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Review

Cosmeceuticals: A Newly Expanding Industry in South Africa

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Abstract: Africa is counted amongst the cosmetic market contributors; however, South Africa's remarkable plant diversity is still largely untapped in terms of its potential for medicinal and cosmetic purposes. Thus, we aim to provide a critical assessment of the advancements made in South African cosmeceuticals with emphasis towards online local companies/brands that are manufactured by small, medium and micro enterprises (SMMEs). For the current study, we limited our search of herbal cosmeceutical products to SMMEs with online websites, or products traded in other online cosmetic directories such as 'Faithful to Nature' and 'African Botanicals' using a simple Google search. We recorded more than 50 South African SMME companies/brands involved in the trade of cosmeceuticals. Skin and hair care were the major product categories widely traded in these online platforms. Furthermore, few patents were recorded from South African researchers and institutions thereof, which is quite alarming considering the extensive research that has been undertaken to study these commercially valuable plants. Based on the increasing number of new products and the wide pool of economically important plants coupled to their associated rich indigenous knowledge systems, the cosmeceutical sector can contribute to the economy, job creation, entrepreneurship skills, socio-economic development and intellectual property generation.

Keywords: aloe; cosmetics industry; cosmeceutical patents; natural products; rooibos; skin physiology

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1. Introduction

The cosmetics industry, made up of skincare, haircare, fragrances, colour cosmetics, and personal care, is one of the key thriving industries globally. In the last two decades, the industry has contributed to the development of ground-breaking innovative products as consumers continue to seek cosmetics of natural origin, influenced by new trends in fashion, media and television, marketing, and changing lifestyles [1]. As the ideology of beauty changes from glamour towards youthfulness and healthy lifestyles, consumers are shifting their focus into purchasing cosmetic products that promote emotional and mental well-being, considered as self-care products. Furthermore, the paradigm shift towards natural products among consumers for the promotion of a healthy lifestyle has caused a shift in demand from products (mascara, lipsticks, foundation, lotion, creams) formulated from synthetic compounds to safe cosmetic products, especially of natural origin, with specific health purposes (such as anti-dandruff shampoo, anti-acne creams, anti-inflammatory lotion, and healing creams). The lifestyle change of consumers has greatly influenced the industry, leading to the development of cosmetic products with active ingredients sourced from nature.

Cosmeceuticals incorporate biologically active ingredients with therapeutic benefits (medicinal or drug-like) intended for external use or use on teeth and the mucous membranes of the oral cavity. These products use ancient knowledge of beauty techniques, rituals/traditions, and indigenous ingredients known to have healing and cleansing properties. Generally, the main active ingredients in cosmeceuticals are of plant, animal, and/or microorganism origin, of which herbal ingredients make up the largest category of additives relative to animal-derived and microorganism by-products. The active compounds (such as phenolics, flavonoids, alkaloids, terpenoids, saponins, etc.) in herbal ingredients offer valuable bioactivities such as antioxidant, photo-protection, antimicrobial, healing, and anti-ageing agents, as well as anti-inflammatory action useful for skin, hair, and dental care [2–5]. Herbal products are also rich in nutrients, for instance, vitamins, minerals, carotenoids, and anthocyanins, that keep skin healthy and glowing, repair DNA, slow down ageing, and protect against UV skin damage [6]. The benefits of phytochemicals, herbal nutrients, and minerals, amongst others, had led to the formulation of UV filters such as sunscreen products, but nowadays, UV filters are incorporated in different cosmeceutical products, e.g., moisturizing creams, anti-ageing creams, aftershave products, and make-up, due to the detrimental effect of skin exposure to UV radiation caused by sunlight [7].

Now, the paradigm shift of beauty perception, motivated by the "inside-out" ethos in cosmeceuticals, is well-established, as dermatologists recognize the value of external (topical) and internal (dietary) factors that might contribute to healthy hair and skin [8]. This is not new to the African continent as the majority of the medicinal plants used for skin disorders are applied externally as ointments, pastes, and poultices, while few are taken orally as infusions. Due to South Africa's long history of herbal use, there are quite a number of medicinal plants used in the treatment of various skin disorders and as beautifying agents. For instance, Lall and Kishore [9] reported on 117 plant species distributed in South Africa that are traditionally used for several skin disorders. A survey carried out by Ndhlovu et al. [10] recorded 49 plant species belonging to 31 families, used by Vhavenda women (in the Vhembe district, Limpopo, South Africa) as natural-based cosmetics and cosmeceuticals. Several other publications have reported on a number of medicinal plants widely used in South Africa as herbal-based cosmeceuticals [11–16]. Accordingly, research on a handful of these plant species in South Africa is starting to yield positive results, as some of the plants have been brought into commercialization in a form of cosmeceuticals for skin, hair, personal, and dental care. These products are gradually getting global recognition and a number of them have been well received locally by consumers, as some of the products cater for the diversity of South African (black, white, coloured and Indian populations) skin and hair care.

Thus, the current review aims to highlight some of the advancements made in South African herbal cosmeceuticals with emphasis on online local brands. This new untapped domain can be advantageous for South African cosmetic industries towards economic growth, job creation, and the generation of intellectual property (IP; patents) through the use of ancient traditional knowledge of medicinal plants. The review also details some of the available cosmeceutical patents developed from South Africa using endemic medicinal plants. The need for sustainability and conservation of plants used in cosmeceuticals from the formal and informal market is also emphasized.

2. Global Cosmetic Industry Transformation and Market Trends

In the past two decades, the global beauty market has seen major changes that are reflected in the economic, social, and cultural transformation [17]. The rise in environmental awareness changed the behaviour of consumers in reference to sustainable products. Concerns have been raised on the harmful impact caused by the cosmetic industry on the environment, human health, and animal testing. Thus, the global trends towards natural cosmeceuticals, with an increasing interest in eco-friendly products that have minimal or no side effects/adverse reactions, and are not harmful to the environment, have become the major drivers of the cosmetic industry. Such trends have also been linked to the need for

self-care, such as health-care-promoting products that are beneficial for one's emotional and mental well-being, as highlighted by the Gen Z (generation born between 1997 and 2012) and Millennials (generation born between 1981 and 1996) [18]. The need for transparency in beauty product labels is another important factor that Millennials (40%) demand as they seek natural skin and hair care products [19]. Beauty products free of chemicals, e.g., parabens, silicones, and sulphates are the preferred choice [19]. Recent research indicated that nearly half of Millennials started using cosmeceutical skin care products with organic, sustainable, or herbal-based features that were free of synthetic chemicals, while 59% mainly purchased hair care products that were free of synthetic chemicals [19]. Moreover, the desire for 'green' features amongst women of different ages (15–70 years) worldwide has escalated, whereby 64% prefer organic ingredients, 60% prioritize sustainable products, and 52% prefer vegan ingredients when purchasing beauty products [20]. Another drastic change that has revolutionized the cosmetic industry, brought by the Millennials and Gen Z generations, is online shopping through avenues such as Amazon, beauty specialty, online beauty specialty, and natural/specialty grocery stores (Figure 1a,b). Such trends in consumer behaviour have been brought about by the influence of social media, as social networks play a critical role in shaping consumer opinions, influencing attitudes and purchasing decisions [21]. The powerful role of social media has been noted in a global study conducted in 2019, which showed that 37% of the consumers learnt about new online brands through social media ads, 33% via recommendations and comments, 22% through following expert blogger posts, 22% through following online product brand companies, and another 22% from following online endorsed celebrities [21]. The cosmetics industry needs to understand consumer's attitude and their buying behaviour for continued market growth.

