Biomedical Research 2017; 28 (15): 6561-6566 *ISSN 0970-938X*
www.biomedres.info

Bioactive compounds from natural product extracts in Taiwan cosmeceuticals-Mini review.

Chien-Hsing Lee[1], Guan-Cheng Huang[2*], Chung-Yi Chen[3*]

[1]Department of Pharmacology, Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

[2]Department of Internal Medicine, Division of Hematology and Oncology, Yuan's General Hospital, Kaohsiung, Taiwan

[3]Department of Nutrition and Health Science, School of Medical and Health Sciences, Fooyin University, Kaohsiung, Taiwan

Abstract

Botanicals (herbal materials and extracts) are primarily added to the formulations due to different related properties such as antioxidant, anti inflammatory, antiseptic and antimicrobial effects. The bioactive compounds from natural product extracts have been successfully utilized in various applications of the skin care. The bioactive compound from natural product extracts does not possess any side effects on the human body instead of providing the body with nutrients and other useful minerals. The cosmetic industry takes the advantages of natural extracts for cosmetics products to promise a gentler, less side effects to beauty compared to synthetic cosmetics. Therefore, the market of bioactive compounds from natural product extracts is increasing rapidly in cosmeceuticals. This review attempts and emphasizes the natural product extracts in Taiwan cosmeceuticals.

Keywords: Botanicals, Cosmeceuticals, Natural product extracts.

Accepted on May, 27, 2017

Introduction

In recent years, alternative medicine and complementary have become increasingly popular and even considered a highly acclaimed practice in the world. Botanicals, which by definition are plant-derived products, play an important role in the market for natural remedies. They are extremely ancient and have been used in various cultures for centuries, representing the earliest medications used by humans. The current popularity of bioactive compound from natural product extracts has occurred for several reasons, and is based on a greater public access to health information, which has led to the formulation of wild selection and assumptions of allopathic medicine as well as concerns about the side effects of chemical drugs. In contrast, the opinion of bioactive compound from natural product extracts is introduced by patients into a ''natural'' source, which they associate with safety.

Several of the available products derived from bioactive compound from natural product extracts have been applied for their dermatologic benefits, especially in cosmetics. The natural-based cosmetics are collectively referred to as "cosmeceuticals" introduced by Albert Kligman two decades ago [1]. Cosmeceuticals are defined as intermediary substances between drugs and cosmetics. They do not require Food and Drug Administration (FDA) approval before being marketed. A discussion of all the currently available bioactive compounds from natural product extracts used in dermatology and dermatologic formulations would far exceed the scope of this article. Therefore, we focused on a select group of the most popular bioactive compounds from natural product extracts in Taiwan cosmeceuticals in the review.

Bioactive compounds from natural product extracts

The term "botanicals" subsumes numerous preparations derived from herbs, roots, stems and other materials of botanical origins. Botanicals are used for cosmetic purposes in the form of fresh plants or extracts. The use of plant extracts and herbs has feet in ancient times, with the earliest records coming from ancient China and Egypt. The cosmetic industry is taking good advantages of this trend by introducing plant extracts from seeds, herbs, flowers and fruits to their products, promising a gentler approach to beauty. The guiding principle of bioactive compounds from natural product extracts is that the naturally occurring mixture of active compounds in plants is more effective and safer than individual molecules and manufactured combinations of synthetic molecules [2]. These products with active compounds are referred to as "cosmeceuticals" [3].

Bioactive compounds from natural product extracts are focused on improving the total "body condition". Botanical sales in 2002 in the United States exceeded $4.3 billion and grew by

one-third over only 6 years. Taiwan's online cosmeceuticals market is worth around NT$36 billion (US$1.2 billion) a year, with sales showing steady year-on-year growth. Bioactive compounds from natural product extracts growth has increasing to now consume 25% of all health- and lifestyle-related dollars [2]. Now over 60 various bioactive compounds from natural product extracts are formulated into cosmeceuticals. Most bioactive compounds from natural product extracts possess several effects and often display different simultaneously, such as antioxidant, anti-inflammatory, anticarcinogenic, and pigment-lightening activity. Various herbal crude drugs with their parts used for cosmeceuticals are given below. This article mainly reviews the bioactive compounds from natural product extracts in Taiwan cosmeceuticals.

