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AN OVERVIEW OF RECENT ELASTIC SKIN BIOACTIVE ENHANCERS

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Abstract

Natural products are commonly used in cosmetics to maintainhealthy skin and improve visible signs of aging due to great confidence that they are harmless. Nowadays, the therapeutic benefit of skin bioactive components has been well identified, and some of them have been established as drugs that target different kinds of skin diseases. A review of the literature was conducted using peer-reviewed journal articles toidentify laboratory, animal, and clinical studies that have studied the most recent and advanced innovations in the bioactive properties and skin applications of the different dermatological active natural ingredients that could be implemented in the development of various skin active products that could invade the photoaged skin. The provided data in this article aims to get the picture of the most recent investigations, and it might be helpful for dermatologists and other experts in cosmeceutical manufacturing companies. Despite the several advances in this field, additional development would enable scientists to develop new skin-active antiaging products.

Keywords: *Natural bioactive, Skin aging, Reactive oxygen species, Skin elasticity*

Introduction

Aging is multifactorial and yields physiological changes in organs, tissues, and cells over time. In the skin and cartilage, aging causes a decrease in the buildup and changes in the organization of proteoglycans and collagen, as well as the loss of glycosaminoglycans, which are accountable for the integration of these tissues. The marks of aging are most evident on the epidermis, dermis, and subcutaneous tissue. As skin ages, the epidermis becomes thinner, and collagen production in the dermis declines with the brutality of photodamage [1]. Collagen embraces 90% of the dermis, it provides elasticity to the skin and is responsible for its mechanical firmness [2]. Collagen is decomposed by collagenase, such as matrix metalloproteinase (MMP), triggering wrinkles, reduced elasticity, and sagging of the skin [3]. MMPs are metalloproteinases, and these are commonly classified into collagenases, gelatinases, stromelysins, matrilysins, membrane-type MMPs, and other MMPs [4]. Light absorbed into the skin conveys its energy to plastids, such as melanin. Then, the plastid yields free radicals that form a harmful reactive oxygen species (ROS) [5]. Large production of ROS results in overexpression of MMP-1 causing collagen and elastin degradation, that precipitate skin aging. Besides, keratinocytes release cytokines including interleukins and tumor necrosis factor (TNF)-α through exposure to UV light [6]. MMP- 1 is a collagenase that identifies its substrate through a hemopexin-like domain and cuts native fibrillar collagen [7]. MMP-2 and MMP-9 are gelatinases that destroy ECM components, including types I and IV collagen. Numerous types of MMPs that are expressed by ROS hydrolyze the collagen chain, skin connective tissue, and accelerate the formation of wrinkles [4]. Hence, the way of preventing aging is by hindering the oxidative stress caused by ROS [8]. Melanin is a dark-colored polymer pigment that is produced by melanocytes in the epidermis. Its main purpose is to block ultraviolet (UV) rays to protect the skin. Otherwise, its undue production can cause pigment darkening, such as age spots [9-11]. Tyrosinase is a major enzyme that catalyzes the production of melanin through dopachrome during melanin biosynthesis [12]. Therefore, it is widely accepted to decrease melanin production through the prevention of tyrosinase activity to enhance the fading effect of cosmetics [13]. The increase in UV radiation triggers the active production of reactive oxygen species (ROS) in the human body, such as superoxide anions, hydrogen peroxides, and hydroxyl radicals. Such species have endorsed the oxidation of tyrosine, causing increased production of melanin. Hence, inhibition of melanin secretion and collagen breakdown through the lessening of ROS generation has been the main focus for skin whitening and wrinkle prevention [14]. Bioactive ingredients are derived from collagen, peptides, proteins, vitamins, minerals, and plant extracts. These ingredients have potential applications for skin regeneration and photoprotection. With growing interest in natural antioxidants to overcome the limitations of conventional anti-wrinkle ingredients, Plant-derived extracts have been actively used to develop bioactive compounds for safe whitening and anti-wrinkle cosmetics [15]. Natural phytoactive compounds have antioxidant properties [16, 17]. They can act as ROS scavengers and lipid peroxidation inhibitors. They can be incorporated into cosmetic formulations as anti-wrinkle and depigmentation ingredients, thus preventing damage from UV radiation.

