

Review Article

Natural active ingredients used in topical cosmetic formulations for anti-ageing: A systematic review

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Abstract

Smooth, even-complexed and radiant skin without wrinkles and dark spots characterizes healthy skin. Ageing is a natural biological process of becoming older. As a largest organ in the body, skin is prone to aging due to exposure to the external and internal damages. Skin ageing is characterized by wrinkles, fine lines and dark spots that appear on the skin surfaces. Cosmetics nowadays not only associated with beauty but also younger looking skin. The demand for anti-ageing cosmetics with natural ingredients are projected to boost the cosmetics industry contributing to global market growth due to an increase in global ageing populations. There are many cosmetics in the market offered product line for anti-ageing. Despite giving positive result in a longer period, natural ingredients are more preferred as active ingredients compared to synthetic ingredients which are notoriously known for causing complications as mild as minor irritations to more severe anaphylactic reactions, lethal poisonings, or long-time effects to users due to accumulated toxins. In this study, natural active ingredients will be discussed in terms of their sources, mechanisms, and anti-ageing properties. Systematic searches of PubMed, ScienceDirect, NCBI and Medline databases were carried out using various keywords. Through screening, 40 studies out of 70 studies were selected. Based on this review, a large variety of natural active ingredients could be obtained from plants, animals, and marines compared to singly synthesized artificial alternatives. The benefits, safety and efficacy of the ingredients were also evaluated, and it is found that they are indeed better constituents compared to synthetic ingredients to be used in cosmetic formulations.

Keywords: ageing, cosmetic formulations, natural, active ingredient, anti-ageing

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1.0 Introduction

Ageing is a natural biological process that cause changes to all the body organs especially the skin as it is the largest and visible one. Binic *et al* (7) reported that, chronological ageing and photoaging are two different forms of changes occurring in the skin (7). Generally, signs of ageing can be characterized with features of a mixture of multiple grades of dry skin intensity, visible fine lines and wrinkles, uneven skin pigmentation, lack of elasticity and skin sagging (8). The skin ageing can be determined through two common factors which are intrinsic and extrinsic factors (9). Intrinsic factors are from inside the individual, such as genetics and hormonal changes which occur naturally over lifetime. Meanwhile, the extrinsic factors are from environment that can induce skin ageing such as UV rays, pollution, and unhealthy lifestyle such as cigarette smoking. Although both factors can contribute to the ageing of the skin, the principal factor is the extrinsic influence from the climate (10).

Younger, healthy, and glowing looking skin can boost confidence and self-esteem especially for the ageing population. According to Mavon, (8), one of every nine people around the world is 60 or older. This is expected to rise by 2050 to one in five. Population aging is one of the 21st century's most notable megatrends. Sadly, the skin's natural cycle of healing is not enough because the exterior surface still faces harsh external factors such as UV rays, pollutants, and chemical exposure (8). While the population ages, dermatological emphasis needs to change from increasing the superficial effects of skin ageing to decreasing the actual morbidity associated with skin ageing problems (11). Hence by using cosmetics, the ageing process can be slowed down.

Treatment of aged skin may be through oral supplements, but it is typically through topical treatments such as creams, lotions, and ointments as appropriate to the form of

ageing signs observed (12). The cosmetics industry is worth tens of billions of US dollars worldwide and is actively looking for new and better natural ingredients to use as suitable raw materials, competing with artificial synthetic alternatives or introducing new bioactivities (13).

According to the US related statistics Census data and the National Consumer Survey of Simmons (NHCS), 25.32 million Americans used lotions 14 times or more in 2019 (14).