Botanical antioxidants

Soy: Soy belongs to the pea family (Leguminosae) can be obtained by eating tofu or soybeans and drinking soymilk. It has been used for food and medicinal purposes for 5000 years in East Asia. The soybean trypsin inhibitor and Bowmann-Birk inhibitor, derived from soymilk, can induce skin depigmentation by inhibiting protease-activated receptor-2 (PAR-2) activation, which is responsible for the regulation of the ingestion of melanosomes by keratinocytes [4-6]. In large randomized, double-blind, vehicle-controlled study, a novel soy moisturizer containing nondenaturated soybean trypsin inhibitor and Bowmann-Birk inhibitor, demonstrated a significant improvement in mottled pigmentation, blotchiness, dullness, fine lines, overall texture, skin tone and appearance [7-9]. Furthermore, several preliminary *in-vivo* human studies have demonstrated that the skin-lightening effect of nondenatured soy extracts [10,11].

Silibinin: Silibinin, also known as silybin or silibin in literature, is a polyphenolic flavonoid or flavonolignan compound that can be extracted from the seeds of the milk thistle plant *Silybum marianum* and also in artichoke (*Cynara scolymus*). It is used clinically as an antihepatotoxic agent and a supplement. Silibinin has antioxidant, anti-inflammatory, and anticarcinogenic properties [12-14]. Several studies have demonstrated photoprotective effects of topically applied silibinin prior to, or immediately after, ultraviolet (UV) irradiation [15-17]. They showed a reduction in thymine dimer-positive cells and an up-regulation of p53-p21/Cip1, which they believe may ultimately inhibit cell proliferation and apoptosis [18-20], suggesting that mechanisms other than sunscreen effects are integral to the efficacy of silibinin against UV-induced skin damage [21]. Silibinin is included in various antiaging and sun-protective skin care products [22]. In addition, silymarin/silibinin is found in a number of high-end moisturizers to prevent cutaneous oxidative damage and photoaging. RosaCure+, is sold as an anti-redness cream with silymarin, decreases the appearance of facial redness as in rosacea-prone skin, sooth reactive skin and even out skin tone [15].

Pycnogenol: Pycnogenol is extracted from the bark of the French maritime pine tree Pinus pinaster. The extract is rich with flavonoids and monomeric phenolic compounds, such as catechin, epicatechin, taxifolin, and procyanidins, also called proanthocyanidins. Proanthocyanidins are well-known potent free radical scavengers, and the free radical-scavenging effects of pycnogenol have been well documented [23,24]. Oral supplementation with pycnogenol has been shown that photoprotection in humans was demonstrated by a significantly increased UV radiation level needed to reach one minimal erythema dose. The mechanism is through the inhibition of nuclear factor-κB-dependent gene expression by pycnogenol has also been discussed [25]. Pycnogenol can also be used as a depigmentation agent. In clinical trial, 30 women showed a significant decrease in the average surface area of melasma with melasma supplemented with 25 mg of pycnogenol in three meals a day [26]. Pycnogenol is included in sunscreens and various other skin care products.

Curcumin: Curcumin is native to India and other Asian countries, which is the active compound in turmeric. Turmeric is widely applied in various fields such as cooking, medicine, beauty, and health products [27-33]. In South Indian, women used turmeric for skin care owing to its multibeneficial activities including in natural beauty products with yellow pigments, moisture retention, antiaging, and antioxidant activity [34-39]. In addition, turmeric has been improved to enhance the bioavailability in cosmeceutical product and increase antioxidant activity owing to nanodelivery techniques such as solid lipid nanocarriers, nanoliposomes, nanoniosomes, and nanoemulsions [40-42].