Collagen-derived bioactive peptides and natural antioxidant compounds

Nutraceuticals comprising collagen peptides, antioxidants, vitamins, and minerals are inventivefood supplements that have been clinically shown to have positive effects on skin hydration and elasticity. The interactions between collagen peptides (0.3–8 kDa) and other constituents present in liquid collagen-based nutraceuticals have been examined for normal primary dermal fibroblast function in a novel, cell culture model packed with macromolecular dextran sulfate. Collagen peptides expressively increased fibroblast elastin synthesis while considerably inhibiting the release of MMP-1 and MMP-3 and elastin deprivation. The optimistic effects of the collagen peptides on these reactions and fibroblast propagation were improved in the presence of the antioxidant components of the products. Providing a cell-based basis for the

positive effects of these collagen-based nutraceuticals on skin properties, they signify the enriched formation of stable dermal fibroblast-derived extracellular matrices after their oral consumption [18].

JasminumSambac Extract

The anti-aging activities of *Jasminumsambac*extract (JSE) have been considered. The phytochemical assay was accomplished with the modified Farnsworth method. Antioxidant assays were measured by 2,2-diphenyl-1- picrylhydrazyl (DPPH) scavenger, Ferric Reducing Antioxidant Power (FRAP), and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS)-reducing activities. Anti-aging properties were measured through the inhibitory activities of elastase, collagenase, and hyaluronidase. The phytochemical analysis revealed the presence of triterpenoids, flavonoids, and phenols at a low level and terpenoids at a high level. JSE presented higher DPPH-scavenging activity than eugenol but less than hesperidin. JSE demonstrated the lowest ABTS activity compared to hesperidin and eugenol. The FRAP-reducing activity of JSE, hesperidin, and eugenol showed JSE had the lowest activity at the highest concentration. JSE exhibited the lowest anti collagenase activity, anti-elastase, and anti-hyaluronidase relative to hesperidin and eugenol. Generally, JSE has low antioxidant activity compared to hesperidin and eugenol, besides low anti-collagenase, anti-elastase, and anti-hyaluronidase activities [19].

Lactic and lactobionic acids

Alpha-hydroxy and polyhydroxy acids (AHA and PHA) have excellent antioxidant and moisturizing properties. These compounds are valuable in terms of both cosmetic and dermatological treatments. The hydrating properties of lactobionic and lactic acids have been evaluated. AHA and PHA can bind large amounts of water and serve as potent antioxidant agents through the prevention of matrix metalloproteinases and strong chelating properties. Lactic acid (LAC) and lactobionic acid (LA) can maintain epidermal integrity and, thus, they possess the opportunity to be applied to various sensitive skin types. They are substances that cause quite a similar effect on the skin. AHA and PHA possess pronounced surface activity, they have exfoliating properties but with very mild and moisturizing features. Due to their highly hydrophilic nature, neither acid can penetrate deeply into the skin. In comparison with other hydroxy acids used in cosmetology, the higher moisturizing properties of both substances originate from a large number of hydroxyl groups of lactobionic acid and the high compatibility of lactic acid with normal skin. It is considered one of the major components of the natural moisturizing factor (NMF). AHA and PHA are considered distinctive humectants; they have great potential to attract water in the stratum corneum [20].

Mangosteen Peel Extract

Mangosteen peel extract (MPE) has been widely studied and has achieved various biological activities. Physical and chemical characterization of the Mangosteen peel revealed various xanthones., including alpha-mangostin, gamma-mangostin, and garcinone C. The antioxidant properties and inhibitory activity of MPE and its compounds against aging-relatedenzymes were examined. MPE and its compounds were subjected to ferric reducing antioxidant power (FRAP), hydroperoxide (H_2O_2) scavenging, anti-collagenase, anti-elastase, anti-hyaluronidase, and anti-tyrosinase assays. MPE possesses the highest anti elastase activity at IC50 7.40 µg mL−1. Also, MPE has the highest FRAP 116.31 ± 0.60 µMFe(II) µg−1 extract. Alpha-mangostin showed potent anti-collagenase activity (IC50 9.75 µgmL−1). Whereas gamma-mangostin showed potent anti-hyaluronidase (IC50 23.85 µgmL−1) and anti-tyrosinase(IC50 50.35 µgmL−1). IC50 of MPE on H_2O_2 scavenging activity was 54.61 µg mL−1. Accordingly, there is scientific evidence for possible usage of mangosteen extract and its compounds could be usedas an antioxidant and antiaging agent [21].