There are many types of cosmetic items available on the market recently. However, the cosmetic products may exhibit health risks and repeated adverse effects due to the toxic substances found in their formulations (15). Most of the non-natural product initially gives the skin positive results in a short period of time. Unfortunately, when toxic chemicals like heavy metals pile up or accumulate in the skin, this may pose significant problems to the health of the skin in the long term. As stated by Siti Zulaikha *et al* (16), While the presence of toxic metals in cosmetics was in small quantities, it is understood that these metals are accumulated toxins in which the slow release of these metals into the human system can be detrimental to the biological system as they can accumulate over time because these metals can accumulate in the organs of the body due to their long half-life (16).

The global warming is the main contribution to the aging of the skin nowadays. Photoaging is intensified in areas exposed to sunrays where the combination of short wavelength (UVB) damage to the outer layers of the skin (epidermis) and long wavelength (UVA) damage to the middle layers (dermis) (8). Therefore, because of their competitive efficacy and lower toxicity effects, the industry is actively looking for ingredients from natural sources.

Hasmida and Siti Zamidah (17), stated that natural sources may include polyphenols, terpenes, fatty acids, and vitamins that boost several bioactivities and may be beneficial when used in cosmetics. Natural cosmetic products thus provide the skin with better anti-ageing benefits as compared to non-natural

industrial cosmetic products (17). This review will discuss the variety of natural ingredients from plant and animal sources and their properties, the anti-aging mechanism.

2.0 Materials and method

2.1 Search strategy

In this review, PubMed, ScienceDirect, NCBI, Medline were used for the searching of data. The key terms that were used were “natural ingredient”, “cosmetics”, “formulations”, and “anti-ageing”. Besides that, a few textbooks were used to search extra information regarding the topics which was related with the anatomy and physiology of the skin. Exclusion criteria were lack of outcome measures and detailed information.

2.2 Data extraction

From the articles searched, in the data extraction, the inclusion and exclusion criteria were used. The included criteria consist of various databases sites with all review articles, abstract articles, full text articles, literature review articles and experimental studies that were associated with natural actives ingredients in anti-ageing cosmetic formulations. The information extracted from the textbooks were also used to get the required data for this review. The extracted data were on the information on the basic knowledge of the skin anatomy and physiology.

3.0 Results

A total of 20 studies from ScienceDirect, 20 studies from PubMed, 30 studies from NCBI and 30 studies from Medline were appointed. 70 studies remained after duplicates were detached. After evaluating their titles and abstracts, 18 studies were removed. The remaining 52 studies were assessed a more detailed manner for eligibility by evaluating the whole text of the articles and journals. Among these, 7 studies were excluded due to lack of outcome measures and 5 studies were excluded due to lack of detailed information. At the end, 40 studies were utilized for the final data extraction. The flowchart of literature search is presented in the Figure 1. The extracted data from the final 40 studies

were organised into the tabulated forms according to the type of active ingredients that are commonly used in the cosmetic formulations, to date. Other relevant information such as the sources, therapeutic values, functions, and their references were also included in the tables 1 and 2.

3.1 Plant-based active ingredients

3.1.1 Alpha hydroxy acids (AHAs)

Alpha hydroxy acids (AHAs) are natural active ingredients that can be obtained from plants and animals. These ingredients include lactic acids, glycolic acids, and malic acids. Glycolic acid can be obtained naturally from sugarcane. Some of them can be synthetically produced, but natural ingredients are preferable by the consumers nowadays. Generally, AHAs are mild exfoliants. They work on the skin surface by peeling of the dead skin. AHAs cause desquamation, plasticization, and normalization of epidermal differentiation by interfering with intercellular ionic bonding, reducing the cohesion of the corneocytes, and thereby inducing keratolysis (24). Thus, making the skin look radiant and youthful. It was reported that there were a reduction of rough texture and fine wrinkling, reduction of solar keratoses and slight lightening of solar lentigines in 41 volunteers with topical application of glycolic acid after 5 weeks of treatment (24).