Ginseng: Ginseng is a representative medicinal herb belonging to the Araliaceae family, which is seven major species of ginseng distributed throughout East Asia, Central Asia, and North America [43]. Several reports have been shown that ginsenosides as potential cosmeceutical agents due to their beneficial effects on skin health. Ginsenosides have been used for 1000 years and are one of the safest and most potent natural antiaging agents for skin in terms of skin cosmetology. Several works of traditional literature have mentioned that ginsenosides possesses the skin protective and improving effects [44-47], antiwrinkle formation, as well as protection against excessive sun exposure using *in vitro* [44,48] and *in vivo* models [47,49,50]. Among the various ginsenosides, ginsenoside Rd and compound K, in particular, have received increased attention for their natural antiaging effects to as cosmeceutical ingredients.

Botanical anti-inflammatories

Ginkgo biloba: Ginkgo biloba is the last member of the Ginkgoaceae family, which grew on earth some 200 to 250 million years ago. The plant leaves contain unique polyphenols including in terpenoids (ginkgolides, bilobalides), flavonoids, and flavonol glycosides with anti-inflammatory effects. In experimental fibroblast models, the antiradical and antilipoperoxidant effects have been demonstrated to associate with the anti-inflammatory effects [51]. Furthermore, Ginkgo

flavonoid fractions such as quercetin, kaempferol, sciadopitysin, ginkgetin, and isoginkgetin have been shown to induce human skin fibroblast proliferation *in vitro* [52,53]. Thus, ginkgo extracts are applied to many cosmeceuticals as antioxidants and promoters of collagen synthesis after resurfacing based on nonhuman models of oxidative damage.

Green tea: Green tea originates in China and has been consumed as a popular beverage in Asia for many years. It recently has gained great popularity in the West resulted from its antioxidant and anticarcinogenic effects [54]. Green tea is derived from the Camellia sinensis plant through special preparation of the tea leaves in the short steaming and no fermentation situation which preserve the antioxidant activities of polyphenols. The active ingredients identified in the leaves are flavanols, commonly known as catechins consists of four major polyphenolic catechins [55,56]. (-)Epigallocatechin-3-O-gallate (EGCG) is the most abundant and biologically active component, and is mainly responsible for the antioxidant effects, down-regulate UV-induced expression of AP-1 and NF-kB, as well as suppress metalloproteinase [57-60].

In human skin, the photoprotective effects of polyphenols have been demonstrated to decrease in UV-induced erythema, a decline in the number of sunburn cells, protection of epidermal Langerhans cells and decrease in DNA damage [61]. The molecular mechanisms involved in Ras and activator protein-1, both of which are a part of the mitogen-activated protein kinase pathway [62]. In addition, EGCG has been shown to reduce interleukin-10 production and increase interleukin-12 production, two major cytokines mediating UV-induced immunosuppression, thus reducing UV-induced immunosuppression [63]. Meanwhile, the augmentation of interleukin-12 further leads to increase synthesis of enzymes repairing UV-induced DNA damage [64]. EGCG also seems to reduce collagen degradation, which leads to photodamage by down-regulating the UV-induced expression of activator protein-1, nuclear factor-κB and the suppression of metalloproteinases [65]. Green tea polyphenols administered orally pre-exposure were shown to inhibit UV-B-induced protein oxidation and expression of matrix-degrading matrix metalloproteinases *in vivo* [59]. These data support the role of green tea polyphenols as a potent antiphotoaging compound. Meanwhile, the over-the-counter skin care products of green tea are included in shower gels, toothpastes, depilatories, shampoos, perfumes, and popular soft drinks.

Botanical skin-soothing agents

Aloesin: Aloesin is a C-glycosylated chromone derived from Aloe vera [66]. It acts as a competitive tyrosinase inhibitor, reducing both the hydroxylation of tyrosine to dihydroxyphenylalanine and oxidation of dihydroxyphenylalanine to dopachinone [67]. Aloesin showed a dose dependent decrease in tyrosinase activity in cultured normal melanocytes [68]. When administered four times a day for 15 days for hyperpigmentation in human skin after UV radiation, aloesin suppressed pigmentation by 34% compared with the control [69].

