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Skin Penetration Ability of Active Substances from Plant Extracts

Introduction

Plant extracts have been used in medicine and body care since the beginning of human civilisation. The ancient man collected step by step knowledge, which plants possessed high medicinal and cosmetic value and which of them had to be avoided.
Nowadays, application of herbal extracts in modern cosmetics became very trendy. Again and again the market requires cosmetics that include mixtures of natural origin.
In the view of these facts one important question appears – do ingredients of natural origin play only the marketing role? Definitely not. And this is just where the problem begins. What is their real cosmetic value? Do they display the same properties while being studied *in vitro* and *in vivo*? All these questions lead us to the problem of skin penetration process of active substances contained in plants.
The paper introduces the main groups of active substances that are present in plant extracts such as polyphenols, phenolic acids, phenolic glycosides, terpenes, saponins, carbohydrates and their cosmetic activity in a view of skin penetration ability of these compounds.

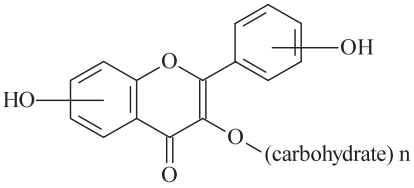
Plant Extracts – Amazing Wealth of Chemical Structures

Plant extracts are mixtures composed of many constituents of different chemical structure, existing side by side and displaying very wide spectrum of chemical and biological activity. Extracts produced for cosmetic purposes are manufactured from different parts of plant: leaves, flowers, roots, seeds and nuts. Composition of this mixture depends very often on the plant origin, climate, seasons and other factors [1].
A lot of plant extracts have found wide application in cosmetic industry. One of the most common appears to be green tea, plant rich in catechins and other flavonoids [2]. Other, not less important are camomile, ginseng, grape leaves, ginkgo biloba, rosemary, birch, horse chestnut and sage [3].
Which features make them so priceless and irreplaceable, why did they become an integral part of many cosmetic formulations?
To answer these questions we have to plunge into their chemical composition. The enormous volume of substances doesn't permit a full listing what forced us to distinguish only the main groups.

Active Compounds of Plant Origin

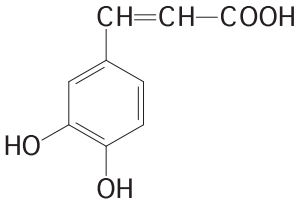
- **Polyphenols**

One of the most numerous groups belonging to polyphenols are flavonoids, compounds occurring in the plant kingdom both in glycoside and in aglycone form. The scientific approaches report that these molecules display beneficial influence on human body, including skin [4]. Flavones, flavone glycosides, flavonols, flavonol glycosides, flavanons, isoflavons and other compounds create huge and various group of substances belonging to flavonoids. The general formula of flavonol glycosides, which are very common in plants, has been introduced below:
One of the most widespread substances of aglycone nature is quercetin, which is an integral part of large number of cosmetic extracts. Quercetin is present in calendula, camomile, linden, green tea and other extracts, which have found broad application in cosmetic industry [5]. The other groups of flavonoids of special significance for the cosmetology are catechins – compounds occurring in high concentration in green tea extract. A good representative for glycosides can be rutin, which can be easily found in gingko biloba, grape leaf and green tea. Taking into account bio-chemical properties of these molecules, all of them seem to be priceless from the cosmetological point of view. The literature reports that flavonoids are very effective free radical scavengers, anti-oxidising agents and very good UV radiation protectors as well as very effective anti-alergenic, anti-inflammatory and anti-mutagenic substances. Flavonoids can act as anti-oxidants both by free radical scavenging and inhibition of enzymes involved in oxidative chain. It has been proven that these molecules can affect the permeability and fragility of microvessels and blood platelet aggregation [6, 7]. Flavonoids have been shown to influence the wide variety of enzymes including ATPases, phosphodiesterases, hydrolases, lipoxygenases and many others. It is known that the main mechanism of this activity involves the formation of flavonoid-metal complexes by chelation of metal ions. Extracts containing flavonoids have found application in almost all branches of cosmetic industry.



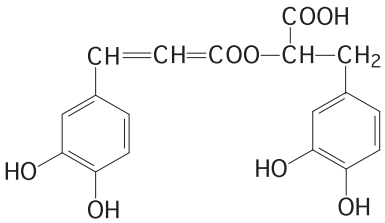
- **Phenolic acids**

Phenolic acids are compounds that include phenolic hydroxyl group and carboxyl group in the structure. These substances occur in the nature in mixtures, both in bounded and unbounded form.
The good example phenolic acids occurring in extracts that have found wide application in cosmetic industry can be caffeic acid:



Caffeic acid

Caffeic acid can be easily found in Ivy, which is very common ingredient of slimming and anti-cellulite products as well as in balm mint. The other molecule belonging to this group is rosmarinic acid.