3.1.2 Catechin

Catechin is an active ingredient found in green tea leaf. Camellia sinensis green tea leaf plays an important part on the cosmetics market. The flavanols or catechins present in tea infusions make up as many as 20-30 per cent of the dry matter of tea (21). Tea leaf is well known for its numerous benefits such as for body slimming and anti-ageing of the skin. Campa and Baron (18), stated that the potential properties of green tea mediated anti-ageing effects are antioxidant, photoprotective, immunomodulatory, anti-angiogenic, and anti-inflammatory. It has also been reported that there was an increase in epidermal thickness, skin elasticity and moisture of the skin when combining green tea extract with Ginkgo biloba

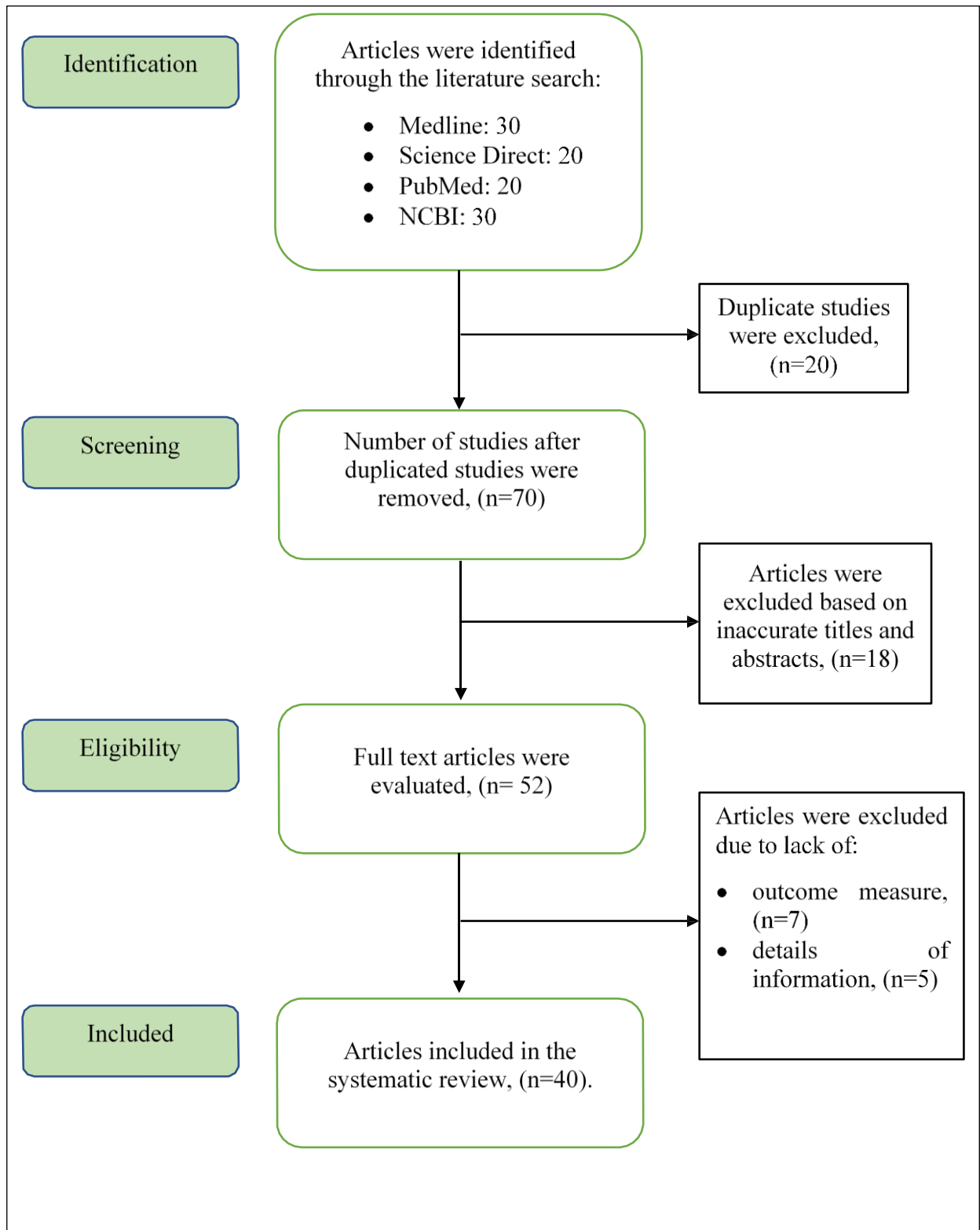


Figure 1: Flow diagram of study selection process

Table 1: Plant-based anti-ageing ingredients.

Therapeutic value	Sources	Bioactive Ingredients	Functions	Route	References
Anti-ageing	Argan oil	Vitamin E	Improve elasticity	Oral, Topical	(18)
	<i>Cecropia pachystacha</i> leaves	Flavonoid	Antioxidant	Topical	(19)
	Citrus fruit	Vitamin C	Antioxidant	Oral, Topical	(20)
	Coconut oil	Phenolic acid	Antioxidant	Topical	(18)
	Green tea	Catechins	Photoprotective	Oral, Topical	(21)
	Panax Ginseng	Ginsenoside	Anti-wrinkle	Oral, Topical	(22)
	Pomegranate	Ellegic acid	Dyspigmentation	Topical	(18)
	Pubescent oak	Phenolic acid	Moisturizing Effects	Topical	(23)
	Shea butter	Vitamin A	Anti-wrinkle	Topical	(23)
	Soy	Isoflavone	Anti- wrinkle	Topical	(18)
	Sugarcane	Alpha hydroxy acids (AHAs)	Natural Exfoliants	Topical	(24)
	Wheat	Niacinamide	Antioxidants	Topical	(25)

Table 2: Animal or Marine-based Anti-ageing Ingredients

Therapeutic value	Sources	Bioactive Ingredients	Functions	Route	References
Anti-ageing	Brown algae	Hyaluronic acid	Moisturizing effect	Topical	(26)