Allantoin: Allantoin is approved by the German Commission E to treat blunt injuries owing to the activity of triterpene saponins, tannins, and silicic acid, as well as allantoin [2]. Allantoin has been extracted from the comfrey root and leaves but is now commercially manufactured. Allantoin is an antiphlogistic, antioxidant, and soothing keratolytic that has an antitrichomonal effect and induces cell proliferation. It is listed in the FDA over-the-counter monograph as a safe and effective skin protectant at 0.1 to 2.0% [2]. Allantoin and/or comfrey-based products are used to treat wounds, ulcers, burns, dermatitis, psoriasis, impetigo, and acne. When formulated with surfactant and benzalkonium chloride, allantoin is an effective hand sanitizer and onychomycosis therapy [70]. Allantoin formulated with onion (*Allium cepa*) extract in a proprietary topical formulation improved the signs and symptoms of scars and keloids [71]. No photoaging clinical trials using topical allantoin have been published.

Camphor: Camphor ((1R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one) is obtained from turpentine oil or extracted naturally from the oil distillated flower and leaves of Camphor tree belong to Cinnamomum camphora family Lauracae [72,73]. It has a long-valued history for a traditional medicine in treatment of sprains, swelling, and inflammation [74]. In addition, camphor is used commercially as a moth repellent and as a preservative in pharmaceuticals and cosmetics [75]. A recent study has shown that the benefit of camphor in skin health through inducing fibroblast proliferation, maintaining or recovering collagen and elastin production in UV exposed skin, and preventing thickening of the epidermis and subcutaneous fat layer [74]. Therefore, camphor is a potent antiwrinkle agent with considerable potential for use in cosmeceuticals.

Discussions

Synthetic ingredients in cosmetics effected skin even faster than bioactive compounds from natural product extracts. Therefore, manufacturers are striving to develop natural products containing all natural ingredients. Plant materials may be a viable alternative owing to a significant source of active constituents with a high level of antimicrobial activity compared to synthetic ingredients. Consumers consider these materials more beneficial to the body and less toxic than synthetics. Meanwhile, this use is concordant with the all-natural concept ingredients the personal care and cosmeceutical industries. However, plant derived ingredients are limited. The plants produced toxic metabolites, the plants grow too slow as a result of a seasonal harvesting and the concentration of plant constituents is instable due to the different harvest or the unpredictable factor such as climate and pests.

Conclusion

This discussion of bioactive compounds from natural product extracts has reviewed some of the currently popular botanicals in Taiwan cosmeceuticals, their biologic effects, and currently available scientific data. What all discussed bioactive

compounds from natural product extracts have in common is a need for controlled clinical trials in humans to prove what has been shown so far *in vitro* or in animal models. Furthermore, scientific data obtained on the respective bioactive compounds from natural product extracts *in vitro* and/or *in vivo* should also be estimated in the final cosmetic formulation.

