Plant polyphenols in cosmetics – a review

European Journal of Medical Technologies
2019; 3(24): 1-10

www. medical-technologies.eu
Published online 29.09.2019

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Abstract

Polyphenolic compounds constitute a diverse group of natural components commonly occurring in various plant species. These include phenolic acids, tannins, flavonoids, anthocyanins, lignans and neolignans. Due to the chemical structure of the molecules (e.g. the presence of ortho-diphenol groups in aromatic rings), these compounds have antioxidant properties, which may delay the aging process. The mechanism of their antioxidant activity is mainly related to the scavenging of free radicals. Additionally, polyphenols possess antimicrobial and antiallergic, as well as vasoactive (sealing capillary walls) properties, which allows them to be used as ingredients of dermocosmetics for acne, sensitive and capillary skin. The use of creams containing natural antioxidants can effectively improve skin condition and prevent its aging. This paper reviews substances from the group of polyphenols utilized or potentially useful in the production of dermocosmetics as well as current scientific reports on their biological activity.

Key words:

polyphenols, antioxidants, phenolic acids, flavonoids, silymarin, resveratrol, lignans

Polyphenols are one of the most interesting groups of bioactive compounds found in plants due to various aspects of their practical use in food, parapharmaceuticals and cosmetics of natural origin. The latter direction is gaining more and more popularity and intensifies phytochemical research, including searching for new plant sources of these compounds, developing methods for their effective isolation from plant material and qualitative analysis, including spectroscopic evaluation of chemical structures of new little-known compounds. There is also a steady increase in the number of published papers on biological research (*in vitro*, *in vivo* and clinical) on this group of phytochemicals.

Polyphenols are organic compounds that occur commonly in numerous plant species (in their vegetative and generative organs), where they play the role of chemical defense against attack of various parasitic

herbivores. The chemical structure of polyphenolic compounds always contains one or more rings of aromatic hydrocarbons with least two hydroxyl (-OH) groups attached [1,2]. The name "polyphenols" refers to the chemical affiliation of these components to the group of phenols with the simplest molecular structure like hydroxybenzene or phenol. The polyphenols group includes, among others, phenolic acids, tannins, flavonoids, anthocyanins, mono- and oligomeric catechins, lignans and neolignans [3-5]. They show different types of biological effects, including antimicrobial [6], anti-inflammatory, anti-oxidative or photoprotective (anti-UV), that determine corrective or therapeutic activity for the leading brands of dermocosmetics [7,8].

Phenolic acids and their biological properties

Phenolic acids (PhAs) include derivatives of benzoic (gallic, *p*-hydroxybenzoic, protocatechuic, vanillic or syringic) and cinnamic (e.g. caffeic, ferulic, *p*-cumaric, synapic) acids. Herbal substances also contain glycosidic and ester forms of PhAs [9-11].

Caffeic acid (CA) is a representative of this group that shows strong antioxidant properties. It commonly occurs in berries, apples, cereals and coffee seeds [12,13]. This compound reveals anti-inflammatory, antiviral [14] and antibacterial [15] activities and is known as an inhibitor of carcinogenesis and a stimulator of collagen production [16,17]. Therefore, it is used as a component of various skincare cosmetics (peels, butters, tonics). The similar or even stronger dermoprotective properties reveal some CA derivatives, namely chlorogenic, rosmarinic and caffeoyltartaric acids, that are CA esters with quinic, 3,4-dihydroxyphenyl lactic, and tartaric acid, respectively. A very promising skincare and anti-inflammatory agent is also caffeic acid phenylethyl ester (CAPE), that is known as a specific inhibitor of the nuclear transcription factor (NF-κB) and the lipoxygenase via suppressing arachidonic acid metabolism during inflammation [18-23].

Ferulic acid (FA) occurs in rice seeds, cereals, nuts [24], leaves and willow bark (*Salix* sp.) [25]. It has antioxidant and anti-inflammatory [26], as well as radio- [27], neuro- [28], hepatoprotective activities [29]. FA, added as a recipe ingredient of dermocosmetics, determines their anti-aging properties, and affects skin protection against discoloration [30].

Both CA and FA may alleviate skin photosensitization, protect against sunburn caused by UV-B (290-320 nm) or reduce the negative UV-A (320-400 nm) radiation effects (skin photoaging, sun allergies, pigmentation disorders, carcinogenesis risk). These specific abilities of CA and FA have been utilized in sunscreens used in dermocosmetics [27,31].

Protocatechuic acid (PA), also deserves special attention due to its biological effects. Plant sources of PA include vegetables [32], fruits [33,34] and herbal substances with medicinal properties, including rosemary, lemon balm [35], hibiscus flower (Sudan mallow) [36] or St. John's wort [37]. PA shows antiproliferative activity in the process of skin carcinogenesis. It is also known as antioxidant (*in vitro* tests, carried out in rat liver cell cultures treated with *tert*-butyl hydroperoxide, revealed cytoprotective effects of PA in oxidative stress), anti-microbial and anti-inflammatory (being a lipid peroxidation inhibitor) agent [38].