The cosmetic industry generates billions of dollars annually as new advanced and specialized products enter the market. The cosmetic beauty industry shares are made up of five business segments including skin care, hair care, make-up, fragrances, and toiletries. Skin care and hair care are the major product categories. In 2018, skin care products accounted for 39% of the global market, 21% was recorded for hair care products and 19% for make-up products [23]. According to the Fortune Business Insights [24], the global skin care market in 2020 was valued at USD 98.83 billion with a projected growth value of USD 100.13 billion for 2021, and it is expected to reach a growth value of USD 145.82 billion by 2028. Moreover, the global hair care market reached USD 92.52 billion in 2020 with a projected increase of USD 105.14 billion by 2025 [25]. The main cosmetic market contributors are segregated into North America, Europe, Asia-Pacific, as well as Latin America, the Middle East and Africa (LAMEA) (Figure 2), with Asia-Pacific and LAMEA considered as the prominent growth markets [26]. Amongst these regions, the 2016 global data indicated Asia-Pacific (37%) as the major cosmetic market contributor, followed by North America (25%) and Europe (24%), with LAMEA contributing 14% to the global cosmetic market (Figure 2a). The 2020 global data indicated increases in the global market share of Asia-Pacific (39%) and Europe (31%), whereas North America (22%) and LAMEA (7%) experienced a drop in their global market share (Figure 2b). In a recent global breakdown based on cosmetic market geographics, the United States cosmetic industry was valued at USD 39.2 billion in 2020, while China was expected to reach USD 38.9 billion in 2027 [27]. The European skin and hair care product market (2019) was estimated at €20.39 billion (≈USD 23.91 billion) and €14.92 billion (≈USD 17.50 billion), respectively [28]. The cosmetic market industry for developing regions, Africa and the Middle East, was valued at USD 30.37 billion in 2017 [29], and the African market for hair care products was projected to grow by USD 936.32 million, with an estimated 7% compound annual growth rate (CAGR) for the period of 2020–2024 [30]. Geographically, Asia-Pacific, North America, and Europe hold significant shares in the global beauty and personal care market due to a number of factors, such as rising standard of living, foreign direct investments, a growing population and internet exposure, and growth of the e-commerce sector [31]. In the coming years, the cosmetic market is expected to progress at a faster pace due to the

addition and establishment of new products and industry adjustments to new customer demands, originating from outside the Western culture [17].

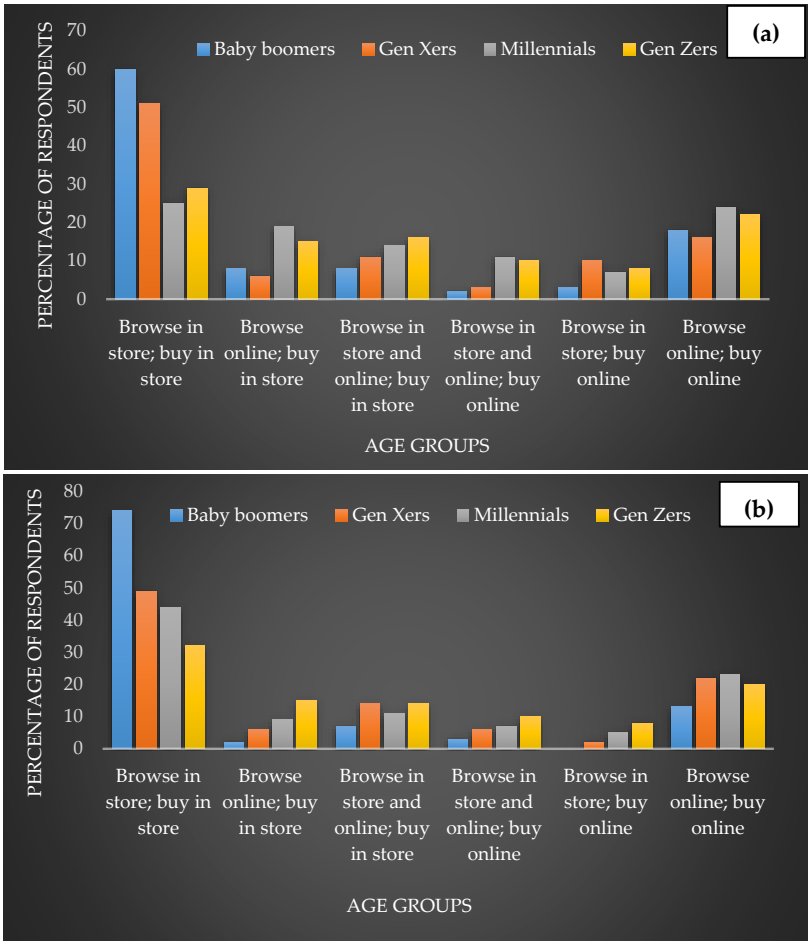

Figure 1. Assessment of in-store and online sales for cosmetic (**a**) and skin care (**b**) products according to different age groups (Baby boomers, Gen Xers, Millennials, Gen Zers); source, McKinsey new age of the consumer generational survey 2019 [22]. Baby boomers (1946–1964); Gen Xers/Z (1965–1980); Millennials (1981–1996); Gen Zers/Z (1997–2012).

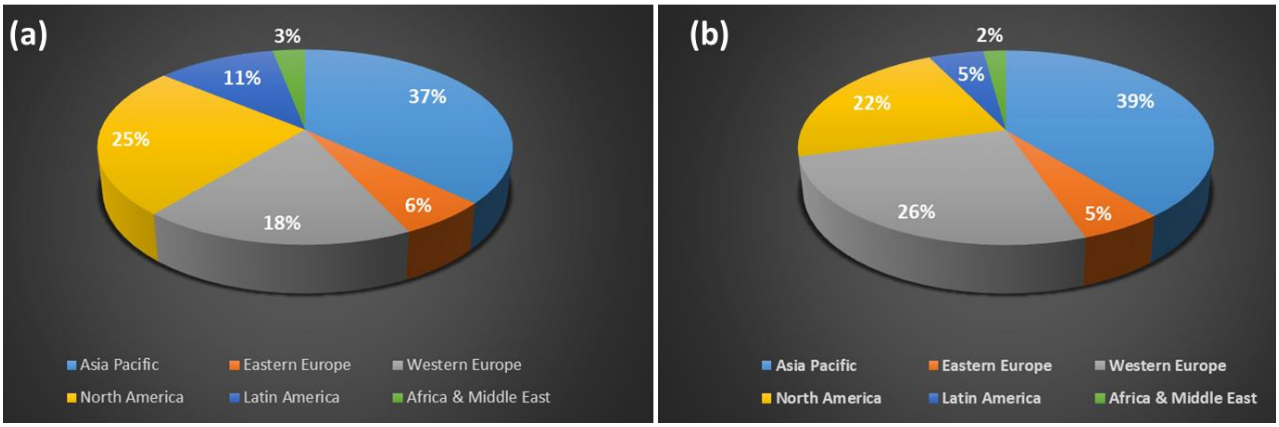

Figure 2. Global cosmetics market value by region, (**a**) 2016 data; from L'Oréal, 2016 (https://www.irinsider.org/economics-business-1/2018/9/29/loral-global-growth-strategy) (accessed on 18 September 2021); and (**b**) 2020 data; source from Statista (https://www.statista.com/statistics/971272/cosmetics-division-market-global/) (accessed on 27 May 2022).

3. South African Cosmetic Market and Progress in the Cosmeceutical Industry

The African continent has a lucrative consumer base for cosmetic, beauty and personal care products. The multi-billion dollar industry was estimated at a 6.6% CAGR during 2018–2020 and the majority of the growth in cosmetics (36%) revenue was concentrated in South Africa [32]. Accordingly, the South African beauty and personal care market industry was valued at USD 3.5 billion in 2018 and is expected to reach USD 6.16 billion by 2024 [33]. The upsurge in the South African beauty and personal care market is due to an ever-increasing consumer demand for new and innovative products, thus generating popular interest in multifunctional personal care products. The beauty and personal care industries are also benefiting from the global shift to online shopping, making it convenient for different enterprises, from multinational giants and entrepreneurial companies to small, medium and large local brands, to get into the market space. Even though online marketing in South Africa was reported to account for 1% of total retail sales in 2016 [34], there was a 2% increase recorded in South Africa's total retail transactions during 2020, and the market is projected to reach a high of 31.6 million South Africans by 2024 [35]. The growth of the South African online consumer market might see several small, medium, and micro enterprises (SMMEs) enter the cosmetic, beauty, and personal care industry. Furthermore, the multiplicity of online cosmetic brands will allow consumers to shop based on affordability, brand loyalty, choice of cosmetic products (e.g., natural, organic or sustainable), and product benefits, amongst others.