Essential oils of *Menthaviridis*

MenthaViridis(MV)is largely used in folk medicine by infusion in tea. North Africa, Australia, Europe, and Central Asia are the principal centers of the *Mentha*genus. Significantly, essential oils (EO) of this

plant showed antioxidant and antimicrobial properties, which are related to the bioactive compounds present in *M. Viridis*. *M. Viridis*contains monoterpenoids like carvone, limonene, menthone, menthol, and pulegone as major compounds. The chemical composition of essential oils from *M. Viridis* has been determinedand their in vitro antioxidant, dermatoprotective, and anti-dermatophyte properties have been studied. Antioxidant activity was estimated by three corresponding methods: DPPH, FRAP, and ABTS. The inhibitory effects of tyrosinase and elastase were used to reveal the dermatoprotective property of MVEO. The chemical composition determination of MVEO revealed the presence of carvone, 1.8-Cineole, and Terpinen-4-ol as the main compounds. MVEO presented remarkable antioxidanteffects by IC50 values of 80.45±1.86 µg/mL, 101.78±3.14 µg/mL, and 139.59±3.12 µg/mL obtained by DPPH, FRAP, and ABTS tests, respectively. Moreover, MVEO demonstrated remarkable inhibition of tyrosinase(IC50= 55.13±1.01 µg/mL) and elastase (IC50= 114.24±1.22 µg/mL). The findings of this work showed that volatile components of MVEO could constitute a new source for antioxidant, dermatoprotective, and antidermatophyte properties [22].

Nylon-Beta Vulgaris

Beta vulgaris extract is widely used in Iran's folk medicine. Engineering of skin tissue that contains a high ratio of a protein named elastin1 requires a polymer substrate with ample elastic properties, including a comparable Young's modulus, to simulate the native skin tissue. Nylon can provide an obvious elasticity to mimic skin properties. A composite membrane of nylon and *B. Vulgaris*extract as a nanofibrous substrate has been studied for skin healing aims. Keratinocytes are a predominant cell type in the epidermal layer of the skin were seeded on the fabricated composite and non-composite scaffolds. It was observed that a composite type scaffold ensures the elastic properties specified for skin providing high biocompatibility. Additionally, the nanostructured surface of the scaffold ensured the proper cell interactions for keratinocytes. Natural ingredients containing polysaccharides have been used as candidates for skin healing properties. An electrospinning setup was proposed for the first time to engineer an efficient composite nanofibrous structure of *Beta vulgaris* (obtained from beet [*Chenopodiaceae* or *Amaranthaceae*]) that belongs to polysaccharides and an elastic polymer named nylon 66. Both Scaffolds, including non-composite and composite types, were studied by Scanning electron microscopy (SEM), FTIR spectroscopy, mechanical assay, and contact angle. Scanning electron microscope examinations have verified the homogeneous structure of the nanofibers containing nylon polymer and *B. Vulgaris* extract. FTIR spectroscopy confirmed the presence of *B. Vulgaris* extracts within the mat of nanofibers. Moreover, the measurement of mechanical properties with cell-laden composite scaffolds confirmed the required similarity between the scaffold and inherent skin tissue. Compared with the nylon nanofibrous scaffold, the composite sample containing *B. Vulgaris* extract has a higher hydrophilic surface. SEM and MTT assays confirmed a higher number of attached cells on the composite electrospun membrane. Using the real-time polymerase chain reaction (PCR) technique, epidermal gene expression was noticed. Besides, immunocytochemistry results showed that the original property of keratinocytes was highly preserved using the composite scaffold [23].

***Ocimum sanctum* extract**

Ocimum sanctum, commonly known as "the Queen of Herbs", has been reported for several biologically beneficial activities. The major constituents of *O. sanctum*, including eugenol, ursolic acid, linalool, and rosmarinic acid, have been reported to exert anti-inflammatory and antioxidant activities. The biological activities of *O. sanctum* extracts related to skin aging, including anti-collagenase, anti-elastase, and anti-hyaluronidase activities, have been investigated. Additionally, this study also examined the content of rosmarinic acid in *O. sanctum* extracts and determined the inhibitory activities against oxidation, inflammation, collagenase, elastase, and hyaluronidase of rosmarinic acid and *O. sanctum* extracts. Anti-inflammatory activity was