In addition to the antioxidant activity, some PhAs have strong antibacterial properties. This group includes rosmarinic acid (RA), which is commonly occurring in some herbal substances from the family Lamiaceae, including the leaves of lemon balm, sage, various mint species or rosemary [39,40]. In addition, RA has antiviral (against herpes or herpes zoster virus), anti-inflammatory, anti-proliferative, immunotropic and weakly antiallergic activities [41,42]. In the *in vivo* studies performed on Swiss Albino mice, the activity of a niosomal gel containing RA was compared to a dermatological preparation with benzoyl peroxide. The product with RA was more effective in reducing the growth of some bacterial strains (*Staphyloccocus aureus* and *Propionibacterium acne*) within the epidermal cells [43].

Oxidative stress and molecular aspects of the antioxidant activity of PhAs

In normal cellular metabolism, endogenous free oxygen radicals or reactive oxygen species (ROS) are produced in the animal body. Exogenous ROS

usually originate from the environment (pollution, pesticides, UV-A radiation). The ROS group is distinguished by anionic superoxide radicals ($O_2^{\bullet -}$), hydroxyl radicals ($OH^{\bullet}$), hydrogen peroxide (H_2O_2), and singlet oxygen. Excess ROS causes increased lipid peroxidation of cell membranes resulting in their damage and accumulation of peroxides. The imbalance between the pro- and antioxidant systems induces oxidative stress, and subsequently the damage of structural and enzymatic proteins and genetic matrix, resulting in the development of various pathomechanisms and diseases [44]. The ROS influence on the skin can cause burns, collagen fiber damage, increased pigmentation and the risk of carcinogenesis. ROS also contributes to the development of inflammatory processes in the skin by activating the synthesis of specific proteolytic enzymes (collagenases), e.g. MMP-1 (metalloproteinase-1) [45].

The antioxidant activity of PhAs is determined by the presence of one or more hydroxyl and /or methoxy groups in their molecules. The presence of a second hydroxyl group in the *ortho*- position relative to the already existing -OH group in the *para*- position (e.g., in CA) increases the antioxidant activity due to additional resonance stabilization and the formation of *o*-quinone) Antioxidant efficiency of *para*-hydroxycinnamic acid (*p*-coumaric acid - PCA) is significantly increased by the presence of one or two methoxy groups substituted at the *ortho* positions relative to the -OH group. Therefore, FA is a stronger antioxidant than PCA, while synapic acid (SA), found in large amounts in the Brassicaceae plants, reveals stronger antioxidant effects than FA [46,47]. The chemical structure of the aforementioned PhAs have been shown in Figure 1.

Tannins and their derivatives - skin effects

Tannins (TNs) are the second group of polyphenols that are important in the production of dermocosmetics. These are high molecular weight compounds (500-3000 daltons), which have the ability to tan the skin, i.e. to create permanent bonds with skin coat proteins. These compounds can be divided into hydrolysing (gallo- and ellagotannins), non-hydrolysing (catechin = condensed TNs) and mixed tannin compounds [11,48]. The plant sources of TNs currently used in cosmetics and medicinal preparations include: oak bark (*Quercus robur* L.), cinquefoil rhizome (*Potentilla tormentilla* Necker), blueberry (*Vaccinium myrtillus* L.), walnut leaf (*Juglans regia* L.), Hamamelis bark and leaf (*Hamamelis virginiana* L.) [49,50]. Cosmetics containing TNs have astringent, disinfecting, anti-inflammatory, anti-haemorrhagic and analgesic properties. Tannin-rich extracts are often the components of intimate hygiene products. Procyanidins and naturally condensed TNs occur in cranberry and hawthorn fruit, whereas florotanins can be found in brown algae [11]. Mixed TNs comprise (-) - epicatechin gallate (ECG) and (-) epigallocatechin gallate (EGCG), which are mainly found in green tea leaves (*Camellia sinensis* L.) [51]. EGCG has anti-inflammatory, antioxidant and photoprotecting properties. It facilitates wound healing and shows bacteriostatic activity on strains of *Streptococcus* sp. and *Escherichia coli* [52-54]. In preclinical studies, EGCG was characterized by anti-wrinkle effects, stimulated hair growth and protected the skin against damage caused by UV-A and UV-B radiation. In *in vitro* studies on human fibroblasts,

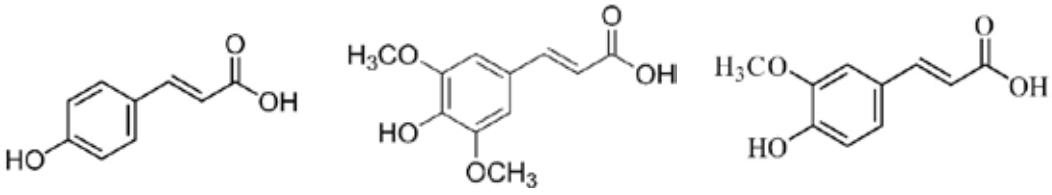

Fig. 1.
Chemical structures of PCA, FA and SA.

