shorter intervals indicating better spreadability [141]. Between two glass slides, the formula was applied and pressed to achieve a uniform film thickness. Following that, a weight of 10 g was added to the pan, and the top plate was pulled using a string attached to a hook. The time it takes for the upper glass slide to travel 10 cm over the lower plate is recorded, and the spreadability (S) is calculated using the formula [142].

$$\text{Spreadability} = \frac{\textit{Weight tied to upper slide} \times \textit{glass slide length}}{\textit{Time taken to separate slides}} \quad (1)$$

5.6. Saponification Value

The saponification value is a measure of saturation, with higher values indicating shorter chain fatty acids in the glycerol bond [143]. Meanwhile, Saraf et al. (2011) stated that the saponification value is a measurement of the amount of free fatty acid esters in a sample which affects the formulation's stability, pH, and cleaning properties. The formulation's

saponification value should be appropriate; if the fat content is too high, it can contain too much fatty acid, which is susceptible to hydrolysis and may lead to rancidification and microbial growth [144]. Two grams of substance were refluxed for 30 min with 25 mL of 0.5 N alcoholic KOH; then, 1 mL of phenolphthalein was applied and titrated with 0.5 N HCl right away, marking the result as 'a'. The procedure was repeated, this time omitting the material to be tested, marking the result as 'b' in the reading [70].

$$\text{Saponification value} = \frac{(b-a) \times 28.05}{weight\ of\ subtance\ (gram)} \quad (2)$$

5.7. Density

This is the proportion of a substance's mass to the volume it takes up. This parameter is an indication of air incorporation or the loss of volatile ingredients in liquids or semi-solids. A graduated cylinder and a balance were used to determine the (apparent) density of the formulations. The test was performed in triplicate with 10 mL of each formulation, and an average was determined. The apparent density is correlated with the recipient's capacity [109].

5.8. Light Test

The formulations were placed in clear plastic containers and exposed to intense light for 15 days using a daylight bulb with a photoperiodicity system consisting of 16 h of light and 8 h of dark. The samples were analyzed for any changes in physical properties, such as clarity, appearance, or color, as well as liquefaction, at the end of the exposure period. Any visible phase separation or color change is an indication of product instability [109].

5.9. Acid Value

The acid value is a measurement of the amount of free acid in fats or oils that causes rancidity upon exposure to heat or light [145]; 10 g of substance was dissolved in a precisely weighted 50 mL mixture of equal parts alcohol and solvent ether. The flask was attached to a reflux condenser and slowly heated until the sample was fully dissolved; 1 mL of phenolphthalein was added and titrated with 0.1 N NaOH until the appearance of a slightly pink color after 30 s of shaking [70].

$$\text{Acid value} = \frac{no.of\ mL\ of\ 0.1\ \text{N KOH solution} \times 5.61}{weight\ of\ subtance\ (gram)} \quad (3)$$

5.10. Viscosity

The viscosity is used to evaluate the formulation's stability with regard to consistency and as a result, to predict how the substance will behave over time [109]. The Brookfield Viscometer can be used to calculate the viscosity of formulated creams [70]. Viscosity values are calculated by multiplying the dial reading with correction factors in the Brookfield viscometer. Increased viscosity during storage indicates kinetically unstable emulsions, in which free-moving droplets collide and appear to coalesce [135].

5.11. Homogeneity

Shows the distribution of materials in the formula [135]. Touch and visual appearance were used to check for homogeneity [70]. The homogeneity of cream can be assessed by smearing 50 mg of preparations onto a clean object-glass, showing a homogeneous arrangement with no clear grain observation [135]. Homogeneity and texture were conducted simultaneously by Chen et al. (2016) by pressing a small amount of the formulation between the thumb and index finger to assess the presence of coarse particles. The immediate skin feel was also assessed, which includes stiffness, grittiness, and greasiness [146].