South Africa is one of the richest, flora-diverse countries with extensive knowledge related to the traditional use of natural resources in industries such as cosmetics, medicine, and food. Therefore, the possibility of discovering new compounds of commercial value in cosmeceuticals is eminent for South African companies or indigenous people. In the past years, the cosmeceutical industry has invested immensely into the formulation of natural and safe cosmetic products, based on consumer preference, by using plant materials or active compounds isolated from plants, as well as plant ingredients/extracts as alternatives to synthetic compounds. South African SMMEs have also ventured into cosmeceutical product development using the vast history of knowledge on medicinal plants and scientific reports establishing plant extract/essential oil efficacy and safety. The products are readily available in online stores making it easier for SMMEs to establish themselves and promote their products at lower input costs.

The South African cosmetic industry is extremely competitive due to several high-profile international players such as Estee Lauder, Nivea, Clinique, Garnier, Dove, L'Oréal and Revlon. The industry tends to favour multinational giants that prioritize the development of scientifically validated products, unlike small and medium brands with less available resources. Product quality testing and safety tests might prove challenging for SMMEs to promote their products at an international scale. Therefore the South African Department of Trade, Industry and Competition has committed to facilitating safety analysis on such cosmetic products to promote and support new market entrants [36]. In addition to some 'generic' requirements, there may be different requirements in different regions of the world for the production and registration of cosmeceutical products. These products can only be sold internationally once quality research has been conducted on their safety in different population groups (EU, Asia, etc.), for which some of the SMMEs might need assistance through the Department of Trade, Industry and Competition or collaborating with established companies and/or institutions that can conduct such research in several regions. According to the Department of Trade, Industry and Competition [37], South African small business manufacturers producing different cosmetic products can tap into the international market and be able to meet international export demands as their products are of high quality and very affordable. In order to meet such demands, South African small business manufacturers need to work on competitive pricing and strategic planning to boost their chances of expanding into the European markets and competing with multinational giants in cosmetics. The growth of the South African cosmetic sector, at R 27 billion (≈USD 1.81 billion), and its manufacturing division, valued at R 20 billion

(≈USD 1.34 billion), are proof that South African brand owners can expand to meet global demands [37].

The cosmeceutical industry in South Africa is yet to be fully exploited by local companies and brands. Yet, a number of international cosmetic companies have created various products using South African medicinal plants as active ingredients, due to the high volume of natural resources exported by South Africa. These products are 'unfortunately' sold to South African retailers at exorbitant costs and they benefit the international cosmetics industry more than the South African economy. With increased growth projections estimated for the next coming years in the cosmetics industry, it is pertinent for South Africa to be a key exporter of developed products, in order to compete at an international level, boost economic growth, stimulate an innovative culture, create jobs, and foster enterprise development. Such initiatives will require the South African Department of Trade, Industry and Competition to further invest in SMMEs, help build entrepreneurship skills, and invest into research and development of innovative products, as these factors can contribute extensively to revenue generation. At this stage, few local companies/brands have entered the South African cosmeceutical industry to sell their products in renowned retailers (such as Shoprite, Checkers, Pick n Pay, and Spar), pharmacies (Clicks and Dis-Chem) and a few clothing stores. There is, however, an increasing number of new companies/brands choosing to sell via online platforms, either through company websites or the promotion of products through different social media platforms. The use of social media platforms for the promotion of start-up businesses is becoming more common as newcomers gain visibility and promote their products with minimal costs incurred, relative to the high cost of advertising via TV, newspapers, and magazines, while saving costs from building store rentals. In the current section, we limited our search of South African cosmeceutical products to companies/brands with online websites, those sold in other online directories, or those products found using a simple Google search. Therefore, products primarily promoted on social media (e.g., Twitter, Facebook, Instagram, Pinterest, etc.) alone were not included in this review.

Tables 1 and 2 highlight some of the South African cosmeceutical products traded by different companies/brands using online platforms. Our primary focus was on products with active ingredients developed from plants that are widely distributed (native/naturalized) in South Africa and parts of Africa, or plants that are found globally and are extensively exploited for their essential oils. There are several benefits of online shopping. These include the ease of finding products, price comparison, and saving time through online browsing in the comfort of one's own home. Since online shopping is still relatively new to a number of South African consumers, few platforms are available for consumers to browse different products and make purchases without logging on to the company/brand website. 'Faithful to Nature' and 'African Botanicals' are some of the online directories that make it easy for South African consumers to find different cosmeceutical products. According to the founder of 'Faithful to Nature', a business established in 2006, the company holds a 'strict ingredient policy' to confirm if each and every product adheres to the green and safe regulations stipulated by the company and claimed by the product. They offer a diverse range of body and beauty care products, which they consider to be green, clean, 'cruelty-free' and eco-conscious cosmeceuticals. 'African Botanicals' is another cosmeceutical online directory that serves to promote and market African medicinal herbs and traditional remedies, with more than 50 plants in their directory. There are however, a number of online brands who have registered their own websites for consumers to browse different products and understand the brands' vision, the types of herbal ingredients used in the formulation of their products, and to get to know the manufacturers of the cosmeceutical brand. These include Olive Handmade Soaps, Aloeunique, Portia M, Crede Natural Oils, Antjies Handmade Naturals, Isivuno Naturals and Skimmelberg, just to name a few. Some of these brands/companies prefer to have a signature plant in their diverse collection of products, for examples, African Extracts Rooibos uses rooibos, Plush Organics has a Moringa product range, BaoCare uses baobab oil serums, and Alcare and AloeFerox

produce products from aloe extracts. Other brands or products mentioned that they avoid the use of animal ingredients and produce vegetarian and vegan-friendly products, such as Africa Organics, Antjies Handmade Naturals, BaoCare, and Africa Organics, among others. Some cosmeceutical products are formulated without the use of parabens, sulphates, preservatives, artificial ingredients and synthetic fragrances/chemicals; however, some products do not disclose such information. The detailed description of online products allow consumers to purchase cosmeceutical products based on their benefits, ingredients used, and their value on the skin, while noting that some of the products also include information on scientific findings conducted on the products. The lengthiness of such information makes it impractical to find it on product labels when shopping in stores. Moreover, some of these cosmetic online sites have a section on their websites for reviewer comments, where consumers can read/write about product satisfaction or dissatisfaction, which at times can influence other consumers' decision to purchase a product or not.

It should be noted that the list of companies/brands in the presented Tables are not comprehensive, as few extensively used medicinal plants have been systemically analysed. In Tables 1 and 2, a number of products are listed, based on the company/brand herbal cosmeceutical product development. The different skin and hair care products commonly sold online are as follows:

- Skin care products: Moisturizer/lotion, cream, serum, toner, facial mask, sunscreen, aftershave soother, balm
- Hair care products: Shampoo and conditioner, scalp treatment ointments
- Cleansing products: Soap, cleanser, scrub, shower gel, bath salts

A summary of the therapeutic benefits of cosmeceutical product ingredients based on plant extracts/essential oils is also provided in Tables 1 and 2. Some of the therapeutic benefits of the products include their UV protection, anti-wrinkle, anti-ageing, skin repair, wound healing, and anti-hyperpigmentation properties, as well as treatment/prevention of stretch marks, eczema, acne, and scalp irritation. The benefits of these products may be due to possible synergistic effect of their constituent plant extracts/essential oils, and a number of these medicinal plants have been scientifically proven to possess antioxidant, wound healing, anti-inflammatory, anti-ageing, antimicrobial, and anti-wrinkle properties, as well as treating dermal irritation and skin ulcers (Table 3). For instance, aloe gel is used in the treatment of burns and acne, and as a moisturizer for dry skin because of its diverse and effective bioactive compounds e.g., aloe-emodin, aloin A and B [2]. The antioxidant effect of rooibos and honeybush helps fight against free radicals in the skin, caused by environmental impact, and to repair damaged skin, soothe irritation from sunburn, reduce the appearance of wrinkles, and improve skin elasticity and hydration [3,38]. The ancient use of Marula oil in Africa has gained momentum in the cosmeceutical industry due to the oil's emollient properties, UV protecting effect, and anti-ageing and wound healing benefits [39,40]. Geranium (native to subtropical southern Africa) is another plant that has been widely cultivated globally due to the oil's biological activity, which helps to reduce acne breakouts, and prevent skin irritation and infections [41,42]. Cannabis legalization in many parts of the world and cannabinoid (CBD) oil extraction has led to the development of cosmeceutical products widely used for acne, ageing, scalp irritation, eczema, and psoriasis, based on the oils' biological properties, which include antioxidant, anti-inflammatory and antimicrobial activities [43].

Table 1. South African cosmeceutical products developed from native/naturalized medicinal plant extracts, their therapeutic benefits, and companies/brands involved in their production.