EGCG significantly limited cell aging [55]. *In vitro* and *in vivo* assays on human dermal papilla cells (tissue cultures and scalp in the occipital part) showed an increase in dose-dependent dermal cell proliferation, a three-fold increase in the expression of proteins involved in the proliferation of human epidermal keratinocytes and a 180% increase in hair follicle length after 10 days of EGCG administration [56]. In *in vivo* studies, using guinea pigs and hairless mice, the protective effect of EGCG (1%) and vitamin E (1%) has been demonstrated on the skin of animals under the conditions of UV-A and UV-B exposure. At the same time, a 2.9-fold decrease in lipid peroxidation in the guinea pig skin under the influence of this compound was documented, as well as reduction of erythema and inhibition of collagenase activity. The structure of the guinea pig skin, protected with EGCG containing formulation, turned out to be less flaccid and its surface less rough compared to the control group [57,58].

Flavonoids and flavonolignans

Flavonoids are a group of polyphenolic compounds that are benzo-4-pyrone derivatives – Figure 2 [59].

Due to the antioxidant and anti-inflammatory effects, they constitute a valuable component of skincare products used in a broad spectrum of dermatological diseases [60]. Antioxidative activity is determined by the presence of hydroxyl and carbonyl groups as well as the double bonds in a flavone molecule. The hydroxyl groups in both benzene rings are hydrogen and electron donors for hydroxyl, peroxyl and peroxynitrite free radicals. They cause their stabilization and the formation of a fairly stable flavonoid radical. Increasing the number of substituents in benzene rings, e.g. hydroxyl groups and placing the substituents in the *ortho-* and *para-* position causes an increase in the antioxidative activity of flavonoids, while the addition of a sugar moiety reduces free radical scavenging properties of these compounds [61-64]. Table 1. presents selected flavonoid compounds and their use in cosmetics.

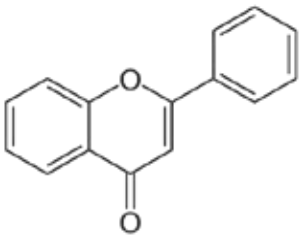

Fig. 2.
Molecular structure of benzo-4-pyrone (flavone)

Flavonolignans, represented by silymarin (SLM), constitute a set of ingredients (silibinin, silychristin, silidianin and others) found in the fruit of milk thistle (*Sylibum marianum* L. Gaertn.), It is known for hepatoprotective [65], antioxidant [66], anti-inflammatory and antiviral activities [67]. In *in vivo* studies, SLM showed a protective effect on the skin in SKH-1 mice with a skin cancer induced by UV-B radiation. While administered topically or *per os*, before or after exposure to UV-B, SLM significantly inhibited the development of sunburn, tissue edema and the process of skin cell apoptosis. It also reduced the activity of proinflammatory enzymes, namely catalase, cyclooxygenase and ornithine decarboxylase [68]. In cosmetology, SLM is used as a component of anti-UV filters, a brightening agent for skin tone and as a curative agent for rosacea (Pharmaceris brand).

Anthocyanins

Anthocyanins (ACs), like flavonoids, are natural dyes, that are stable in plant cells in the glycosidic form. They exhibit anti-inflammatory and sealing effects on capillaries [69]. ACs improve blood circulation within the eyeball [70] and have antioxidant properties [71,72]. The main herbal sources, rich in ACs and used in medicine and cosmetics, are blueberry (*Vaccinium myrtillus* L.), elderberry (*Sambucus nigra* L.) and black currant (*Ribes nigrum* L.) fruits and the flowers of cornflower (*Centaurea cyanus* L.), hibiscus (*Hibiscus sabdariffa* L.) and hollyhock (*Althaea rosea* var. *nigra* L.). ACs, as vasoactive components, are used in gel and creams applied to the skin under the eyes to limit exudative processes and tissue swelling.

Table 1.
Flavonoids – their occurrence, biological activity and application in cosmetic products

Flavonoids	Plant source	Biological activity	Cosmetic products and their brands
Rutoside	*Sophora japonica* L.	capillary wall sealant, antioxidant	creams for vascular skin (Bielenda, Norel, Farmona)
Quercetin	*Crataegus monogyna* L.	anti-inflammatory, antioxidant	Sesderma C-Vit
Diosmin, hesperidin or hesperidin methyl chalcone	citrus fruits	sealing capillary walls, antio-edematous	creams and concentrates for capillary skin, gels for heavy legs (Iwostin, Lirene, RedBlocker)
Baicalin	plant species of the genus *Scutellaria* L.	antioxidant, antiviral, antibacterial, anti-inflammatory	Vichy cream, Baikadent – a series of medicinal products used in dental diseases
Apigenin	*Chamomilla recutita* L., *Helichrysum arenarium* L., *Thymus vulgaris* L.	antiallergic, anti-inflammatory	Bioderma and Ecolab dermocosmetics
Kaempferol	*Camellia sinensis* L.	anti-inflammatory, antiallergic and antifungal	Apis – a series of bee products
Naringenin	*Prunus* sp., *Citrus* sp.	antiallergic, UV-protecting, sealing capillaries	haircare dermocosmetics (Pharmaceris H)
Genistein	*Glycine soja* Sieb.&Zuch.	estrogenic	anti-aging cosmetics (Auriga, Fitcomfort)