	Snail secretion	Glycosaminoglycans	Anti-wrinkle	Topical	(22)
	Seahorse	Peptides	Antioxidant	Topical	(26)
	Starfish powder	Ceramide	Dyspigmentation	Topical	(22)

in mouse model (18). According to Puri et al (27), maltose microneedling technique in topical cosmetical delivery enables the administration of green tea catechins to deeper layers of the skin without degradation due to light exposure (27).

3.1.3 Ellegic acid

Ellegic acid is an active ingredient naturally can be found in *Punica granatum* or also known as pomegranate. Pomegranate is a popular fruit due to its numerous nutrients and vitamins. Pomegranate extracts have been an interesting potential ingredient in cosmetic formulations because of their high antioxidant content (18). Ellegic acid is a major compound in the pomegranate extracts. A study showed reduced melanin and decreased erythema in 11 subjects with the topical application of a pomegranate extract microemulsion using polysorbate surfactant (28). According to Parveen *et al* (29), the skin lightening effects of ellagic acid was due to the chelation of copper ions at the active site of tyrosinase enzymes. This prevent the synthesis of melanin.

3.1.4 Flavonoid

Flavonoid is an active ingredient that is well-known for its anti-ageing effects. According to Fernandes *et al* (19), there is an interest in searching for bioactive compound derived naturally from *Cecropia pachystachya* as antiaging agents. Flavonoid has an antioxidant property. The elevated production of reactive oxygen species results in an accelerated skin aging. Flavonoids are recognized as tissue protector against reactive oxygen species (ROS) and are believed to be the defense against premature skin aging (19). As reported by Duque et al (30), antioxidant activity was associated with the topical gels containing the ethyl acetate extract of *Cecropia pachystachya* (ECP).