Plant Species (Scientific Name)	Formulation Type/Cosmetic Product Category	Therapeutic Benefit of Developed Products	Company/Brand
African potato (*Hypoxis hemerocallidea* Fisch. and C. A. Mey.)	Cream, gel cleanser, moisturizer, aftershave soother, soap, toner, body lotion	Athlete's foot, boils, eczema, wounds, psoriasis, eczema, acne, rashes, sunburn and minor burns, bed sores, warts, stretch marks, scars, dry skin, cracked heels, boost skin hydration, anti-ageing	Phyto-Force, Down To Earth, Zinplex, Eskamel, Africology
Aloe (*Aloe ferox* Mill., *A. vera* Mill.)	Moisturizer, day and night cream, cleansers, toner, sun lotions, shampoos, conditioner, toothpaste and mouthwash, lightening cream, soap	Burns, anti-ageing, sun damage/sunburn, acne-prone skin, strengthens and protects hair, insect bites, stings, cuts and bruises wrinkles, rash, eczema, healthy gums	Faithful to Nature, Natraloe, Alcare, Aloeunique, Howlistic Pets, AloeFerox, Down To Earth, Olive Handmade Soaps
Baobab (*Adansonia digitata* L.)	Shampoo, conditioner, sheet mask, body wash, hydrotherapy, facial toner, anti-ageing SPF cream, clay wash, serum, lightening cream, deep cleansing powder, tonic, powder	Sun damage/sunburn, detoxify and hydrate skin, rejuvenate skin, cell renewal, refines pores, removes impurities, reduce wrinkle depth, smooth fine lines, protect against harmful UVA and UVB damage, promote collagen stimulation, after-shave tonic	Africa organics, Iwori Beauty of Africa, Howlistic Pets, Skin Creamery, Isivuno Naturals
Buchu (*Agathosma betulina* (P. J. Bergius) Pillans)	Soap, moisturizer and aftershave soother, cream, bath salts, gel, serum, balm, soap, African clay mask	Reduce skin sensitivity, soothe razor-burn and irritation, wounds, bites, burns, eczema, bruising, anti-ageing, hydrate, nourish and brighten skin, anti-ageing, itches, scratches, bruises, acne	Antjies Handmade Naturals, Le Naturel, Skimmelberg, Olive Handmade Soaps, Salty Sistas
Bulbine (*Bulbine frutescens* (L.) Willd.)	Cleanser, sunscreen, day and night cream, moisturizer, toner, soap, soothing spray, Bulbine frutescens extract, anti-ageing, toner, soap	Discoloration and uneven skin tone, sun damage/sunburn, cuts, insect bites, stimulate collagen production, hydrate skin, grazes, acne, burns, blisters, cold sores, cracked lips, rashes, ringworm	Afari, Essentially natural, Timola, Nautica, African Botanicals
Cancer bush (*Sutherlandia frutescens* (L.) R. Br.)	Cream, soap, lotion, topical gel	Eczema, insect bites, psoriasis, shingles, acne, herpes, lesion, ageing, dark pigmentation, pimples and marks	Phyto-Force, Lady K cosmetics, Faithful to Nature, African Botanicals
Honeybush (*Cyclopia intermedia* E. Mey.)	Conditioner, shampoo, soap, fynbos mask, bath oil, hand and body cream, hand and body wash, body scrub, bath crystals, beard wash, moisturizer	Strengthens hair, soothes scalp irritation, exfoliate skin	Back 2 Nature, Antjies Handmade Naturals, Harmony Honeybush
Marula (*Sclerocarya birrea* (A. Rich.) Hochst.)	Shampoo, clay face mask, firms and brightens skin, lip balm, soap, purifying face mask, serum, cream, body lotion, body wash gel, face wash, toner, body scrub, shampoo and conditioner	Strengthens and protects hair, nourish dry and chapped lips, anti-blemish, soft and hydrated skin, even skin tone, minimizes appearance of pores, skin exfoliate, strengthen and protect hair	Africa organics, The Victorian Garden, Lulu and Marula, Portia M, Iwori Beauty of Africa
Moringa (*Moringa oleifera* Lam.)	Collagen boosting cream, anti-ageing cream, soothing cream, body and facial wash/cleanser, soap, sunscreen, body butter mousse, conditioner, serum, toner, eye serum	Skin repair, collagen booster, even tone skin, damaged skin, skin irritation, insect bites, protect from harmful rays, chronic skin disorders, anti-ageing	Howlistic Pets, Moringa 5000, African Botanicals
Rooibos (*Aspalathus linearis* (Burm.f.) R.Dahlgren.)	Toner, facial scrubs, facial mask, cleanser, moisturizer, bath and shower gel, shampoo, conditioner, acne cream, hydrotherapy bathing powder, serum	Cellulite, healthier, younger looking skin, soft, shiny and smooth hair, dark circles, detoxify and hydrate skin, puffiness and fine lines	Natraloe, African Extracts Rooibos, Faithful to Nature, Skimmelberg, Iwori Beauty of Africa
Sausage tree (*Kigelia africana* (Lam.) Benth.)	Cream, gel, serum, scalp and body lotion, shampoo and shower gel, moisturizer	Eczema, psoriasis, sunburn, skin pigmentation, sores wound healing, cold sores and fever blisters, Athlete's foot, shingles, moles, Molluscum contagiosum (viral infection), firmer and smoother complexion, skin repair, anti-ageing, scalp irritation	Phyto-Force, The Victorian Garden, Medico Herbs, Basix Skin Care, Katavi Skincare, African Botanicals, Down To Earth

Table 2. South African cosmeceutical products developed from essential oils of African/global origin, product benefits, and companies/brands involved in the production.

Essential Oils (Plant Species)	Formulation Type/Cosmetic Product Category	Therapeutic Benefit of Developed Products	Company/Brand
Essential oils from plants of African origin/endemism			
Argan oil (*Argania spinosa* (L.) Skeels.)	Conditioner, Argan oil	Strengthen and repairs hair, dry skin, wrinkles, skin radiance, marks, scars, acne	The Victorian Garden, Isivuno Naturals, Essentially Natural, Soil, Crede Natural Oils, Umuthi Botanicals
Baobab oil (*Adansonia digitate* L.)	Baobab skincare, soap, shower gel, nourish tissue oil, lotion, hand wash, Baobab and Marula day cream, shower/bath oil, serum, body scrub, wrinkles	Eczema, after-shave balm, skin breakouts, dry red, itchy, scaly skin, psoriasis, stretch marks, scars, dry skin, cell regeneration, damaged skin	BaoCare, Antjie's Artisan Cosmetics, The Victorian Garden, Skin Creamery, Iwori Beauty, Isivuno Naturals, Salty Sistas, Timola, Pure Indigenous
Buchu oil (*Agathosma betulina* (P. J. Bergius) Pillans.)	Soap, Buchu oil, Serum, topical gel	Acne, wounds, bruises, burns, nappy rash, eczema	Antjies Handmade Naturals, Salty Sistas, Skimmelberg, African Botanicals
Geranium oil (*Pelargonium graveolens* L'Hér.)	Body lotion, hand wash and cream, facial massage oil, Geranium essential oil, soap, roll-on deodorant	Toned and brightened complexion, re-hydrate dry skin, regenerate skin cells, blemishes	The Victorian Garden, Africology, Pure Simple, Isivuno Naturals
Jojoba Oil (*Simmondsia chinensis* (Link) C.K. Schneid.)	Jojoba oil, scrub beads, topical gel, face cleanser, hydrating oil	Acne, skin renewal, dry and sensitive skin, pimples, cold sores, athletes foot, eczema, psoriasis, brighten complexion, anti-wrinkle	Soil, Crede Natural Oils, Isivuno Naturals, Umuthi Botanicals, Essentially Natural, eOil, Soil, Ozone Company, Hey Gorgeous, Victorian Garden, Skin Creamery
Kalahari melon oil (*Citrullus lanatus* (Thunb.) Matsum. and Nakai.)	Gel face cleanser, Kalahari melon seed oil, body wash, body lotion	Itchy scalp, dandruff, skin cell growth, regenerate and hydrate hair and skin, acne, blemishes, sensitive skin, anti-ageing	The Victorian Garden, Isivuno Naturals, Pure Indigenous, Timola, Soil, Africa Organics
Marula oil (*Sclerocarya birrea* (A. Rich.) Hochst.)	Marula oil, clay face mask, tissue oil, body lotion, hand wash, hydrating body mist, cleansing gel, eye make-up remover, SPF 15 day cream	Wrinkles, inflamed skin, boost collagen, firms and brighten skin, scars, stretch marks, repairs skin cells, ageing, dry cracking skin, dry damaged hair	Kudu Cosmetica, The Victorian Garden, Portia M, Kalahari Lifestyle, Iwori Beauty, Pure Indigenous, Timola, Isivuno Naturals
Mongongo oil (*Schinziophyton rautanenii* (Schinz) Radcl.-Sm.)	Mongongo oil, hair treatment mask, hair oil, conditioner, shampoo	Skin elasticity, healing, scars, damaged skin, skin elasticity, wrinkles, sunburn, skin, rashes, repair brittle or split hair ends, dry, damaged hair	Pure Indigenous, Essentially Natural, Iwori Beauty
Essential oils of plants with global distribution			
Cannabis sativa oil, CBD and hemp oil (*Cannabis sativa* L.)	Anti-ageing cream, scalp treatment oil, body oil, CBD/Moringa balm	Skin health, anti-ageing, soothes irritated scalp, cellulite, stretch marks, scars, eczema, psoriasis	Back 2 Nature, Moringa 5000, Isivuno Naturals
Moringa oil (*Moringa oleifera* Lam.)	Moringa oil, Moringa/CBD balm, Moringa/CBD cream, exfoliator, Moringa tissue oil, Ben oil, body cream	Anti-ageing, acne, anti-ageing, eczema, psoriasis, removes dead skin cells, hydrate skin, hair and nails, scars, acne damaged skin, dark spots, blemishes, blackheads, wrinkles, dark spots	Plush Organics, Moringa 5000, Kudu Cosmetica, Timola, African Botanicals
Rosehip (*Rosa canina* Siev.)	Rosehip oil, serum	Anti-ageing, acne, eczema, wrinkles, fine lines, acne scars, dark spots	Victorian Garden, Isivuno Naturals, Standard Beauty
Tea tree (*Melaleuca alternifolia* (Maiden and Betche) Cheel.)	Conditioner, Tea Tree oil, shampoo, body wash, toothpaste, deodorant, liquid soap, shaving cream	Damaged hair, acne, dry scalp, athlete's foot, healthy gums, blemishes, soothe irritation, pimples, insect bites	Wellness Warehouse, Earthsap, Africology