Resveratrol

Resveratrol (*trans*-3,5,4'-trihydroxystilbene – RSV) is a polyphenolic compound, found mainly in red grapes and the root of the knotweed (*Polygonum cuspidatum* Sieb. et Zucc.) but also in mulberry or peanuts. The active form of RSV (*trans*-) is transformed into the inactive (*cis*-) under the influence of UV radiation. RSV has antioxidant, anti-proliferative, anti-inflammatory and estrogenic activity [73-75] It was shown that this compound activates the SIRT1 gene coding for sirtuin-1 protein, which is involved in cell proliferation, apoptosis and aging processes. RSV is also responsible for normal growth and metabolism, the repair of damaged DNA, chromosomal stability and response to stress factor in skin cells [76]. It is often utilized as a component of anti-wrinkle creams (Sesderma, Caudalie, Dermomedica).

Lignans and neolignans

Lignans (LGs) belong to phenylpropane derivatives with a dimeric molecular structure (Figure 3). They contain two C6-C3 units and a β'-β 'linkage in position 8-8' [77]. Naturally, they occur in free form, rarely as glycosides. Neolignans are formed by the biosynthesis of two Ar-C3 units with the loss of one or two carbon atoms as a result of decarboxylation [78,79].

LGs occur in oilseeds, cereals, plant resins and herbal medicinal substances deriving from some botanical genera, including *Magnolia* L., *Eleutherococcus* L., *Schisandra* L. or *Linum* L. Significant biological activity has been documented for a few lignan compounds, e.g. secolariciresinol, lariciresinol, pinoresinol, matairesinol, magnolol, honokiol and others.

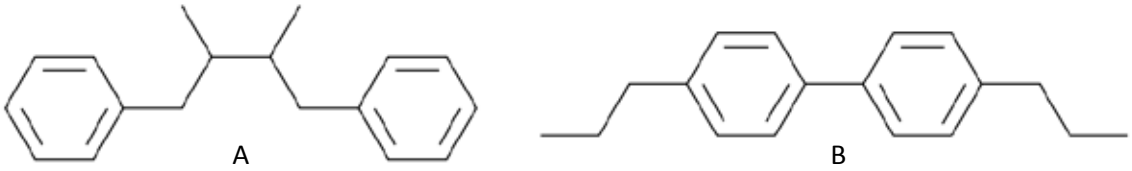

Fig. 3.
Chemical structure of lignan (A) and neolignan (B)

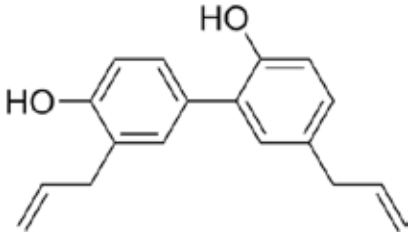

Fig. 4.
Chemical structure of honokiol

Honokiol (HKL), shown in Figure 4, is one of the best known lignan representatives found in the bark and flowers of magnolia (*Magnolia officinalis* Rehder et. Wilson) [80].

The hydrophilic cream with the addition of HKL, applied locally to the skin of SKH-1 mice exposed to UV radiation, protected skin tissues against photocarcinogenesis. In immunoenzymatic and Western blotting tests, HKL was shown to inhibit the formation of proinflammatory factors in the skin, induced by UV-B, including: COX-2, prostaglandin E2, cytokines and interleukins (IL-1β and IL-6) [81].

The extract from the bark of *Magnolia grandiflora* L. (ME), rich in LGs, was examined as an ingredient of anti-aging cosmetics. In clinical studies, women applied the cream with 0.5% addition of ME to the face skin showing extensive erythema and edema. In the group of patients, where *verum* was administered, the redness decreased by half. Additionally, the application of this cream to the skin around the eyes (over a period of 2 months), resulted in increased skin elasticity and reduced fine wrinkles (so-called "crow's feet"). The extract also increased the amount of adipocytes and stimulated the synthesis of the adiponectin, being the hormone regulating collagen metabolism in facial skin fibroblasts [82,83]. Huang et al. [84] studied the effect of ME on the process of inhibiting the skin biosynthesis of melanin and its potential in the treatment of discoloration, hyperpigmentation, age spots or freckles. ME reduced tyrosinase expression involved in the melanin production and inhibited the formation of this pigment in B16F10 mice skin cell lines as well as showed significant antioxidant activity. The results of the studies confirmed the suitability of ME in production of dermocosmetics that are developed as the skin colour brightening agents.