3.1.5 Ginsenoside

Ginsenoside is a bioactive compound that occur naturally in *Panax ginseng* known as red ginseng. According to Kim *et al* (31), red

ginseng is used as cosmetic and food ingredient that protects against UVB-induced cell death, improves skin hydration, prevents wrinkles, and has antioxidant effects. Ginsenosides in red ginseng extracts are responsible for the anti-ageing and anti-wrinkle effects on the skin (31). A study reported a decrease in epidermal skin thickness, wrinkle formation, and skin elasticity after UV-B irradiation in a mouse model with topical application of ginsenosides (22). The mechanism of anti-ageing by red ginseng are as follows: reduced wrinkle formation by increasing Col-I and MMP-1, MMP-2 and MMP suppression, increased skin-related rates of AQP3 and HAS2 and promoted expression of SPT, CERS3 and FLG, which are essential for skin moisturization (31).

3.1.6 Isoflavone

Isoflavone is a bioactive component that is commonly used in cosmetic formulations for anti-ageing effects. Isoflavones are found in high concentration in soybean. According to Campa and Baron (18), the oestrogen-like effects are due to isoflavone diphenolic structure and may potentially counteract some of the skin aging effects of menopause. Genistein is a soy isoflavone with antioxidant and anti-wrinkle activity (18). A research found an increase in the amount of facial collagen of both type I and type III by the end treatment with topical oestrogen and genistein on postmenopausal women's facial skin collagen (32).

3.1.7 Niacinamide

Niacinamide is a natural active ingredient that is used recently in the anti-ageing formulations. It is the amide of nicotinic acid, which is a water-soluble vitamin found in meat, fish, and wheat, that is responsible for these effects (25). The anti-inflammatory property in niacinamides can be used to reduce hyperpigmentation that cause dark spots on the aging skin. Niacinamide is naturally safer than synthetic hydroquinone. In addition, it improves the skin's elasticity, strengthens the epidermis and increase the

fatty acids in the skin that leads to plumper effects to the skin. A study showed significant reductions in the Fitzpatrick wrinkle score and significant improvements in elasticity parameters that support the niacinamide test cream's potential anti-ageing benefits (33).

3.1.8 Phenolic acid

Phenolic acid is a bioactive compound that can be used in cosmetic formulations for anti-ageing. It is naturally obtainable in coconut oil obtained from *Cocos nucifera*'s dried fruit. Coconut oil can moisturize the aging skin by applying it topically onto the skin. According to Campa and Baron (18), phenolic acids are associated with antioxidant activity which work against UV-induced damage. According to Plainfossé et al (23), *Quercus pubescens* willow leaves extract known as pubescent oak also contains phenolic acids that are responsible for anti-ageing effects.

3.1.9 Vitamin A (Retinols)

Vitamin A is a natural form of retinol that has a potent anti-ageing property. Commonly, retinols also are included in the cosmetic formulations including serums and creams. Shea butter contains essential fatty acids and is considered to be naturally rich in vitamins A, E and F, as well as additional vitamins and minerals which help the skin to smooth, hydrate and balance (34). Retinols help to fight aging of the skin by triggering the collagen production, making the skin more elastic and firmer. Zasada and Budzisz (35), stated that the anti-wrinkle properties of retinoids stimulate proliferation of keratinocytes, enhance the defensive role of the epidermis, restrain trans epidermal water loss, protect collagen from degradation and inhibit metalloproteinase activity. Due to its ability to penetrate the epidermis and dermis, a fat-soluble retinol frequently used in cosmetic formulations for anti-ageing (35). A clinical study in 49 volunteers with application twice a day of either 15% or pure shea butter had discovered that shea butter prevented photo-aging (36).