References

1. Kligman A. The future of cosmeceuticals: an interview with Albert Kligman, MD, PhD. Interview by Zoe Diana Draelos. Dermatol Surg 2005; 31: 890-891.
2. Thornfeldt C. Cosmeceuticals containing herbs: fact, fiction, and future. Dermatol Surg 2005; 31: 873-880.
3. Choi CM, Berson DS. Cosmeceuticals. Semin Cutan Med Surg 2006; 25: 163-168.
4. Paine C, Sharlow E, Liebel F, Eisinger M, Shapiro S, Seiberg M. An alternative approach to depigmentation by soybean extracts via inhibition of the PAR-2 pathway. J Invest Dermatol 2001; 116: 587-595.
5. Babiarz-Magee L, Chen N, Seiberg M, Lin CB. The expression and activation of protease-activated receptor-2 correlate with skin color. Pigment Cell Res 2004; 17: 241-251.
6. Scott G, Deng A, Rodriguez-Burford C, Seiberg M, Han R, Babiarz L, Grizzle W, Bell W, Pentland A. Protease-activated receptor 2, a receptor involved in melanosome transfer, is upregulated in human skin by ultraviolet irradiation. J Invest Dermatol 2001; 117: 1412-1420.
7. Wallo W, Nebus J, Leyden JJ. Efficacy of a soy moisturizer in photoaging: a double-blind, vehicle-controlled, 12-week study. J Drugs Dermatol 2007; 6: 917-922.
8. Gao XH, Zhang L, Wei H, Chen HD. Efficacy and safety of innovative cosmeceuticals. Clin Dermatol 2008; 26: 367-374.
9. Huang MT, Xie JG, Lin CB, Kizoulis M, Seiberg M, Shapiro S, Conney AH. Inhibitory effect of topical applications of nondenatured soymilk on the formation and growth of UVB-induced skin tumors. Oncol Res 2004; 14: 387-397.
10. Hermanns JF, Petit L, Martalo O, Piérard-Franchimont C, Cauwenbergh G, Piérard GE. Unraveling the patterns of subclinical pheomelanin-enriched facial hyperpigmentation: effect of depigmenting agents. Dermatology 2000; 201: 118-122.
11. Levin J, Momin SB. How much do we really know about our favorite cosmeceutical ingredients? J Clin Aesthet Dermatol 2010; 3: 22-41.
12. Svobodova A, Psotova J, Walterova D. Natural phenolics in the prevention of UV-induced skin damage. A review. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2003; 147: 137-45.
13. Zhao J, Sharma Y, Agarwal R. Significant inhibition by the flavonoid antioxidant silymarin against 12-O-tetradecanoylphorbol 13-acetate-caused modulation of antioxidant and inflammatory enzymes, and cyclooxygenase 2 and interleukin-1alpha expression in SENCAR mouse epidermis: implications in the prevention of stage I tumor promotion. Mol Carcinog 1999; 26: 321-33.
14. Zi X, Mukhtar H, Agarwal R. Novel cancer chemopreventive effects of a flavonoid antioxidant silymarin: inhibition of mRNA expression of an endogenous tumor promoter TNF alpha. Biochem Biophys Res Commun 1997; 239: 334-339.
15. Singh RP, Agarwal R. Cosmeceuticals and silibinin. Clin Dermatol 2009; 27: 479-484.
16. Singh RP, Agarwal R. Flavonoid antioxidant silymarin and skin cancer. Antioxid Redox Signal 2002; 4: 655-663.
17. Singh RP, Agarwal R. Mechanisms and preclinical efficacy of silibinin in preventing skin cancer. Eur J Cancer 2005; 41: 1969-1979.
18. Fotedar R, Bendjennat M, Fotedar A. Role of p21WAF1 in the cellular response to UV. Cell Cycle 2004; 3: 134-137.
19. Huang LC, Clarkin KC, Wahl GM. Sensitivity and selectivity of the DNA damage sensor responsible for activating p53-dependent G1 arrest. Proc Natl Acad Sci U S A 1996; 93: 4827-4832.
20. Pontén F, Berne B, Ren ZP, Nistér M, Pontén J. Ultraviolet light induces expression of p53 and p21 in human skin: effect of sunscreen and constitutive p21 expression in skin appendages. J Invest Dermatol 1995; 105: 402-406.
21. Dhanalakshmi S, Mallikarjuna GU, Singh RP, Agarwal R. Silibinin prevents ultraviolet radiation-caused skin damages in SKH-1 hairless mice via a decrease in thymine dimer positive cells and an up-regulation of p53-p21/Cip1 in epidermis. Carcinogenesis 2004; 25: 1459-1465.
22. Allemann IB, Baumann L. Botanicals in skin care products. Int J Dermatol 2009; 48: 923-934.
23. Packer L, Rimbach G, Virgili F. Antioxidant activity and biologic properties of a procyanidin-rich extract from pine (Pinus maritima) bark, pycnogenol. Free Radic Biol Med 1999; 27: 704-724.
24. Rohdewald P. A review of the French maritime pine bark extract (Pycnogenol), a herbal medication with a diverse clinical pharmacology. Int J Clin Pharmacol Ther 2002; 40: 158-168.
25. Saliou C, Rimbach G, Moini H, McLaughlin L, Hosseini S, Lee J, Watson RR, Packer L. Solar ultraviolet-induced erythema in human skin and nuclear factor-kappa-B-dependent gene expression in keratinocytes are modulated by a French maritime pine bark extract. Free Radic Biol Med 2001; 30: 154-160.
26. Ni Z, Mu Y, Gulati O. Treatment of melasma with Pycnogenol. Phytother Res 2002; 16: 567-571.
27. Agrawal R, Sandhu SK, Sharma I, Kaur IP. Development and evaluation of curcumin-loaded elastic vesicles as an effective topical anti-inflammatory formulation. AAPS PharmSciTech 2015; 16: 364-374.
28. Balasubramanian S, Roselin P2, Singh KK3, Zachariah J4, Saxena SN5. Postharvest Processing and Benefits of Black