5.12. Dye Test

To determine the type of emulsion [133]. A drop of cream was placed on a slide after the cream was mixed with scarlet dye. Then, the slide was covered with a coverslip and examined under a microscope; o/w creams have dispersed globules that appear red and the ground is colorless and vice versa for w/o creams [70].

5.13. After Feeling Test

After application of a fixed amount of cream, the slipperiness, emollience and residue left were assessed [70].

5.14. Type of Smear

The smear pattern developed on the skin after the cream application was assessed [70].

5.15. Irritancy Study

This test determines the characteristics of produced formulations in terms of skin irritation [147]. On the left-hand dorsal surface, draw a 1 sq.cm section. The cream was applied to the designated location, and the duration was recorded. Erythema, irritation and edema were assessed and recorded at regular intervals for up to 24 h [70]. Another type of skin irritation test was conducted using albino rabbits. During the test time, these animals were held in separate cages and given fresh food and water; 24 h before the test, the fur on the neck and thighs was shaved to reveal a sufficiently wide test area. Surgical spirit was used to disinfect the test site briefly. The test area was then covered with cream. For 24 h, 48 h, and 72 h after application, the test site was monitored for erythema and edema [141]. Irritancy studies should be performed on animals prior to human studies. Once the prepared formulation demonstrated high compliance in animal tests, then it could be applied to healthy human volunteers to determine its safety for topical use [148]. Both animal and human studies are preferably conducted in skin irritancy tests as some substances are harmful to rabbits but not to humans, and vice versa [148,149].

5.16. Spectrophotometric Test

It is another form of stability testing involving the dilution of formulations in ultra-pure water at a ratio of 1/100 (m/v); then they are analyzed using spectrophotometry in the UV-VIS region (210 nm to 600 nm), with the spectrum compared to the control formulation's reference spectrum. Formulation instability is described as variations in intensity or absorption bands' wavelength. This indicates that some changes have occurred in the color intensity or even modification of the coloring content [109].

5.17. Microbial Stability

The microbial contamination test was used to assess the formulations' microbial stability. After preparing the bacteria and yeast culture medium, it was autoclaved for 20 min at 125 °C, and then 20 mL of the culture medium was poured into a sterile Petri dish. The Petri dishes were then inoculated with 0.2 g of each formulation in the center of each plate, and incubated for 3 days at 37 °C or 25 °C, depending on the inoculated microorganisms. Plates were removed after the incubation period and tested for microbial growth, which indicates contamination [109].

5.18. In Vitro Occlusivity Test

The occlusion factor was used to assess the formulations' occlusivity. When the occlusion factor is zero ("0"), there is no occlusion effect when compared to the reference; "100" is the highest occlusion factor, indicating complete surface coverage by the topical formulation [150,151]. Creams with a higher occlusion effect result in more moist skin that is more pliable and maintains its moisturizing effect [151]. Each beaker with a height of 4.6 cm and a diameter of 3.2 cm was filled with 10 g of distilled water. Then, the open end was covered with Whatman filter paper (0.45 pore size) on which 200 mg of the sample

was uniformly distributed. After that, the beakers were set at 37 ± 2 °C/607 ± 5% RH for 48 h. The in vitro occlusivity of all formulations, prototype formulations, and the negative control in which the filter paper was left uncovered were investigated to determine the water flux. The occlusion factor F was determined as follows [152]:

$$F = \frac{A - B}{A} \times 100$$

where A = Water flux via uncovered filter (percent water loss) and B = Water flux via filter when covered by test preparation (percent water loss).

5.19. Accelerated Stability Study

According to ICH guidelines, all formulations were subjected to accelerated stability testing for a duration of 2 weeks at a temperature of 25 ± 2 °C and 40 ° ± 2 °C, with two relative humidity conditions, specifically 60 ± 5% RH and 75 ± 5% RH. The cosmetic formulations were examined for organoleptic characteristics (texture, smell, color, phase separation and consistency) and their pH value was determined after 8 days. At the end of the storage period, the process was repeated [70,109].