3.1.10 Vitamin C

Vitamin C is a well-known active ingredient that is also commonly used in cosmetic formulations for anti-ageing. According to Schagen *et al* (20), Ascorbic acid is used topically in a number of cosmetics, such as dyspigmentation, anti-ageing and sunscreen formulations. Fresh fruits and vegetables such as citrus fruits, blackcurrant, rose hip, guava, chili pepper or parsley are the best natural sources of vitamin C (20). Usually, vitamin C that is used in the formulations come from citrus fruits such as lemons, orange, lime, and grapefruits. Vitamin C is a powerful antioxidant. It works by neutralising the free radicals that cause damages to the skin. According to Telang (37), vitamin C is an effective antioxidant drug that can be used topically in dermatology to treat and prevent photoaged related changes.

3.1.11 Vitamin E

Vitamin E is an active ingredient that can be found naturally. The source of vitamin E can be from various plant-based oils or butter. The increasingly famous one recently is argan oil. Argan oil is plentiful in Morocco and is extracted from *Argania sponosa* L seeds (18). According to Schagen *et al* (20), vitamin E topical application is described to reduce erythema, sunburned cells, and chronic UVB-induced skin damage. Vitamin E works by neutralising oxidant from free radicals that can cause wrinkles to the skin. Consequently, the skin can maintain its healthy and youthful looking skin. A study showed an improvement of skin elasticity with daily consumption or topical application of argan oil in a group of post- menopausal women (38).

3.2 Animal or Marine-based active ingredients

3.2.1 Hyaluronic acids

Hyaluronic acids (HA) are natural active ingredients that are well known to be added in the cosmetics formulations for its moisturizing effects. According to Saranraj and Naidu (39), low molecular weight hyaluronic acid can penetrate easily through the skin.

Hence, hyaluronic acid is one of the most common ingredients used in the formulations for anti-ageing. According to Hameury *et al* (40), some clinical studies proved the numerous beneficial activities of algae-derived ingredients on the skin including anti-aging, free radical scavenging, soothing, preventing redness, depigmenting, and slimming. Brown algae known as *Macrocystis pyrifera* of the Laminariaceae family, is one of the common ingredients used in the cosmetic formulation for its bioactive compound of natural hyaluronic acid. It is widely used for skin care against ageing. An aqueous extract of the brown alga is available on the market for its properties as inducers of hyaluronic acid synthesis, which triggers syndecan-4 synthesis, another essential extracellular matrix (26).

3.2.2 Glycosaminoglycans

Glycosaminoglycans are active ingredients that can be found in the secretion of brown garden snail. The secretion or slime has become popular and trending in the cosmetic markets nowadays especially in Korean and Japan. Brown garden snail is known as *Cryptomphalus (Helix) aspersa*. The growth factors and active glycosaminoglycans contained in the secretions have many dermatological advantages including rejuvenation due to antioxidative, cellular proliferative, extracellular matrix remodelling properties, as well as antimicrobial effects (15). The antioxidant properties in the slime contribute to the anti-ageing effects on the skin. A study by Brieve *et al* as cited in Juhász *et al* (22) has stated that a secretion of the mollusk *Cryptomphalus aspersa* (SCA) contained antioxidant bioactives which possesses skin-regenerative properties. Another study reported that with the active snail extract treatment, it appears to be effective in improving signs of skin aging in women 45 to 65 years old (41).

3.2.3 Peptides

Peptides is a protein that is used as active ingredients in cosmetic formulations. Bioactive peptides obtained naturally as extracts, hydrolysates and individual peptides have biological properties including antioxidant,

antimicrobial, and anti-inflammatory activity, and inhibit aging-related enzymes such as elastase, collagenase, tyrosinase, and hyaluronidase (42). Peptides extracted from seahorses (SHP-1) have been reported to stimulate collagen release through inhibition of collagenases 1, 3 and 13 (26). Varani *et al* as cited in Fu *et al* (42) stated that photoaging is partially caused by damage to the skin's connective tissues through increased collagen-degrading metalloproteinases and reduced collagen synthesis. The origins of MMPs inhibitors can be obtained from seahorses in marine resources such as the natural peptide. Matrix metalloproteinase inhibitors (MMPs) can be of potential use as a cosmetic anti-wrinkle product (26).