Table 3. Bioactive compounds and biological efficacy of medicinal plants used in product development (in reference to Tables 1 and 2).

Plant Species (Common Name)	Bioactive Ingredients	Extract, Compound or Essential Oil Biological Activity	References
Aloe (*Aloe ferox* Mill., *A. vera* Mill.)	Aloe-emodin, aloetic acid, anthranol, aloin A and B (barbaloin), isobarbaloin	Wound healing, anti-inflammatory, tissue burn, antioxidant, anti-ageing, antimicrobial, dermal irritation, skin ulcers, antiseptic	[44–48]
African potato (*Hypoxis hemerocallidea* Fisch. and C. A. Mey.)	Hypoxoside, rooperol, β-sitosterol, ergosterol, stigmasterol	Antimicrobial, antioxidant, anti-inflammatory, antinociceptive	[49–51]
Baobab (*Adansonia digitata* L.)	Terpenoids, flavonoids, sterols, vitamins, lipids	Antibacterial, anti-inflammatory, antioxidant, analgesic, healing effect	[52–54]
Buchu (*Agathosma betulina* (P. J. Bergius) Pillans.)	Limonene, menthone, diosphenol, l-pulegone, pseudo-diosphenol	Antimicrobial, anti-inflammatory, antioxidant	[55,56]
Bulbine (*Bulbine frutescens* (L.) Willd.)	Anthraquinones, flavonoids, phenolics, triterpenes	Wound healing, antioxidant, anti-inflammatory, anti-proliferative	[5,57–59]
Cancer bush (*Sutherlandia frutescens* (L.) R. Br.)	Flavonoids, triterpenoid saponins	Antibacterial, antioxidant, inflammation, pain and wounds, analgesic	[60–62]
Cannabis sativa (L.) oil, CBD and hemp oil	Δ9-tetrahydrocannabinol, (THC), cannabidiol (CBD), α-humulene, (E)-caryophyllene, caryophyllene oxide	Antimicrobial, skin health, antioxidant, anti-inflammatory, insecticidal, pain	[43,63–65]
Geranium oil (*Pelargonium graveolens* L'Hér.)	Terpenoids, flavonoids, phenolics, coumarins, cinnamic acids, tannins, alkaloids	Antimicrobial, antioxidant, anthelmintic, anti-dermatophyte, anti-ageing	[41,66–69]
Honeybush (*Cyclopia intermedia* E. Mey.)	Xanthone mangiferin, hesperitin, isokuranetin, isomangiferin, polyphenols	Antioxidant, anti-wrinkle, skin hydration effects, antimicrobial, chemopreventive	[3,38,70–72]
Marula (*Sclerocarya birrea* (A. Rich.) Hochst.)	β-caryophyllene, ascorbic acid, α-humulene, terpinen-4-ol, pyrrolidine aromadendrene, gurjunene, polyphenols, sesquiterpene hydrocarbons	Antibacterial, antifungal, antioxidant, anthelminthic, anti-inflammatory, analgesic	[39,73,74]
Moringa (*Moringa oleifera* Lam.)	Flavonoids, quercetin, β-sitosterol, zeatin, alkaloids, carotenoids, anthocyanins, proanthocyanidins tannins, anthraquinones	Anti-inflammatory, antioxidant, antitumor, antifungal, antibacterial, wound healing, anthelmintic, antinociceptive, analgesic, local anesthetic	[75,76]
Rooibos (*Aspalathus linearis* (Burm.f.) R. Dahlgren.)	Dihydrochalcones (aspalathin, nothofagin), aspalalinin, flavones (isoorientin, orientin)	Antioxidant, anti-ageing, antimicrobial, dermatological effects, anti-inflammatory	[3,4,77]
Sausage tree (*Kigelia africana* (Lam.) Benth.)	Naphthaquinones, iridoids, sterols, coumarins, flavonoids, kigelinone, vernolic acid, kigelin	Antimicrobial, antioxidant, analgesic, wound healing, anti-inflammatory	[78–82]

4. Pathophysiology and Importance of Cosmeceuticals in Skin Disorders

Mammalian skin is a physical barrier that protects the host from infiltration by pathogenic microbes and prevents permeability of harmful chemicals, retains water and electrolytes, regulates body temperature, and detects external stimuli [83,84]. The epidermis, dermis and hypodermis are the three layers that make up mammalian skin and are separated by the basal membrane [83,85]. The hypodermis is primarily composed of connective and adipose tissue, while the cellular components of the dermis are vast and

include fibroblasts, collagen, elastin, macrophages, adipocytes, mast cells, and Schwann cells [86]. The epidermis is the uppermost layer and is predominantly composed of stratified squamous keratinocytes and, to a lesser extent (10%), of melanocytes, Langerhans cells, Merkel cells, and inflammatory cells [83,85,87]. The protective barrier afforded by the epidermis has evolved as a result of cornification, the process through which keratinocytes from the basal cell layer of the epidermis produce a cornified envelope (CE) [88]. Cornification is a highly organized process of sequential proliferation, differentiation, and death of keratinocytes, and is mediated by specific proteins including filaggrin, involucrin, loricrin, small proline-rich proteins, and late CE proteins [87,88]. The mechanisms involved in the normal development of the stratum corneum are depicted in Figure 3. However, dysfunctions or abnormalities in these proteins and associated enzymes, as well as ceramides, have been linked to the development of various skin disorders. Human skin is the outward component of beauty and visible skin disorders are often associated with psychological conditions including depression and anxiety [88]. Furthermore, considering the increased vulnerability to environmental damage and the development of diseases such as skin cancer, skin disorders associated with ageing have gained increased attention from dermatologists. Photo-ageing skin and skin disorders including acne, vitiligo, psoriasis, eczema, hyperpigmentation, and skin lesions have thus led patients to consider the use of cosmetic products for improved skin condition [83,85]. Cosmeceuticals have gained popularity because of the widespread acceptance of the apparent safety and reduced side effects of compounds isolated from natural sources. Here, we discussed the mechanistic role of cosmeceutical products in the treatment of skin disorders.