investigated according to the inhibition of nuclear factor kappa B (NF-κB) expression and interleukin-6 (IL-6) secretion. The ethanolic extract of *O. sanctum* had the highest yield (6.5%), and it contained the highest rosmarinic acid and the highest total phenolic content. Moreover, it possessed the most potent antioxidant activity with the Trolox equivalent antioxidant capacity of 270.1 ± 15.1 µM/mg, the equivalent concentration of 459.3 ± 91.4 µM/mg, and inhibition against 2, 2-diphenyl-1-picrylhydrazyl radical of 34.0 ± 0.7%. The ethanolic extract also showed the highest anti-inflammatory activity with inhibition of IL-6 secretion and NF-κB expression. Furthermore, it also exerted the highest inhibition against matrix metallopeptidase-1 and hyaluronidase, with inhibition of 77.7 ± 9.0% and 98.1 ± 0.1%, respectively. Rosmarinic acid was considered as the major compound liable for anti-aging properties. Thus, the ethanolic extract of *O. sanctum* is an optimistic natural source of skin-anti-aging components in the cosmeceutical industry [24].

Collagen peptides combined with vitamins and other bioactive compounds

Daily oral supplementation with a liquid nutraceutical containing hydrolyzed fish collagen, vitamins, antioxidants, and other active ingredients (such as L-carnitine, glucosamine, and chondroitin sulfate) has been hypothesized to improve skin texture and elasticity. A double-blind, randomized, placebo-controlled clinical trial was conducted on 120 subjects who consumed either the test product or placebo daily for 90 days. Subjects taking the test product had an overall significant increase in skin elasticity (+40%; P < .0001) when compared to placebo. Histological analysis of skin biopsies showed positive changes in the skin design, with a decrease in solar elastosis and enhancement in collagen fiber arrangement in the test product group. Furthermore, the consumption of the test product decreased joint pain by -43% and increased joint mobility by +39%. Oral supplementation with collagen bioactive peptides combined with chondroitin sulfate, glucosamine, L-carnitine, vitamins, and minerals considerably improved the clinical manifestations related to skin aging and, thus, might be an effective solution to slow down the signs of aging [25].

***Siegesbeckiaglabrescens* extract.**

*Siegesbeckiaglabrescens*has been traditionally used to treat inflammation. The anti-photoaging effects of S. glabrescens extract and kirenolwere studied in UVB-induced photoaging in vitro and in vivo models, respectively. The anti-photoaging effects of standardized *Siegesbeckiaglabrescens* extract (SGE) and its major active compound, kirenolwere examined using Hs68 human dermal fibroblasts and hairless mice, respectively. UVB-irradiated hairless mice that received oral SGE (600 mg/kg/day) demonstrated minimized wrinkle formation and skinfold thickness compared to the UVB-irradiated control. Moreover, SGE treatment raised the mRNA levels of collagen synthesis genes (COL1A1, COL3A1, COL4A1, and COL7A1) and enhanced antioxidant enzyme (catalase), whereas inhibiting matrix metalloproteinase (MMP-2, -3, -9, and -13) expression. In Hs68 fibroblasts, kirenol expressively prevented MMP expression while elevating the expression of COL1A1, COL3A1, and COL7A1. Therefore, both SGE and kirenol diminished UVB-induced photoaging in hairless mice and fibroblasts through suppression of the mitogen-activated protein kinases and nuclear factor kappa B pathways, providing that SGE could act as a natural anti-photoaging nutraceutical [26].

Compound K

CK which is a ginsenoside of Panaxginseng has antiatopic dermatitis activity. It has also been able to suppress MMP-1 in UVB- or tumor necrosis factor-a-stimulated dermal fibroblasts. The antiaging effect of compound K (CK) has been assessed. Under UVB irradiation conditions, matrix metalloproteinase-1, cyclooxygenase-2, and type I collagen expression levels were measured. Under UVB irradiation conditions, CK inhibited skin aging and depletion of collagen by regulation of MMP1 and COX-2 expression. RT-PCR was used to test the skin-hydrating effect of CK. Assays of melanin content and secretion and tyrosinase activity were done. CK treatment alleviated the production of matrix metalloproteinase-1 and cyclooxygenase-2 in UVB irradiated NIH3T3 cells and improved type I collagen expression levels. Expression of skin hydrating factors such as filaggrin, transglutaminase, and

hyaluronic acid synthases-1 and -2d was increased by CK and was modified through the inhibitor of kBa, c-Jun N-terminal kinase, or extracellular signal-regulated kinases pathway. In the melanogenic response, CK did not adjust tyrosinase activity or melanin secretion, but increased melanin content in B16F10 cells was noticed. CK has hydrating and anti-aging properties. CK could be used to increase the skin moisture levels in cosmetic preparations and to protect against UVB rays [27].