Pepper, Coriander, Cinnamon, Fenugreek, and Turmeric Spices. Crit Rev Food Sci Nutr 2016; 56: 1585-1607.

29. Deb L, Laishram S, Khumukcham N, Ningthoukhongjam D, Nameirakpam SS, Dey A, Moirangthem DS, Talukdar NC, Ningthoukhongjam TR. Past, present and perspectives of Manipur traditional medicine: A major health care system available for rural population in the North-East India. J Ethnopharmacol 2015; 169: 387-400.
30. Kocaadam B, Åžanlier N. Curcumin, an active component of turmeric (Curcuma longa), and its effects on health. Crit Rev Food Sci Nutr 2017; 57: 2889-2895.
31. Kumar A, Chetia H, Sharma S, Kabiraj D, Talukdar NC, Bora U. Curcumin Resource Database. Database (Oxford) 2015; 2015: bav070.
32. Nimgulkar C, Ghosh S, Sankar AB, Uday KP, Surekha MV, Madhusudhanachary P, Annapurna BR, Raghu P, Bharatraj DK. Combination of spices and herbal extract restores macrophage foam cell migration and abrogates the athero-inflammatory signalling cascade of atherogenesis. Vascul Pharmacol 2015; 72: 53-63.
33. Yun T, Liu Y, Gao D, Linghu E, Brock MV, Yin D, Zhan Q, Herman JG, Guo M. Methylation of CHFR sensitizes esophageal squamous cell cancer to docetaxel and paclitaxel. Genes Cancer 2015; 6: 38-48.
34. Agarwal R, Gupta SK, Srivastava S, Agarwal P, Agrawal SS. Therapeutic potential of Curcuma longa, the golden spice of India, in drug discovery for ophthalmic diseases. Expert Op Drug Disc 2009; 4: 147-158.
35. Goel A, Aggarwal BB. Curcumin, the golden spice from Indian saffron, is a chemosensitizer and radiosensitizer for tumors and chemoprotector and radioprotector for normal organs. Nutr Cancer 2010; 62: 919-930.
36. Gupta SC, Kismali G, Aggarwal BB. Curcumin, a component of turmeric: from farm to pharmacy. Biofactors 2013; 39: 2-13.
37. Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin: lessons learned from clinical trials. AAPS J 2013; 15: 195-218.
38. Prasad S, Gupta SC, Tyagi AK, Aggarwal BB. Curcumin, a component of golden spice: from bedside to bench and back. Biotechnol Adv 2014; 32: 1053-1064.
39. Prasad S, Tyagi AK, Aggarwal BB. Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: the golden pigment from golden spice. Cancer Res Treat 2014; 46: 2-18.
40. Golubovic-Liakopoulos N, Simon SR, Shah B. Nanotechnology use with cosmeceuticals. Semin Cutan Med Surg 2011; 30: 176-180.
41. Meghea A. Pharmaceuticals and cosmeceuticals based on soft nanotechnology techniques with antioxidative, immunostimulative and other therapeutic activities. Recent Pat Nanotechnol 2008; 2: 137-145.
42. Tavano L, Muzzalupo R2, Picci N3, de Cindio B4. Co-encapsulation of lipophilic antioxidants into niosomal carriers: percutaneous permeation studies for cosmeceutical applications. Colloids Surf B Biointerfaces 2014; 114: 144-149.