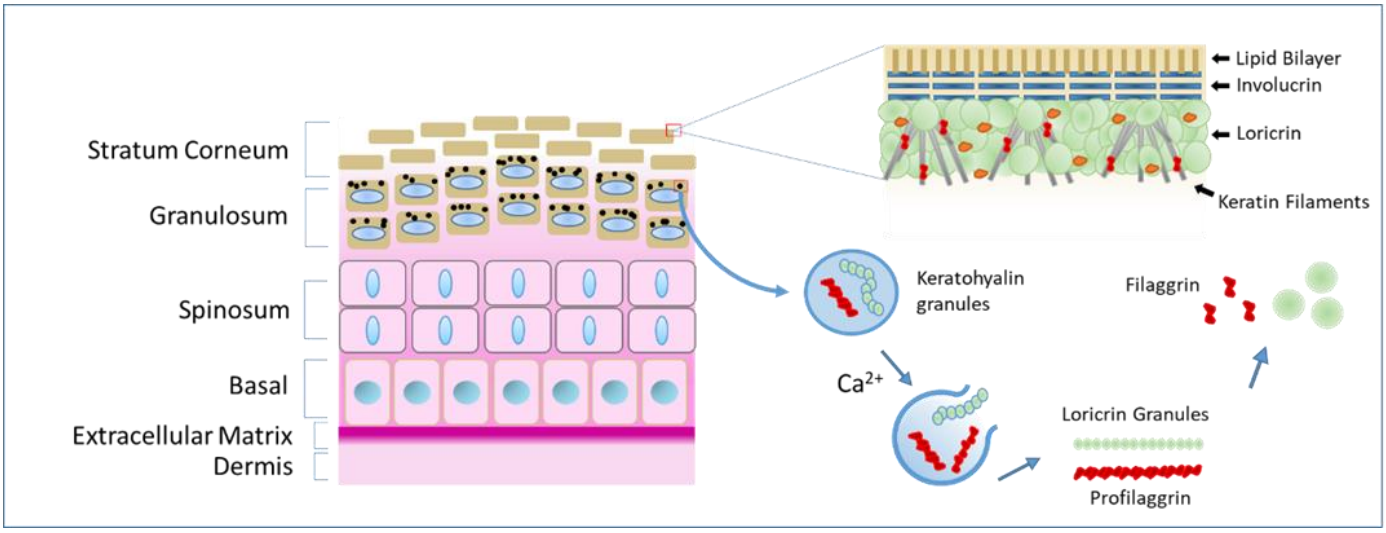

Figure 3. Normal development of the stratum corneum. Cornification follows the breakdown of keratohyalin granules to produce FLG (filaggrin) monomers and loricrin. Proteins including involucrin, loricrin and filaggrin, are crosslinked with transglutaminases, keratin filaments and lipids to form the protective barrier.

The development of dry skin conditions (eczema, xerosis, dermatitis, and psoriasis) are associated with defects in the hydration of the stratum corneum (cornified layer) [89]. Several structural and functional proteins within the epidermis, and proteins responsible for the regulation of the innate immune response, have been identified as key instigators in the development of dry skin [90]. For instance, the proteolysis of filaggrin, a late epidermal differentiation protein encoded by *FLG* gene, produces amino acids and hygroscopic molecules that make up the natural moisturizing factor [91]. However, mutations in the *FLG* gene result in defects in the stratum corneum barrier function, leading to dry skin disorders including atopic dermatitis (synonymous with eczema) [90,91]. Similarly, the absence of involucrin, a component of the CE as a substrate of transglutaminase, has been linked with a delay in the maturation of the CE and hyperkeratotic dry skin [92].

Studies have demonstrated the ability of aloe (*Aloe vera*) extracts to regulate the expression of the proteins involved in the production of CE. Razia and colleagues recently treated human epidermal keratinocytes with a water extract of the *Aloe vera* flower [91]. The extract displayed a multi-target mechanism to enhance skin moisturization. Furthermore, the authors observed enhanced expression of protein kinase C, p38, and ERK1/2, thereby upregulating involucrin in the epidermal layer. The expression of other essential structural proteins, including filaggrin and aquaporin, were also improved, while also modulating hyaluronan, a key regulator of inflammation in the extracellular matrix [91]. The authors further identified isoorientin, a *C*-glucosyl flavone derivative of the biologically active glucoside present in rooibos (*Aspalathus linearis*), as the active component after molecular modelling. Several cosmetic companies have developed moisturising products including African Extracts Rooibos, Natraloe, SKOON SKIN®, and JOMAR Natural Skincare® using rooibos extracts as a key ingredient in their formulations. Atopic dermatitis (AD) is associated with excess immunoglobulin E production and inflammation is a characteristic indication of the disorder [93]. Topical steroids are used as standard treatments to reduce inflammation in patients presenting with AD [94]. Although topical steroids provide rapid relief, their use has been associated with significant adverse effects including atrophy, hypopigmentation, acne, excessive hair growth, and others, as reviewed by Ellis et al. [94]. The anti-inflammatory properties of aloe, including their role in dermatitis, are well documented. Finberg and colleagues evaluated the anti-inflammatory activity of *A. ferox* and *A. vera* gel extracts and reported a reduction in cutaneous inflammatory responses in 2,4-dinitrochlorobenzene-challenged mice models after topical treatment [93]. The authors identified a reduction in serum immunoglobulin E (Ig E) levels, which is an important antibody that has been linked with AD [93,95]. Several compounds from *A. vera* influence inflammatory pathways. For instance, *C*-glucosyl chromone was isolated from *A. vera* as a topical anti-inflammatory agent that seemed to exhibit activities equivalent to hydrocortisone in in vivo mice models [96]. The gels and phytochemical constituents of *A. vera* may thus be promising alternatives to topical corticosteroids in the treatment of AD.

Chronic inflammation has also been closely linked with ageing skin [97]. Skin ageing is influenced both by intrinsic and extrinsic factors that result in the loss of structural integrity and physiological function [98]. While intrinsic ageing is attributed to natural physiological changes that occur over a lifetime, extrinsic ageing may be attributed, most notably, to UV radiation exposure [98,99]. Chronic inflammation as a result of sun exposure occurs in response to the release of proteolytic enzymes including tumour necrosis factor-α, and interleukin-6 (IL-6) from keratinocytes that disrupt the permeability of the stratum corneum [98,99]. Pharmaceuticals targeted at reversing chronic inflammation have thus been recommended as plausible regimes for the treatment of photo-ageing [97]. The use of rooibos and honeybush (*Cyclopia intermedia*) in the treatment of skin disease has gained popularity worldwide. In addition to their rich antioxidant content, the anti-inflammatory properties of these species have bolstered their pharmaceutical appeal. Magcwebeba et al. [77] described the anti-inflammatory activity of methanolic and aqueous rooibos, and honeybush extracts in terms of their ability to inhibit UVB-induced accumulation of IL-α and the promoted apoptosis of cells that accumulated excess IL-α. Fermented honeybush extracts displayed similar activity against UVB-induced damage in HaCaT keratinocytes where the expression of IL-1β, IL-6, and IL-8 were suppressed [100]. The extract was capable of upregulating the activity of epidermal barrier proteins including involucrin, filggrin, and loricrin, and as the barrier function of the skin is improved, so is the structural integrity of the skin.