Pheophorbidea derivatives

Pheophorbidesproduced by the majority of photosynthetic plants and microalgae as degradative products of chlorophyll upon fruit ripening. Pheophorbidea (PA) exerts antioxidant and anti-inflammatory properties. PA is intensely absorbed light energy at 650-700 nm. PA has an antiwrinkle effect in UV-induced skin tissue through suppression of MMP-1 and MMP-3 expression (Granted patent: US 20170189292). Further, PyroPA a derivative of Pheophorbidea shows higher photobleaching efficiency than PyroPA-ME. The antiwrinkle effects of PA and its derivatives, including PyroPA and PyroPA-MEhave been surveyed and compared using UVB-exposed CCD-986sk human fibroblasts. Additionally, the molecular mechanism underlying the effects of these pheophorbideswas clarified. PA, PyroPA, and PyroPA-ME successfully suppressed the accumulation of reactive oxygen species in UVB-exposed CCD-986sk fibroblasts. Furthermore, all three pheophorbides reduced UVB-induced matrix metalloproteinase (MMP)-1 secretion and mRNA expression of MMP-1, MMP-2, and MMP-9. Using pheophorbides in treatments resulted in increased procollagen synthesis in CCD-986sk cells. These antiwrinkle properties were more effective with PA and PyroPA than with PyroPA-ME. Also, PA and PyroPA inhibited UVB-induced phosphorylation of extracellular signal-regulated protein kinase and c-Jun N-terminal kinase. Besides, all three pheophorbides inhibited NF-_B p65 phosphorylation. Consequently, these pheophorbides, especially PA and PyroPA, can be used in functional cosmetics as natural anti-wrinkle ingredients [28].

Peanut Shell

Peanut (*Arachishypogaea*) is a plant belonging to the legume family. Peanuts are rich sources of protein (25%), lipids (47%), and carbohydrates (16%), as well as minerals, vitamins, niacin, unsaturated fatty acids, and oleic acids [20]. As a byproduct, more than 1.5 million tons of peanut shells are discarded each year. Nevertheless, it is important to produce richly-added materials using peanut shells to overcome the problem of byproducts. Anti-inflammatory properties of peanut shell extracts have been reported. Herein, the bioactive compounds from a peanut shell were extracted using ultrasound-assisted extraction (UAE) to approve their antioxidant, whitening, and anti-wrinkle effects, and an optimal UAE condition using the response surface method (RSM) and increased the functionality of extracts was optimized to settle the prospect of their use as cosmetics and medical ingredients. Response surface methodology was employed to optimize the ultrasound-assisted extraction (UAE) conditions for simultaneous optimization of dependent variables, including DPPH radical scavenging activity (RSA), tyrosinase activity inhibition (TAI), and collagenase activity inhibition (CAI) of peanut shell extracts. A reverse transcription-polymerase chain reaction showed that peanut shell extract decreased mRNA levels of tyrosinase-related protein-1 and matrix metalloproteinase-3 genes in B16-F0 cells. Consequently, the skin-whitening and anti-wrinkle effects of peanut shell extracts at protein as well as gene expression levels were determined. According to the results, the peanut shell is a promising cosmetic material for skin-whitening and anti-wrinkle effects. Depending on this study, peanut shell, which was considered a byproduct, can be used effectively for the production of medicines, and cosmetics [29].

Conclusion

Because of the increased demand for natural bioactive compounds that target the skin, many researchers are looking for new entities to use in the development of cosmeceuticals for skincare anti-photoaging therapy. The biologic activity of various natural skin bioactive based on skin anti-

photoaging aging properties have been elucidated, providing mechanisms for how these skin active ingredients may protect against skin photoaging. Further randomized, placebo-controlled, double-blind studies are needed to substantiate many of the claims made about these bioactive-derived cosmetic compounds. There is a need to study combinations of several classes of biofunctional active ingredients that reveal synergistic effects on reversing signs of photoaging.