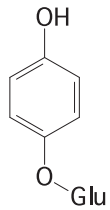


Rosmarinic acid

Rosmarinic acid molecule is a linkage of caffeic and α-hydroxydihydrocaffeic acids and occurs in rosemary and sage. Taking into account anti-oxidant, anti-inflammatory and tonifying properties of these extracts, they found broad application in anti-ageing creams, cleansing and deo preparations.

• Phenolic glycosides

The compound belonging to phenolic glycosides that has to be mentioned in this paper is arbutin. Arbutin is a hydroquinone glucoside, which occurs in bearberry and possesses anti-bacterial and anti-inflammatory activity. The structure of arbutin has been presented below.

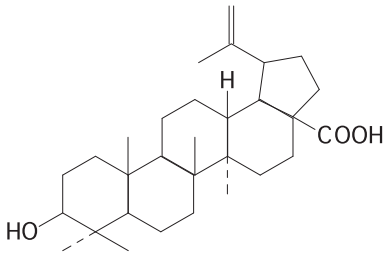


Arbutin

The bearberry extract, so reach in arbutin but containing also ursolic acid is commonly added to skin care cosmetics and products appropriated for the skin whitening treatment.

• Triterpenes

Compounds belonging to the isoprenoid group of cyclic structure and lipophilic character. Betulinic and ursolic acids are very common ingredients of birch, calendula, bearberry, rosemary and other cosmetic raw materials. They are known from anti-bacterial, anti-inflammatory and anti-oxidant activity what makes them very vital for the cosmetic industry. The structure of betulinic acid has been introduced below:

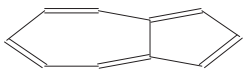


Betulinic acid

• Sesquiterpenes

Sesquiterpenes are groups including various carbohydrates and their oxygen derivatives: alkohols, aldehydes, acids, lactones and others. The structure of these molecules can be cyclic or aliphatic.

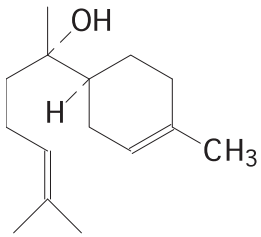
Sesquiterpen of bicyclic structure that has found an application in cosmetology is azulene:



Azulene

Among cosmetic raw materials including azulene are chamomile and yarrow. The other important ingredient of chamomile is α-bisabolol, which displays softening and anti-inflammatory activity. Thanks to these beneficial properties chamomile extract has found wide application in hair care cosmetics as well as in soothing and calming preparations.

The structure of α-bisabolol can be presented as follows:



α-bisabolol

• Saponins

Saponines, named sometimes saponosides are substances of glycoside character, composed of aglycon part (which can be triterpenic or steroid molecule) and carbohydrates. The name of this group originates from the Greek word ”sapo” what means soap. Saponosides occur widely in calendula, ivy, liquorice, and other plants. Seeds of horse chestnut include triterpenic saponin termed escin, which is the compound decreasing the fragility and permeability of microvascular vessels.

One of the most promising groups belonging to saponins are ginsenosides – triterpenic saponosides from ginseng, that ensure moisturising and regenerating effect. Besides these substances ginseng includes various flavonoids and these ingredients secure beneficial activity. It has been proven that ginseng extract activates dermal blood circulation and skin metabolism as well as prevents the skin from free radicals. Bulk of cosmetics appropriated for hair care contains this raw material.

• Carbohydrates

Carbohydrates are very large and various group of natural substances, which can be divided into monosaccharides, oligosaccharides and polysaccharides. Carbohydrates are present in most of plants and applied to the cosmetic preparation can act as moisturising additives. Simple sugars, like glucose, deoxyribose, arabinose are commonly added with plant extracts to moisturising preparations. Among polysaccharides that have found cosmetic application groups like mucus and gums can be distinguished.

Considering plants that are rich in carbohydrates algae and aloe can’t be left out of account. Algae, plants being so widespread in the cosmetic industry last time, contain various types of polysaccharides, for instance carrageen, alginic acid and agar-agar. Carrageen contains many mucous polysaccharides and can be applied as a moisturising agent.

The other, rich in polysaccharides, raw material that is broadly applied in cosmetics is aloe. In the view of its anti-inflammatory, moisturising, regenerating and anti-oxidising properties, aloe has found wide application in skin and hair care cosmetics.