In addition to ageing and dry skin conditions, patients frequently present with skin hyperpigmentation, a disorder characterised by failure in the pigmentary system in response to several factors. The most frequent hyperpigmentation concerns include periorbital hyperpigmentation, post inflammatory hyperpigmentation, and melisma [101]. Periorbital hyperpigmentation occurs as a result of a genetic predisposition that results in the development of bilateral, round, and homogenous pigments on the skin [102]. Post-inflammatory

hyperpigmentation may occur as a result of superficial damage to the skin including acne lesions, ingrown hairs, wounding, and insect bites [101]. Although the biochemical pathway involved in the development of melisma is not yet fully understood, the disorder is associated with exposure to sunlight, as well as the oral use of contraceptives or hormone treatments (melasma) [102]. Hyperpigmentation is often treated with the application of skin-lightening agents that target hyperplastic melanocytes and inhibit important dysfunctional biochemical pathways in melanin synthesis [103]. However, concerns over the safety of current cosmetics, including hydroquinone, mequinol, and kojic acid, have highlighted the need for alternative products in the treatment of the skin condition (hyperpigmentation). Molecular mechanisms for the treatment of skin hyperpigmentation involve the inhibition of tyrosinase, which is an essential enzyme in the synthesis of melanin [104]. Tyrosinase acts within melanocytes to convert L-tyrosine to L-3,4-dihydroxyphenylalanine (L-DOPA) [105]. Yagi and Takeo [106] demonstrated the ability of aloesin (from *Aloe* sp.) to inhibit tyrosine hydroxylase and DOPA oxidase activities, suggesting a possible role for the compound as a skin-lightening cosmeceutical. Wang and colleagues later described similar activity in reconstructed three-dimensional human skin equivalents where aloesin reduced tyrosinase activity and melanin content [107]. Further, isolation of aloeresin A and plicataloside (*Aloe plicatilis*, *A. chabaudii*) were documented as adequate substrates for mushroom tyrosinase [108]. The pigment-altering activity of *Aloe* species has prompted the incorporation of plant gels into a range of cosmeceutical products including Aloeunique, AloeFerox, Aloe Mastercare®, etc.

5. Cosmeceutical Patents Developed from South African Plants

The discovery of new drugs, cosmeceuticals, and nutraceuticals from medicinal plants based on indigenous knowledge systems sparked a crucial debate into the ownership of intellectual property (IP). Since the adoption of the Convention on Biological Diversity, several developing countries have introduced IP policies that protect ethnobotanical knowledge from which new pharmaceuticals are developed [109]. South Africa developed and adopted the Indigenous Knowledge System (IKS) policy in 2004 to prevent the misappropriation of the country's traditional knowledge of medicinal plants from IKS holders. The policy intends to establish fair and sustained recognition of communities for their knowledgeable inputs, and benefit sharing from pharmaceutical companies or end users, as well as to stimulate innovation and socio-economic development within local communities [109,110]. Several studies have demonstrated the cosmeceutical potential of a vast array of South African medicinal plants and their components [9]. However, patents filed in this context are limited to the preparation of extracts with activity within the cosmeceutical domain. In order to identify patents filed from South Africa, we conducted a thorough search employing the WIPO (World Intellectual Property Organization) IP portal using a combination of search terms such as: "skin/skincare", "cosmetic/cosmeceutical", "dermatology", "medicinal plant extract/compounds", "eczema", "psoriasis", and "hydration". The results thereof are presented in Table 4. A total of seven patents were filed within the first decade after the adoption of the IKS policy while only three were published subsequent to this period. The first patent detailed the extraction of a biologically active extract of *Kigelia africana* with potential against inflammatory diseases of the skin and solar keratosis [111]. Following this, researchers detailed the inhibition of phosphodiesterase-4 (PDE4) and serotonin uptake by extracts of *Sceletium tortuosum* that contained mesembrenol and mesembrenone [112]. The PDE-4 enzyme is an important mediator of pro-inflammatory and anti-inflammatory mechanisms and plays a crucial role in the expression of AD [113]. A study by Ahluwalia et al. [113] reported reduced cyclic adenosine monophosphate (AMP) levels in patients with AD as a direct result of higher than normal PDE-4 activity. Inhibitors of PDE-4, as in the case of the mesembrine alkaloids present in *S. tortuosum*, have thus presented interesting therapeutics against AD and related skin disorders.

Table 4. South African endemic botanical extracts and processes patented for use in the cosmeceutical domain.

Patent Name and Source	Year	Applicant	Plant Species	Extract (s)	Proposed Compounds	Biological Action	Cosmetic Application
W02006002443A1 [111]	2006	Karl R. Schleipfer	*Sausage tree* (*Kigelia africana* (Lam.) Benth.)	Unstated	Unspecified	Unspecified	Inflammatory disease of the skin, solar keratosis
W0/2010/106495 [112]	2010	H.L. Hall and Sons Limited Nigel Gericke, Alan Harvey, Alvaro Viljoen, Deon Hofmeyr	Kanna (*Sceletium tortuosum* (L.) N.E.Br.)	Aqueous, ethanol	Mesembrenol, mesembrenone	PDE4/serotonin-uptake inhibitors	Psoriasis, atopic dermatitis, eczematous dermatoses, hypersensitivity, etc.
W0/2013/150406 [114]	2013	Integral Bioceuticals (PTY) LTD	African ginger (*Siphonochilus aethiopicus* (Schweif.) B.L. Burt)	Aqueous, ethanol, glycerine, propylene glycol, natural oils	Unspecified	Unspecified	Skin moisturizing
W0/2013/171720 [115]	2013	University of Pretoria, South Africa	Woolly bottlebrush (*Greyia radlkoferi* Hook. and Harv.)	70% ethanol	5,7-Dihidroxyflavone[(2S)-pinocembrin]; 2′,6′-dihydroxy-4′-methoxydihydrochalcone; 2\4′,6′-trihydroxyhydrochalcone; 3,5,7-trihydroxyflavone and 4,57-trihydroxyisoflavone	Tyrosinase inhibitor	Skin hyper-pigmentation
W0/2013/072855 [116]	2013	University of KwaZulu-Natal, South Africa	Unstated	Unstated	Morelloflavone, morelloflavone-7″-sulphate, sargaol	Reduction in melanin content in melanocytes	Skin lightening
W0/2014/053944 [117]	2014	University of the Witwatersrand, South Africa	* Moringa (*Moringa oleifera* Lam.) *Moringa ovalifolia* Dinter and A.Berger)	Aqueous extract	Kaempferol quercetin	Antioxidant	Topical cosmetics
W0/2014/020575 [118]	2014	University of Pretoria, South Africa	Oldwood (*Leucosidea sericea* Eckl. and Zeyh.)	Ethanol, methanol, ethyl acetate, acetone	Phytol acetate, triacontanol, phytol, alpha kosin	Antibacterial activity of *Propionibacterium acnes*. Skin hydration capability	Anti-acne and skin hydration
WO2017098426A1 [119]	2017	University of Pretoria, South Africa	African boxwood (*Myrsine africana* L.)	Ethanol, methanol, butanol, aqueous	Unspecified	Inhibition of elastase enzyme, porcine pancreatic elastase	Anti-wrinkle cosmetic
W0/2020/152577 [120]	2020	University of Pretoria, South Africa	False or Bastard Olive (*Buddleja saligna* Willd.)	Ethanol, methanol, butanol	Oleanolic acid, ursolic acid	Reduction in cytokine synthesis, inhibition of cyclooxygenase-2, induction of apoptosis in UCT-MEL-1 and HaCaT cells	Reduce damages resulting from UV radiation
W0/2020/121187 [121]	2020	University of Pretoria, South Africa	*Plectranthus aliciae* (Codd) Van Jaarsv. and T.J. Edwards	Ethanol, methanol, aqueous, diethyl ether, hexanol, acetone, propylene glycol, ethyl acetate, dichloromethane, chloroform, petrol	Vitexin, isovitexin, luteolin, quercitrin, Vanillic acid, syringic acid, caffeic acid, epicatechin, ferulic acid, propyl gallate, Catechin, rosmarinic acid, isoquesrcitrin, 4-hydroxybenzoic acid, protocatechuic acid and orientin	Antibacterial activity directed towards *Cutibacterium acnes*	Anti-acne preparations

* Not of South African origin.

The inhibition of tyrosinase has been implemented clinically to successfully treat skin hyperpigmentation. A patent published in 2013 sought to detail the isolation of known tyrosinase inhibitors from *Greyia radlkoferi* [115]. The authors isolated five phenolic compounds that exhibited differing levels of tyrosinase inhibition and the incorporation of the extract into a topical cream/lotion/ointment was proposed for the treatment of skin-hyperpigmentation. An invention related to skin lightening was published by researchers at the University of KwaZulu-Natal, South Africa, who described reduced melanin content in melanocytes with several compounds including morelloflavone, morelloflavone-7''-sulphate and sargaol [116]. Although the authors did not mention from which plant species these compounds were isolated, the morelloflavones are typically isolated from *Rheedia edulis* and *Garcinia* species including *G. dulcis* and *G. livingstonei* [122,123]. More recently, a patent invention published by the University of Pretoria, South Africa, detailed the inhibition of the elastase enzyme and porcine pancreatic elastase by ethanolic extracts of *Myrsine africana* [119]. Elastase was identified as an attractive target for the development of anti-ageing cosmetics given the protein's role in the breakdown of elastin and collagen [124]. In an in vivo study, the invention indicated reduced visioscan and visioface wrinkles after 28 and 14 days of topical application, respectively.