3.2.4 Ceramides

Ceramide is a natural active ingredient usually included in moisturizing preparations. Ceramides is a lipid derived from animal sources. According to Lazzara *et al* (43), Around 1500 starfish species worldwide, mainly found in Southeast Asian waters contain bioactive substances such as steroid glycosides, glycosaminoglycans, cerebroside and ceramides. Starfish powder from species of *Asterine pectinifera* is one of sources for ceramides. Starfish powder is beneficial for photorejuvenation and dyspigmentation in cosmeceuticals. They restore the natural lipid on the skin that are lost due to the environmental factors. In terms of aging, ceramides moisturize the skin, making it hydrates and hence, the skin looks more youthful (43). According to Juhász *et al* (22), *A. pectinifera* extracts can be beneficial additions to skin brightening and hyperpigmentation treatment regimens (22).

4.0 Discussion

Our systematic literature review identified 20 studies concerning the natural active ingredients used in cosmetic formulation that possess anti-ageing properties. We focused on topical applications which improved skin conditions by actions such as strengthening the skin barrier, enhance skin elasticity,

increase skin density, shield it from radicals, fade wrinkles and reduce age spots. However, there are ingredient that also helped improved the skin's health through the mechanism of peeling (AHA).

Our review showed that some active ingredients could be obtained from multiple sources as well as one source could produce multiple active ingredients. This would allow cosmeceutical industry easy access to produce more effective, nourishing, and safe cosmetic products.

It is known that anti-ageing ingredients are essential components of various cosmetics including creams, moisturizing lotions, tonics, shower gels, beauty products and cosmetic facial masks. Consumers have increasingly become more conscious of the health of cosmetic products on the market. According to Chermahini et al as cited by Liang et al. (44), found that synthetic ingredients in cosmetics effected skin even faster, however most of them react adversely to skin. As a result, cosmetic products made from natural ingredients are becoming more popular than the product made from chemical or non-natural ingredients. The principal difference between natural and non-natural cosmetics are their ingredients. Natural cosmetics are also known as cosmetics of herbal origin. Natural cosmetic products contain natural ingredients from plant sources, animal sources, water and minerals that are considered harmless than artificial substances (45). The formulation of all such cosmetic products includes the addition of various natural additives such as oils, waxes, natural colours, natural fragrances and parts of plants such as leaves or flowers using different techniques of formulation.

The natural cosmetic product provides many advantages such as making the skin healthier and more attractive, as it contains safe ingredients that nourish the skin with vitamins and antioxidants. Natural products, in turn, will reduce exposure to toxic synthetic ingredients such as parabens, formaldehydes, phthalates, fragrances, toluene and heavy metals. The most frequently identified heavy metals in cosmetic products are lead (Pb), cadmium (Cd),

mercury (Hg), chromium (Cr), nickel (Ni) and copper (Cu) used in shampoos, lipsticks, creams, eye shadows and powders (46). Additionally, the chances of skin irritation can be minimized by using natural cosmetic products. Skin irritation may occur because of the higher concentrations of preservatives, colours and fragrances typically used in non-natural cosmetics. Siti Zulaikha *et al* (16), stated that the cosmetic products most commonly cause allergic contact dermatitis due to its fragrance ingredients. Allergic contact dermatitis typically affects the face and hands, so health for work and the individual's quality of life can be affected (16).

5.0 Conclusion

This review evaluated the efficacy of natural active substances used to combat skin ageing. It thus offers complete understanding of the substances' potential to be just as effective as synthesised active chemicals. Some of the most powerful natural ingredients like retinols, alpha hydroxy acids (AHAs), antioxidant and peptides have been industry leading skin aging fighters for its efficacy and safety. Therefore, natural active ingredients are considered the better constituents used in the cosmetic formulation for anti-ageing than the synthetic ingredients.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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