References

1. Tagami, H. (2008). Location-related differences in structure and function of the stratum corneum with special emphasis on those of the facial skin. Int. J. Cosmet. Sci., *30*(6), 413-434.
2. Nishigori, C., Hattori, Y., Arima, Y., &Miyachi, Y. (2003). Photoaging and oxidative stress. Exp. Dermatol., *12*, 18-21.
3. Binic, I., Lazarevic, V., Ljubenovic, M., Mojsa, J., &Sokolovic, D. (2013). Skin ageing: natural weapons and strategies. J Evid Based Complementary Altern Med, *2013*.
4. Poljšak, B., &Dahmane, R. (2012). Free radicals and extrinsic skin aging. Dermatol Res Pract, *2012*.
5. Hwang, K.A., Yi, B.R., Choi, K.C. (2011). Molecular mechanisms and in vivo mouse models of skin aging associated with dermal matrix alterations. Lab.Anim.Res, 27:1:1-8.
6. Arora, S., Tyagi, N., Bhardwaj, A., Rusu, L., Palanki, R., Vig, K., Carter, J.E. (2015). Silver nanoparticles protect human keratinocytes against UVB radiation-induced DNA damage and apoptosis: potential for prevention of skin carcinogenesis. NANOMED-NANOTECHNOL, 11(5):1265-1275.
7. Biesalski, H. K., Berneburg, M., Grune, T., Kerscher, M., Krutmann, J., Raab, W., ...& Schwarz, T. (2003). Oxidative and premature skin ageing. Exp. Dermatol., *12*, 3-15.
8. Liu, S., You, L., Zhao, Y., Chang, X. (2018). Hawthorn polyphenol extract inhibits UVB-induced skin photoaging by regulating MMP expression and type I procollagen production in mice. J. Agric. Food Chem, 66(32):8537-8546.
9. Al-Laaeiby, A., Kershaw, M. J., Penn, T. J., & Thornton, C. R. (2016). Targeted disruption of melanin biosynthesis genes in the human pathogenic fungus *Lomentosporaprolificans* and its consequences for pathogen survival. Int. J. Mol. Sci., *17*(4), 444.
10. Kim, E. J., Shim, M. K., Jeong, A. R., & Kim, A. J. (2019). Anti-photoaging effects of fermented soybean (Bio-Peptone®). J. Soc. Cosmet. Sci. Korea, *45*(1), 27-36.
11. Mungmai, L., Preedalikit, W., Pintha, K., Tantipaiboonwong, P., &Aunsri, N. (2020). Collagenase and melanogenesis inhibitory effects of *perillafrutescens* pomace extract and its efficacy in topical cosmetic formulations. Cosmetics, *7*(3), 69.
12. Huang, H. C., Wang, S. S., Tsai, T. C., Ko, W. P., & Chang, T. M. (2020). Phoenix dactylifera L. Seed Extract Exhibits Antioxidant Effects and Attenuates Melanogenesis in B16F10 Murine Melanoma Cells by Downregulating PKA Signaling. Antioxidants, *9*(12), 1270.
13. Kim, M. J., Kim, S., Hyun, K. H., Kim, D. S., Kim, S. Y., & Hyun, C. G. (2017). Antimelanogenic of *artemisiafukudomakino* extract in melanoma cells. Korean Soc. Biotechnol. Bioeng. J., *32*(3), 233-237.
14. Lee, J. E., Lee, E. H., Kim, B. O., & Cho, Y. J. (2017). Biological activities of extracts from *Caryopterisincana*Miq. J. Appl. Biol. Chem., *60*(1), 61-68.
15. Sinan, K. I., Ak, G., Etienne, O. K., Jekő, J., Cziáky, Z., Gupcsó, K., ...&Zengin, G. (2021). Deeper insights on *Alchorneacordifolia* (Schumach. &Thonn.) Müll. Argextracts: Chemical profiles, biological abilities, network analysis and molecular docking. Biomolecules, *11*(2), 219.
16. Sunoqrot, S., Al-Shalabi, E., Al-Bakri, A. G., Zalloum, H., Abu-Irmaileh, B., Ibrahim, L. H., & Zeno, H. (2021). Coffee Bean Polyphenols Can Form Biocompatible Template-free Antioxidant Nanoparticles with Various Sizes and Distinct Colors. *ACS omega*, *6*(4), 2767-2776.