A recent patent published by the University of Pretoria, South Africa, was formulated for the treatment of skin cancer via the induction of apoptosis in UCT-MEL-1 (human melanoma) cells using *Buddleja saligna* extracts [120]. The authors detailed anti-proliferative activity stimulated by the ethanolic extract to be within the range accepted by the American Cancer Institute for plant extracts. The authors also found that the extract was less cytotoxic to human keratinocytes. Few patents have also been published that provided the detailed extract composition for the development of anti-acne formulations. *Leucosidea sericea* ethanolic extract and its proposed bioactive compounds displayed potent antibacterial activity against *Cutibacterium acnes*, formerly known as *Propionibacterium acnes* [124]. Recently, researchers from the University of Pretoria, South Africa, detailed the inhibition of *Cutibacterium acnes* by *Plectranthus aliciae* extracts with potential for the development of anti-acne preparations [121].

Indeed, these patents hold much promise for the development of cosmeceutical products. However, the expansive gene pools embodied by the mega-diversity of flora in South Africa, as well as the wealth of knowledge related to the traditional use of these resources in skin care, are grossly underrepresented within the patent sphere. Although, under the auspices of the IKS policy, indigenous communities are encouraged to exploit the patent system to commercialise their knowledge and reap the economic benefits, it would appear that several factors have hindered the progress of the policy. These may include broader issues within the South African patent system, issues surrounding communal entitlement to benefits, or an overall lack of information related to the system [109]. These are, however, beyond the scope of the current work.

6. Conservation of Plants Used as Cosmeceuticals

Cosmetic products, especially the synthetic ones, usually contain harmful chemicals, which requires the industry to use advanced testing to check levels of safety in ingredients and finished products [125]. Due to the implemented bans on animal testing in cosmetic industries, in silico approaches have become important for safety tests of cosmetic ingredients and products. The negative impact of many synthetic chemicals has also triggered the use of organic and/or natural products in cosmetics, thus minimising the harmful/side effects to the environment, humans, and animals. Natural products or ingredients applied in cosmetics, such as those from animals and/or microorganisms, have also been linked to safety concerns when used for extended periods, causing allergenic problems and transmitting diseases from their natural source [126]. Therefore, these products should be evaluated for efficacy, toxicology, and compliance with the cosmetics product guidelines and standards established by regulatory agencies [127]. Thus, the use of herbal-based ingredients, although not always entirely safe, is a better option as it contributes to natural resource

sustainability through minimising environmental damage caused by finished products with synthetic chemicals. The growing interest in herbal-based cosmeceuticals is arguably because the products have diverse pharmacological and/or specific biological functions. These include their protective nature as enzyme-reducing agents (collagenases, elastase, tyrosinase, oxidative, and cathepsin), which cause skin degradation and catalyse crucial steps in melanin biosynthesis [128,129]. While herbal-based cosmeceuticals are the most preferred products, there are concerns of over-harvesting and loss of plant biodiversity as the usage of these resources does not correlate with the nature's ability to regenerate. Therefore, sustainability remains a major concern, and conservation practices need to be put in place in order to avoid the extinction of valuable plants.

Environmental pollution, overexploitation, invasive alien species, climate change, and habitat change are major contributors to biodiversity loss and ecosystem changes [130]. Ethical and sustainability strategies in product development should be implemented and maintained, from the sourcing of raw ingredients (alternative green material) to finished products, through the consideration of several factors such as energy and water consumption, waste management, reduction in greenhouse gas emissions, as well as the safety of products and their packaging [127,131]. Sustainability of natural resources include three dimensions, which are environmental, social and economic [130]. Environmental considerations involve the preservation of natural capital, biodiversity and ecosystem integrity, while economic dimensions imply financial feasibility during the application of sustainable strategies. Social dimensions incorporate concepts of equity, accessibility, cultural identity, and institutional stability [132]. The cosmeceutical product supply chain can have an impact on sustainability, thus requiring precise sustainability assessment that aims to identify, predict, and evaluate possible environmental, social, and economic effects. These factors need to be taken into account from the initial stages of product design (raw materials), through manufacturing, packaging, distribution, consumer use, and post-consumer use (disposal or recycling) [131]. As more consumers opt for cosmeceutical products, especially the herbal-based ones, a number of cosmetic companies have shifted to producing green cosmetics, thus bringing benefits such as saving money, increasing sales, improved consumer interest, and brand reputation.

The cosmeceutical industry has adjusted to the adoption of new natural ingredients from herbal-based raw materials (botanicals or waste material), green chemistry, foods, and oleochemistry [127]. The use of these alternative ingredients is not only safe for human use, but mostly safe for the environment and avoids the over-harvesting of plant species, which leads to extinction. Over-collection from the natural environment for commercial production of cosmeceuticals is prohibited and is a threat to biodiversity. Therefore, it is crucial to develop and implement sustainable strategies, to ascertain adequate resources for current and future use. These can include obtaining plant material through wild-crafting, production of cosmeceutical plants by conventional methods (e.g., field or greenhouse), or through the use of biotechnological systems (e.g., microalgae, hydroponics, fermentation, tissue culture) [131]. Regardless of the production system used, the resulting plant material must be tested for quality and reproducibility to maintain the effectiveness of the natural products in cosmeceuticals. Plant species should also be conserved in gene banks to keep the germplasms available for future use. The concept of plant-part substitution (such as leaves for the roots), particularly in cases where non-renewable plant parts are highly targeted, as well as plant species substitution (such as substituting threatened species with relatively abundant species) are plausible approaches for floral diversity conservation.

7. Conclusions

Cosmeceuticals remain part of tradition and a modern trend in the beauty and fashion industries. In the past few years, consumers have shown interest in cosmetics with natural ingredients for their personal care and beauty products, as they are perceived to have minimal side effects. Novel cosmeceutical products have been formulated with the help of traditional knowledge from indigenous people or local communities who hold vast

knowledge, tested over the years, on the bioactivity of genetic resources (plants, animals, or microorganisms), and passed on from generation to generation. The extensive exploitation of ethnobotanical information from indigenous people without any recognition or benefit-sharing arrangement from some cosmetic and pharmaceutical industries has led to the adoption of the IKS policy in South Africa. The policy is not intended to hinder product development but to protect knowledge holders and their communities as their knowledge gives direction for further pharmacological valorisation and equitable use. Besides biological analysis, cosmeceuticals still require testing for stability (colour change, odour, viscosity, precipitation, separation, or degradation of actives), quality, safety, and reproducibility. There are, however, some concerns on the extensive or unsustainable use of natural resources for product formulation, on the environment (deforestation, overharvesting, and potential extinction), animals, and humans. To prevent such problems, the cosmetics industry is becoming greener and applying a number of sustainability strategies to conserve biodiversity, such as minimising pollution and not competing with the food supply. Through sustainability assessment, the impact of the cosmetic supply chain can benefit the companies by saving money, increasing sales, and improving the company's reputation.

For South African small companies/brands to meet the demands for international market trade, developed cosmeceutical products need to be of high quality and affordable. Furthermore, companies/brands need to have competitive pricing and strategic planning in order to operate at an international level with multinational giants of cosmeceuticals. For commercial trading to succeed, policies benefiting IKS holders/communities and companies must be put in place to avoid conflicts when a product expands to international markets. Generation of new IP's is also crucial, along with the number of medicinal plants used in product development and those with a potential to make it into a global market. The current patents of medicinal plants utilized in cosmeceuticals does not reflect the number of medicinal plants used in the industry, both formally and informally. Although under the auspices of the IKS policy, indigenous communities are encouraged to commercialise their knowledge and reap the economic benefits through fair and equitable benefit sharing, as promoted by the Nagoya protocol, it would appear that several factors have hindered the progress of this policy. These may include broader issues within the South African patent system, issues surrounding communal entitlement to benefits, or an overall lack of information or awareness related to the system. These problems need to be resolved urgently in order to give local communities opportunities to showcase what they can produce. Such initiatives will contribute to the South African economy through job creation, entrepreneurship skills, socio-economic development, and IP generation.

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