In other studies, LGs of Schisandra fruit (*Schisandra chinensis* L.) revealed a protective effect on the skin under urban smog conditions, and showed to be useful in creams and other dermoprotective preparations. The contaminants present in the smog penetrate the body through the hair follicles and through the skin. Therefore, they are responsible for the ROS emergence in the skin, the formation of wrinkles around the lips and nose, as well as changes in the skin pigmentation. The contact of the epidermis with air pollution causes a defensive tissue reaction, which manifests itself by the release of inflammatory cytokines and the production of metalloproteinases that accelerate skin aging. *In vitro* studies performed in tissue cultures of human epidermal keratinocytes showed that the Schisandra fruit extract activated the expression of several genes involved in the antioxidant cascade, together with the poison detoxification pathway associated with combating the harmful effects of urban dust on the skin. These activities included activation of superoxide dismutase, glutathione peroxidase and catalase and other endogenous defensive mechanisms, including a biochemical transcription factor (Nrf2) pathway playing a key role in protecting cells from the damaging effects of oxidative stress [85].

Summary

Polyphenols are effective natural antioxidants, used as ingredients in a number of creams and other dermocosmetics. In addition to antioxidant properties, they have shown activities related to the protection of physiological functions of the skin (anti-inflammatory, anti-microbial, antiallergic, diminishing the influence of harmful UV radiation and air pollution, as well as strengthening capillary walls). For the above mentioned properties, these compounds are desirable components in the production of skincare cosmetics, enriching them with additional healing properties. In the last decade, lignans and neolignans emerged as a promising group of polyphenolic antioxidants. Beside strong anti-inflammatory, they also display a broad range of cytoprotective properties, therefore their potential use as inhibitors of aging or even skin carcinogenesis, in novel dermocosmetic formulas, may be considered.

References

1. Ferrazzano GF, Amato I, Ingenito A, et al. Plant Polyphenols and Their Anti-Cariogenic Properties: A Review. Molecules 2011; 16: 1486–1507.
2. Quideau S, Deffieux D, Douat-Casassus C, et al. Plant Polyphenols: Chemical Properties, Biological Activities and Synthesis. Angew Chem Int Ed 2011; 50: 586–621.
3. Zhang H, Tsao R. Dietary polyphenols, oxidative stress and antioxidant and anti-inflammatory effects. Curr Opin Food Sci 2016; 8: 33–42.
4. Abbas M, Saeed F, Anjum FM, et al. Natural polyphenols: An overview. Int J Food Prop 2017; Aug; 20 (8): 1689–1699.
5. Fernandez de Simon B, Perez-Ilzarbe J, Hernandez T, et al.. Importance of phenolic compounds for the characterization of fruit juices. J Agric Food Chem 1992; 40 (9): 1531–1535.
6. Daglia M. Polyphenols as antimicrobial agents. Curr Opin Biotechn 2012, 23:174–181.
7. Nichols JA, Katiyar SK. Skin photoprotection by natural polyphenols: Anti-inflammatory, anti-oxidant and DNA repair mechanisms. Arch Dermatol Res 2010; Mar; 302 (2): 71–83.
8. Friedman M. Chemistry, biochemistry and dietary role of potato polyphenols. J Agric Food Chem 1997; 45: 1523–1540.
9. Kubat K. The role of phenolic compounds in plant resistance. Biotechnol Food Sci 2016; 80 (2): 97–108.
10. Harborne JB, Baxter H, Moss GP. Phytochemical Dictionary: A Handbook of Bioactive Compounds from Plants. 2nd ed. London. Taylor & Francis. London 1999.
11. Soto ML, Falqué E, Domínguez H. Relevance of Natural Phenolics from Grape and Derivative Products in the Formulation of Cosmetics. Cosmetics 2015; Aug; 2 (3): 259–276.
12. Mattila P, Hellström J. Phenolic acids in potatoes, vegetables, and some of their products. J Food Compos Anal 2007; May; 20 (3-4): 152–160.
13. Monente C, Ludwig IA; Irigoyen A, et al. Assessment of total (free and bound) phenolic compounds in spent coffee extracts. J Agric Food Chem 2015; May; 63 (17): 4327–4334.
14. Touaibia M, Jean-Francois J, Doiron J. Caffeic acid, a versatile pharmacophore: an overview. Mini Rev Med Chem 2011; Jul; 11 (8): 695–713.
15. Kim J-H, Yu D, Eom S-H, Kim S-H, et al. Synergistic Antibacterial Effects of Chitosan-Caffeic Acid Conjugate against Antibiotic-Resistant Acne-Related Bacteria. Mar Drugs 2017; 15: 167; doi:10.3390/md15060167.
16. Genaro-Mattos TC, Maurício ÂQ, Rettori D, et al. Correction: Antioxidant Activity of Caffeic Acid against Iron-Induced Free Radical Generation—A Chemical Approach 2015; Plos One 10 (11): e014240.
17. Chung SW, ·Park I-H, Hong S-M,·et al. Role of Caffeic Acid on Collagen Production in Nasal Polyp-Derived Fibroblasts. Clin Exp Otorhinolar 2014; 7 (4): 295–301.
18. Magnani C, Isaac VLB, Correa MA, et al. Caffeic Acid: a review of its potential use for medications and cosmetics. Anal Methods 2013; 6: 3203-3210.
19. Song J-J, Lim HW, Kim K-M, et al. Effect of caffeic acid phenethyl ester (CAPE) on H2O2 induced oxidative and inflammatory responses in human middle ear epithelial cells. Int J Pediatr Otorhin 2012; May; 76 (5): 675–679.
20. Quan W, Tao Y, Lu M, et al. Stability of the phenolic compounds and antioxidant capacity of five fruit (apple, orange, grape, pomelo and kiwi)