5.20. Preference Test

Color, scent and skin sensation were the criteria of preference tests focused on sensory assessment. A numerical scale was used to determine the degree of preference as based on the Table 5 [142]:

Table 5. Different dispensing formulations of moisturizers.

5	like extremely
4	like
3	neutral
2	dislike
1	dislike extremely

6. Uses and Applications

Moisturizers are beneficial for a variety of purposes. There is evidence of biological effects that support the use of moisturizers in medicine [118]. Many moisturizers block cyclooxygenase activity, which inhibits the development of proinflammatory proteinoids, and thus have a calming effect on inflamed skin, leading to their anti-inflammatory action. Mineral oil-based moisturizers have a low-level antimitotic effect on the epidermis, making them effective in inflammatory dermatoses, such as psoriasis, which have increased epidermal mitotic activity. Emollients reduce itching by inhibiting the development of cytokines. In addition, the cooling effect of water evaporating from the skin surface after using water-based moisturizers contributes to the antipruritic effect. Sunscreens with varying sun protection factors are also used in moisturizers, offering extra sun protection (photoprotective action). Moisturizers also have antimicrobial and wound-healing properties [6].

Skin hydration, friction, scaling, and mechanical properties are all affected by moisturizers. A series of changes occur after a single application of a moisturizer, all of which reflects the moisturizer's composition. Initial changes tend to be related to the moisturizer's water content, which includes increased evaporation from the skin surface, decreased temperature, and skin softening. Changes occur with repeated applications over time, which are assumed to be caused by the moisturizer's lipid phase, involving a reduction in scaling, increased hydration and discrete color changes. Specific additives, such as urea, alpha-hydroxy acids, or glycerol, may help to reinforce some of these improvements [118].

Moisturizers are often prescribed as preventative measures and adjunct therapy for a variety of dermatological conditions. Moisturizers seem to be able to reverse some of the barrier defects seen in conditions, such as atopic dermatitis, allowing for improved disease control. Moisturizers have been studied for their adjuvant properties. The use of a moisturizer as an alternative to active corticosteroid treatment of the skin has been shown to minimize the quantity of corticosteroids required, without compromising treatment efficacy. It is postulated that the moisturizer's lipid content may play a role, but the mechanism underlying this remains unclear [118].

There is also a possibility that applying a moisturizer meets an atavistic psychological desire for physical contact, which is reinforced by the moisturizer's immediate physical impact. Using a moisturizer necessitates extensive touching, either by oneself or by another person, resulting in enhanced sensory perception. It is also likely that additional psychological factors may be overlooked when moisturizers are used, such as stress coping and a sense of security, thus reinforcing the use of moisturizers [118].

Moisturizers are often advertised and, as a result, are able to generate significant revenue for all advertising companies. While emolliency is an essential feature of moisturization, advertisement has almost fully replaced the conventional definition of creams or emollients. Marketing concepts promote that skin that is dry and dull is unattractive, while young and attractive skin is supple and moist. Moisture is needed for dry skin, which obviously can be compensated by the usage of moisturizers. Although there is no sufficient evidence of a sex disparity in dryness parameters, the strong focus on this chain of reasoning has persuaded a large number of women that their skin is dry, further promoting the expanded use of moisturizers [118].

7. Conclusions

Moisturizers are often used for both healthy and diseased skin, bridging the gap between medicine and consumer goods. The ability to tailor particular agents to specific dermatological needs will be critical in the future of moisturizer therapy. Knowing the characteristics and interactions of active ingredients with the skin will allow for better utilization of available moisturizers. Dermatologists who have a thorough understanding of moisturizers and have the initiative to explain the importance of moisturization to their patients may improve patient compliance. It is important to keep in mind that moisturizer formulas do not come without flaws. Patients who apply moisturizers on a regular basis can develop contact dermatitis, which is often caused by preservatives or fragrances used in many commercial products. Hence, dermatologists should weigh the risk of allergenicity and irritancy against cost, availability, and customer preferences for patients with sensitive skin or established skin conditions.

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