43. Attele AS, Wu JA, Yuan CS. Ginseng pharmacology: multiple constituents and multiple actions. Biochem Pharmacol 1999; 58: 1685-1693.
44. Fisher GJ, Quan T, Purohit T, Shao Y, Cho MK, He T, Varani J, Kang S, Voorhees JJ. Collagen fragmentation promotes oxidative stress and elevates matrix metalloproteinase-1 in fibroblasts in aged human skin. Am J Pathol 2009; 174: 101-114.
45. He D, Sun J, Zhu X, Nian S, Liu J. Compound K increases type I procollagen level and decreases matrix metalloproteinase-1 activity and level in ultraviolet-A-irradiated fibroblasts. J Formos Med Assoc 2011; 110: 153-160.
46. Kim S, Kang BY, Cho SY, Sung DS, Chang HK, Yeom MH, Kim DH, Sim YC, Lee YS. Compound K induces expression of hyaluronan synthase 2 gene in transformed human keratinocytes and increases hyaluronan in hairless mouse skin. Biochem Biophys Res Commun 2004; 316: 348-355.
47. Kimura Y, Sumiyoshi M, Kawahira K, Sakanaka M. Effects of ginseng saponins isolated from Red Ginseng roots on burn wound healing in mice. Br J Pharmacol 2006; 148: 860-870.
48. Cai BX, Luo D, Lin XF, Gao J. Compound K suppresses ultraviolet radiation-induced apoptosis by inducing DNA repair in human keratinocytes. Arch Pharm Res 2008; 31: 1483-1488.
49. Shin YW, Kim DH. Antipruritic effect of ginsenoside rb1 and compound k in scratching behavior mouse models. J Pharmacol Sci 2005; 99: 83-88.
50. Wang L, Zhang Y, Chen J, Li S, Wang Y, Hu L, Wang L, Wu Y. Immunosuppressive effects of ginsenoside-Rd on skin allograft rejection in rats. J Surg Res 2012; 176: 267-274.
51. Joyeux M, Lobstein A, Anton R, Mortier F. Comparative antilipoperoxidant, antinecrotic and scavenging properties of terpenes and biflavones from Ginkgo and some flavonoids. Planta Med 1995; 61: 126-129.
52. Chan PC, Xia Q, Fu PP. Ginkgo biloba leave extract: biological, medicinal, and toxicological effects. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev 2007; 25: 211-244.
53. Draelos ZD. The art and science of new advances in cosmeceuticals. Clin Plast Surg 2011; 38: 397-407.
54. Hsu S. Green tea and the skin. J Am Acad Dermatol 2005; 52: 1049-1059.
55. Camouse MM, Hanneman KK, Conrad EP, Baron ED. Protective effects of tea polyphenols and caffeine. Expert Rev Anticancer Ther 2005; 5: 1061-1068.
56. Katiyar S, Elmets CA, Katiyar SK. Green tea and skin cancer: photoimmunology, angiogenesis and DNA repair. J Nutr Biochem 2007; 18: 287-296.
57. Wei H, Zhang X, Zhao JF, Wang ZY, Bickers D, Lebwohl M. Scavenging of hydrogen peroxide and inhibition of

ultraviolet light-induced oxidative DNA damage by aqueous extracts from green and black teas. Free Radic Biol Med 1999; 26: 1427-1435.