juices during in vitro-simulated gastrointestinal digestion. Int J of Food Sci and Tech 2018; 53: 1131–1139.
21. Lattanzio V, Kroon PA, Linsalata V, et al. Globe artichoke: A functional food and source of nutraceutical ingredients. J Funct Foods I 2009: 131–144.
22. Natarajan K, Singh S, Burke TR Jr, et al. Caffeic acid phenethyl ester is a potent and specific inhibitor of activation of nuclear transcription factor NF-kappa B. Proc Natl Acad Sci USA 1996; Aug; 93 (17): 9090–9095.
23. Sud'ina GF, Mirzoeva OK, Pushkareva MA, et. al.. Caffeic acid phenethyl ester as a lipoxygenase inhibitor with antioxidant properties. FEBS Lett 1993; 329 (1-2): 21–24.
24. Zhao Z, Moghadasian MH. Chemistry, natural sources, dietary intake and pharmacokinetic properties of ferulic acid: a review. Food Chem 2008; Aug; 109 (4): 691–702.
25. Pobłocka -Olech L, Krauze-Baranowska M, Głód D, et al. Chromatographic Analysis of Simple Phenols in Some Species from the Genus Salix. Phytochem Anal 2010; 21: 463–469.
26. Kikuzaki H, Hisamoto M, Hirose K, et al. Antioxidant properties of ferulic acid and its related compounds. J Agric Food Chem 2002; Mar; 50 (7): 2161–2169.
27. Srinivasan M, Sudheer AR, Menon VP. Ferulic Acid: Therapeutic Potential Through Its Antioxidant Property. J Clin Biochem Nutr 2007; 40: 92–100.
28. Ojha S, Javed H, Azimullah S. et al. Neuroprotective potential of ferulic acid in the rotenone model of Parkinson's disease. Drug Des Devel Ther 2015; 9: 5499–5510.
29. Middleton E, Kandaswami C, Theoharides TC. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease and cancer. Pharmacol Rev 2000; Dec; 52 (4): 673–839.
30. Graf E. Antioxidant potential of ferulic acid. Free Radic Biol Med 1992; 3: 435–513.
31. Ali A. Phenolics for skin photo-aging. Pak J Pharm Sci 2017; Jul; 30 (4): 1389–1394.
32. Mattila P, Hellström J. Phenolic acids in potatoes, vegetables, and a some of their products. J Food Compos Anal 2007; 20: 152–160.
33. Kelebek H, Kadiroğlu P. Demircan N B, et al. Screening of bioactive components in grape and apple vinegars: Antioxidant and antimicrobial potential, J Inst Brew 2017; 123: 407–416.
34. Rajić JR, Dordević SM, Tešević VV, et al. The extract of fennel fruit as a potential natural additive in food industry. J Agric Sci 2018; 63 (2): 205–215.
35. Khan AK, Rashid R, Fatima N, et al. Pharmacological activities of protocatechuic acid. Acta Pol Pharm Drug Res 2015; Jul-Aug; 72 (4): 643–650.
36. Lin W-L, Hsieh Y-J, Chou F-P, et al. Hibiscus protocatechuic acid inhibits lipopolysaccharide-induced rat hepatic damage. Arch Toxicol 2003; Jan; 77 (1): 42–47.
37. Jürgenliemk G, Nahrstedt A. Phenolic Compounds from Hypericum perforatum. Planta Med 2002; 68: 88–91.
38. Szumiło J. Protocatechuic acid in cancer prevention. Postepy Hig Med Dos 2005; 59: 608–615.
39. Lamaison JL, Petitjean-Freytet C, Carnat A. Medicinal Lamiaceae with antioxidant properties, a potential source of rosmarinic acid. Pharm Acta Helv 1991; 66 (7): 185–188.
40. Tang KS, Konczak I, Zhao JM. Identification and quantification of phenolics in Australian native mint (Mentha australis R. Br.). Food Chem 2016; 192: 698–705.
41. Petersen M, Simmonds MSJ. Rosmarinic acid. Phytochemistry 2003; Jan; 62 (2): 121–125.
42. Stansbury J. Rosmarinic Acid as a Novel Agent in the Treatment of Allergies and Asthma. J Restor Med 2014; Apr; 3 (1): 121–126.
43. Budhiraja A, Dhingra G. Development and characterization of a novel antiacne niosomal gel of rosmarinic acid. Drug Deliv 2015; Apr; 22 (6): 723–730.
44. Nimse SB, Pal D. Free radicals, natural antioxidants, and their reaction mechanisms. RSC Adv 2015; 5: 27986–28006.
45. Philips N, Smith J, Keller T, et al. Predominant effects of Polypodium leucotomos on membrane integrity, lipid peroxidation, and expression of elastin and matrixmetalloproteinase-1 in ultraviolet radiation exposed fibroblasts, and keratinocytes. J Dermatol Sci 2003; July; 32 (1): 1–9.
46. Cuvelier ME, Richard H, Berset C. Antioxidative activity and phenolic composition of pilot – plant and commercial extracts of sage and rosemary. J Am Oil Chem Soc 1996; May; 73 (5): 645–652.
47. Rice-Evans CA, Miller NJ, Paganga G. Structure-antioxidant activity relationships of flavonoids and phenolic acids. Free Radic Biol Med 1996; 20 (7): 933–956.