17. Sunoqrot, S., Orainee, B., Alqudah, D. A., Daoud, F., &Alshaer, W. (2021). Curcumin-Tannic Acid-PoloxamerNanoassemblies Enhance Curcumin's Uptake and Bioactivity against Cancer Cells In Vitro. *Int.J.Pharm.*, 121255.
18. Edgar, S., Hopley, B., Genovese, L., Sibilla, S., Laight, D., & Shute, J. (2018). Effects of collagen-derived bioactive peptides and natural antioxidant compounds on proliferation and matrix protein synthesis by cultured normal human dermal fibroblasts. Sci. Rep., *8*(1), 1-13.
19. Widowati, W., Janeva, W. B., Nadya, S., Amalia, A., Arumwardana, S., Kusuma, H. S. W., &Arinta, Y. (2018). Antioxidant and antiaging activities of *Jasminumsambac* extract, and its compounds. J. Rep. Pharm. Sci., *7*(3), 270-85.
20. Algiert-Zielińska, B., Mucha, P., &Rotsztejn, H. (2019). Lactic and lactobionic acids as typically moisturizing compounds. Int. J.Dermatol., *58*(3), 374-379.
21. Widowati, W., Ginting, C. N., Lister, I. N. E., Girsang, E., Amalia, A., Wibowo, S. H. B., &Kusuma, H. S. W. (2020). Anti-aging Effects of Mangosteen Peel Extract and Its Phytochemical Compounds: Antioxidant Activity, Enzyme Inhibition and Molecular Docking Simulation. Trop. Life Sci. Res., 31(3), 127.
22. Bouyahya, A., Lagrouh, F., El Omari, N., Bourais, I., El Jemli, M., Marmouzi, I., ...& Bakri, Y. (2020). Essential oils of *Menthaviridis* rich phenolic compounds show important antioxidant, antidiabetic, dermatoprotective, antidermatophyte and antibacterial properties. Biocatal. Agric. Biotechnol., *23*, 101471.
23. Ranjbarvan, P., Mahmoudifard, M., Kehtari, M., Babaie, A., Hamedi, S., Mirzaei, S., ...&Hosseinzadeh, S. (2018). Natural compounds for skin tissue engineering by electrospinning of nylon-*Beta vulgaris*. ASAIO J, *64*(2), 261-269.
24. Chaiyana, W., Anuchapreeda, S., Punyoyai, C., Neimkhum, W., Lee, K. H., Lin, W. C., ...& Mueller, M. (2019). *Ocimum sanctum* Linn. as a natural source of skin anti-ageing compounds. Ind Crops Prod, *127*, 217-224.
25. Czajka, A., Kania, E. M., Genovese, L., Corbo, A., Merone, G., Luci, C., &Sibilla, S. (2018). Daily oral supplementation with collagen peptides combined with vitamins and other bioactive compounds improves skin elasticity and has a beneficial effect on joint and general wellbeing. Nutr Res, *57*, 97-108.
26. Kim, J., Kim, M. B., Yun, J. G., & Hwang, J. K. (2017). Protective effects of standardized *Siegesbeckiaglabrescens* extract and its active compound kirenol against UVB-induced photoaging through inhibition of MAPK/NF-κB pathways. J. Microbiol. Biotechnol., *27*(2), 242-250.
27. Kim, E., Kim, D., Yoo, S., Hong, Y. H., Han, S. Y., Jeong, S., ...& Park, J. (2018). The skin protective effects of compound K, a metabolite of ginsenoside Rb1 from Panax ginseng. J Ginseng Res, *42*(2), 218-224.
28. Lee, H., Park, H. Y., &Jeong, T. S. (2021). Pheophorbide a derivatives exert antiwrinkle effects on UVB-induced skin aging in human fibroblasts. Life, 11(2), 147.
29. Gam, D. H. H., Hong, J. W. W., Kim, J. H. H., & Kim, J. W. W. (2021). Skin-Whitening and Anti-Wrinkle Effects of Bioactive Compounds Isolated from Peanut Shell Using Ultrasound-Assisted Extraction. Molecules, *26*(5), 1231.