58. Kim J, Hwang JS, Cho YK, Han Y, Jeon YJ, Yang KH. Protective effects of (-)-epigallocatechin-3-gallate on UVA- and UVB-induced skin damage. Skin Pharmacol Appl Skin Physiol 2001; 14: 11-19.
59. Vayalil PK, Mittal A, Hara Y, Elmets CA, Katiyar SK. Green tea polyphenols prevent ultraviolet light-induced oxidative damage and matrix metalloproteinases expression in mouse skin. J Invest Dermatol 2004; 122: 1480-1487.
60. Katiyar SK, Afaq F, Perez A, Mukhtar H. Green tea polyphenol (-)-epigallocatechin-3-gallate treatment of human skin inhibits ultraviolet radiation-induced oxidative stress. Carcinogenesis 2001; 22: 287-294.
61. Elmets CA, Singh D, Tubesing K, Matsui M, Katiyar S, Mukhtar H. Cutaneous photoprotection from ultraviolet injury by green tea polyphenols. J Am Acad Dermatol 2001; 44: 425-432.
62. Stratton SP, Dorr RT, Alberts DS. The state-of-the-art in chemoprevention of skin cancer. Eur J Cancer 2000; 36: 1292-1297.
63. Katiyar SK, Challa A, McCormick TS, Cooper KD, Mukhtar H. Prevention of UVB-induced immunosuppression in mice by the green tea polyphenol (-)-epigallocatechin-3-gallate may be associated with alterations in IL-10 and IL-12 production. Carcinogenesis 1999; 20: 2117-2124.
64. Meeran SM, Mantena SK, Elmets CA, Katiyar SK. (-)-Epigallocatechin-3-gallate prevents photocarcinogenesis in mice through interleukin-12-dependent DNA repair. Cancer Res 2006; 66: 5512-5520.
65. Yoon JY, Kwon HH, Min SU, Thiboutot DM, Suh DH. Epigallocatechin-3-gallate improves acne in humans by modulating intracellular molecular targets and inhibiting P. acnes. J Invest Dermatol 2013; 133: 429-440.
66. Draelos ZD. Skin lightening preparations and the hydroquinone controversy. Dermatol Ther 2007; 20: 308-313.
67. Picardo M, Carrera M. New and experimental treatments of cloasma and other hypermelanoses. Dermatol Clin 2007; 25: 353-362.
68. Jones K, Hughes J, Hong M, Jia Q, Orndorff S. Modulation of melanogenesis by aloesin: a competitive inhibitor of tyrosinase. Pigment Cell Res 2002; 15: 335-340.
69. Choi S, Lee SK, Kim JE, Chung MH, Park YI. Aloesin inhibits hyperpigmentation induced by UV radiation. Clin Exp Dermatol 2002; 27: 513-515.
70. Wadhams PS, Griffith J, Nikravesh P, Chodosh D. Efficacy of a surfactant, allantoin, and benzalkonium chloride solution for onychomycosis. Preliminary results of treatment with periodic debridement. J Am Podiatr Med Assoc 1999; 89: 124-130.
71. Campanati A, Savelli A, Sandroni L, Marconi B, Giuliano A, Giuliodori K, Ganzetti G, Offidani A. Effect of allium cepa-allantoin-pentaglycan gel on skin hypertrophic scars: clinical and video-capillaroscopic results of an open-label, controlled, nonrandomized clinical trial. Dermatol Surg 2010; 36: 1439-1444.
72. Ashby J, Tinwell H, Odum J, Lefevre P. Natural variability and the influence of concurrent control values on the detection and interpretation of low-dose or weak endocrine toxicities. Environ Health Perspect 2004; 112: 847-853.
73. Chen W, Vermaak I, Viljoen A. Camphor-a fumigant during the Black Death and a coveted fragrant wood in ancient Egypt and Babylon--a review. Molecules 2013; 18: 5434-5454.
74. Tran TA, Ho MT, Song YW, Cho M, Cho SK. Camphor Induces Proliferative and Anti-senescence Activities in Human Primary Dermal Fibroblasts and Inhibits UV-Induced Wrinkle Formation in Mouse Skin. Phytother Res 2015; 29: 1917-1925.
75. Schlumpf M, Jarry H, Wuttke W, Ma R, Lichtensteiger W. Estrogenic activity and estrogen receptor beta binding of the UV filter 3-benzylidene camphor. Comparison with 4-methylbenzylidene camphor. Toxicology 2004; 199: 109-120.

***Correspondence to**

Chung-Yi Chen

Department of Nutrition and Health Science

School of Medical and Health Sciences

Fooyin University

Taiwan

Guan-Cheng Huang

Department of Internal Medicine

Division of Hematology and Oncology

Yuan's General Hospital

Taiwan