48. Khanbabaee K, van Ree T. Tannins: classification and definition. Nat Prod Rep 2001; Sep; 18 (6): 641–649.
49. Smeriglio A, Barreca D, Bellocco E, et al. Proanthocyanidins and hydrolysable tannins: occurrence, dietary intake and pharmacological effects. Brit J Pharmacol 2017; Jun; 174 (11): 1244–1262.
50. Hoffmann J, Wölfle U, Schempp CM, et al...Tannins from Potentilla officinalis display anti-inflammatory effects in the UV erythema test and on atopic skin. JDDG 2016; 14 (9): 917–922.
51. Chakrawarti L, Agrawal R, Dang S, et al. Therapeutic effects of EGCG: a patent review. Expert Opin Ther Pat 2016; Aug; 26 (8): 907–916.
52. Karwowska K. Application of tea plant leaves in food and cosmetics industry. Aesthetic Cosmetology 2016; 5: 493–498.
53. Yam TS, Hamilton-Miller JM, Shah S. The effect of a component of tea (Camellia sinensis) on methicillin resistance, PBP2′ synthesis, and beta-lactamase production in Staphylococcus aureus. J Antimicrob Chemother 1998; Aug; 42 (2): 211–216.
54. Okubo S, Sasaki T, Hara Y, Mori F, et al. Bactericidal and anti-toxin activities of catechin on enterohemorrhagic Escherichia coli. Kansenshogaku Zasshi 1998; Mar; 72(3): 211–217.
55. Bae JY, Choi JS, Choi YJ, et al. (–) Epigallocatechin gallate hampers collagen destruction and collagenase activation in ultraviolet-B-irradiated human dermal fibroblasts: Involvement of mitogen-activated protein kinase. Food Chem Toxicol 2008; Apr; 46(4): 1298–1307.
56. Kwon OS, Han JH, Yoo HG, et al.. Human hair growth enhancement in vitro by green tea epigallocatechin-3-gallate (EGCG). Phytomedicine 2007; Aug; 14 (7–8): 551–5.
57. Leo MS, Maibach HI, Sivamani RK. The Cosmetic and Therapeutic Uses for Epicatechin-3-Gallate (EGCG). Cosmeceuticals and Active Cosmetics. CRC Press 2015: 47–54.
58. Kim J, Hwang JS, Cho YK, et al. Protective effects of (–)-epigallocatechin-3-gallate on UVA- and UVB--induced skin damage. Skin Pharmacol Appl Skin Physiol 2001; Jan-Feb; 14 (1):11–19.
59. de Groot H, Rauen U. Tissue injury by reactive oxygen species and the protective effects of flavonoids; Fundam Clin Pharm 1998; Aug; 12 (3): 249–376.
60. Potapovich, AI, Kostyuk, VA, Kostyuk TV, et al. Effects of pre- and post-treatment with plant polyphenols on human keratinocyte responses to solar UV. Inflammat Res 2013; 62: 773–780.
61. Cao G, Sofic E, Prior RL. Antioxidant and prooxidant behavior of flavonoids: structure-activity relationships. Free Radic Biol Med 1997; 22 (5): 749–760.
62. Mora A, Payá M, Rios JL, et al. Structure-activity relationships of polymethoxyflavones and other flavonoids as inhibitors of non-enzymic lipid peroxidation. Biochem Pharmacol 1990; Aug; 40 (4): 793–797.
63. Heim KE, Tagliaferro AR, Bobilya DJ. Flavonoid antioxidants: chemistry, metabolism and structure--activity relationships. J Nutr Biochem 2002; Oct; 13 (10): 572–584.
64. Ratty AK, Das NP. Effects of flavonoids on nonenzymatic lipid peroxidation: structure, activity relationship. Biochem Met Metab Biol 1988; Feb; 39 (1): 69–79.
65. Dvorák Z, Kosina P, Walterova D, et al. Primary cultures of human hepatocytes as a tool in cytotoxicity studies: cell protection against model toxins by flavonolignans obtained from Silybum marianum. Toxicol Lett 2002; Feb; 137 (3): 201–212.
66. Haddad Y, Vallerand D, Brault A, et al. Antioxidant and hepatoprotective effects of silibinin in a rat model of nonalcoholic steatohepatitis. Evid-based Complement Altern Med 2011; 2011 (10); Article ID 647903; doi: 10.1093/ecam/nep164.
67. Polyak SJ, Morishima C, Shuhart MC, et al. Inhibition of T-cell inflammatory cytokines, hepatocyte NF-kappa B signaling, and HCV infection by standardized Silymarin. Gastroenterology 2007; May; 132 (5): 1925-1936.
68. Milića N, Miloševića N, Suvajdžića L, et al. New Therapeutic Potentials of Milk Thistle (Silybum marianum). Nat Prod Commun 2013; 8 (12): 1801–1810.
69. Colantuoni A, Bertugli S, Magistretti MJ, et al. Effects of Vaccinium myrtillus anthocyanosides on arterial vasomotion. Arzneim-Forsch 1991; 41 (9): 905–909.
70. Olmedilla-Alonso B, Estévez-Santiago R, Silván JM, et al. Effect of Long-Term Xanthophyll and Anthocyanin Supplementation on Lutein and Zeaxanthin Serum Concentrations and Macular Pigment Optical Density in Postmenopausal Women.

Nutrients 2018; Jul; 10 (8): 959; doi: 10.3390/nu10080959.
71. Kong JM, Chia LS, Goh NK, et al. Analysis and biological activities of anthocyanins. Phytochem 2003; Nov; 64 (5): 923–933.
72. Castaneda-Ovando A, Pacheco-Hernández ML, Páez-Hernández ME, et al. Chemical studies of anthocyanins: a review. Food Chem 2009; 113: 859–871.
73. Burns J, Yokota T, Ashihara H, et al. Plant Foods and Herbal Sources of Resveratrol. J Agric Food Chem 2002; May; 50 (11): 3337–3340.
74. Afaq F, Adhami VM, Ahmad N. Prevention of short term ultraviolet B radiation- mediated damages by resveratrol in SKH-1 hairless mice. Toxicol Appl Pharmacol 2003; Jan; 186 (1): 28–37.
75. Saraf S, Kaur CD. Phytoconstituents as photoprotective novel cosmetic formulations. Pharmacogn Rev 2010; Jan; 4 (7): 1–11.
76. Knutson MD, Leeuwenburgh C. Resveratrol and novel potent activators of SIRT1: effects on aging and age-related diseases. Nutr Rev 2008; Oct; 66 (10): 591–596.
77. Song Q, Billodeaux DR, Fronczek FR, et al. Futoenone, a neolignan from Magnolia soulangiana. Act Cryst 2001; 57: 1094–1095.
78. Song Q. A Phytochemical Study of Members of the Genus Magnolia (Magnoliaceae) and Biosynthetic Studies of Secondary Metabolites in Asteraceae Hairy Root Cultures; LSU Historical Dissertations and Theses; 5930; Ann Arbor 1995.
79. Moss GP. Nomenclature of Lignans and Neolignans (IUPAC Recommendations 2000). Pure Appl. Chem 2000; Jan; 72 (8): 1493–1523.
80. Khalid S, Khan A, Shal B, et al. Suppression of TRPV1 and P2Y nociceptors by honokiol isolated from Magnolia officinalis in 3rd degree burn mice by inhibiting inflammatory mediators. Biomed Pharmacother 2019; 114; 108777.
81. Vaid M, Sharma SD, Katiyar SK. Honokiol, a phytochemical from the Magnolia plant, inhibits photocarcinogenesis by targeting UVB-induced inflammatory mediators and cell cycle regulators: development of topical formulation. Carcinogenesis 2010; Nov; 31 (11): 2004–2011.
82. Ghys K, De Palma A, Vandevenne A, et al. Magnolia officinalis bark extract, a recently identified contact allergen in 'anti-ageing' cosmetics. Contact Dermatitis 2015; Aug; 73 (2): 130–132.
83. Montaño I, Schmid D. Magnolia Derived Honokiol and Magnolol Fight Against Skin Inflamm' Aging. Mibelle Biochemistry. Buchs 2010.
84. Huang HC, Hsieh WY, Niu YL, et al. Inhibition of melanogenesis and antioxidant properties of Magnolia grandiflora L. flower extract. ISCMR 2012; 12: 72; doi: 10.1186/1472-6882-12–72.
85. Ranouille E, Boutot C, Bony E, et al. Schisandra chinensis protects the skin from global pollution by inflammatory and redox Balance pathway modulations: an in vitro study. Cosmetics 2018; 5: 36; doi:10.3390/cosmetics5020036.