Group	Active ingredients	Plant extracts	Cosmetic activity	Cosmetic application
Polyphenols	Flavonoids (quercetin, rutin, catechin)	Green tea, calendula, chamomile, linden, grape seeds and others	Anti-oxidant, anti-ageing, veinotonic, anti-inflammatory	Skin care, anti-ageing products, after sun prearations
Phenolic acids	Caffeic acid	Ivy, balm mint	Anti-inflammatory, anti-oxidant, anti-ageing	Slimming, anti-cellulite cosmetics
	Rosmarinic acid	Rosemary, sage	Anti-oxidant, tonifying	Anti-ageing creams, cleansing and deo preparations
Phenolic glycosides	Arbutin	Bearberry	Anti-bacterial, astringent	Skin whitening treatment, cleansing preparations, sensitive skin care
Triterpenes	Betulinic and ursolic acids	Calendula, rosemary, bearberry, birch	Anti-oxidant, anti-inflammmatory, anti-bacterial	Soothing products, preparations for oily skin, skin and hair care, treatment of irritated skin
Sesquiterpenes	Azulene	Chamomile, yarrow	Anti-bacterial, anti-inflammmatory	Calming products, anti-dandruff shampoos, skin tonics, soothing cosmetics
	α-bisabolol	Chamomile	Softening, anti-inflammmatory	Hair care cosmetics, calming and soothing products
Saponins	Ginsenosides	Ginseng	Regenerating, stimulating, anti-oxidant	Anti-ageing preparations, skin care
Carbohydrates	Alginic acid, glucuronic acid, polysaccharides (carrageen, glucan)	Cucumber, algae, aloe	moisturising, anti-inflammatory, regenerating	Skin care, soothing, preparations

• **Vitamines –** taking into consideration synthetic origin of the majority of vitamins applied in cosmetics, this group has been left out of account in this paper.

Wide spectrum of different substances that has been presented above does give us some picture about the variety of ingredients distributed in plant kingdom. It is obvious that these species, displaying so different chemical activity possess broad, very often beneficial influence on the human skin. Considering their properties, the one fact has to be remembered: cosmetic activity of these components depends strictly on their ability to overcome *stratum corneum*, which is a skin barrier [8]. If manufacturers of cosmetics want to take advantage of their properties, the creation such a cosmetic system that enables skin penetration of these compounds becomes a necessity.

Skin Permeation Ability as the Key Factor for the Cosmetic Activity of Plant Ingredients

The skin is a very complicated organ, which protects and separates the human organism from the external environment. The most upper layer of the skin, termed *stratum corneum*, determines the skin function as a barrier.

The scientific approaches indicate that large number of different factors influences permeation process. It has been proven that the progress through the horny layer depends on delivery system, lipophilicity, molecular size, concentration, structure of applied compounds and many other factors [9].

One of the most significant factor from these mentioned above is lipophilicity of the permeating molecule, which is advised to be taken into account at the very beginning step of skin penetration ability prediction of particular compound. It has been documented that the correlation between penetrant migration into the horny layer and lipophilicity is directly proportional, but if the whole skin is taken into account the parabolic relationship can be observed. The reason for this situation inheres in the decreased aqueous solubility of lipophilic compounds in epidermis [10]. The possibility of the prediction of active components permeation rate into the skin can be very helpful for the cosmetologists and producers. However, the complex nature of this process causes many troubles to the researchers and scientists [11, 12].

It has been proven that some additives can be regarded as easily penetrating agents-usually these of lipophilic nature. Other components, taking into account their hydrophilic nature or large molecular weight (i.e. sugars) are recognised as weak or non-penetrating molecules. The very promising groups of nature compounds are flavonoids – so wide distributed in plant extracts, but

only a few papers on the skin permeation of these compounds exist. It has been proven that flavonoids can permeate the skin and that the permeation rate of glycosides is lower that aglycones [13, 14]. These results can be explained by more hydrophilic nature of glycosides as well as their larger molecular size. The other molecule of confirmed skin penetration ability is caffeic acid, which capability to permeate through *stratum corneum* have been tested by Italian scientists [15].

Concerning other molecules presented in this article we can suppose, taking into account their structure, that some of them can be better penetrants than others. We can suppose, that unbounded caffeic acid can penetrate *stratum corneum* worse that in the form of ester. The problem is, that without laboratory confirmation our predictions are still in the sphere of suggestions.

Despite of wide application of natural ingredients in cosmetics the literature treats the problem of skin permeation of these molecules with the very little attention.

Conclusion

Skin penetration process of active ingredients of plant origin appears to be very significant both for the researchers and for producers. Prediction of the permeation rate of penetrating molecule, employing only mathematical models seems to be insufficient. The permeation of molecule into the skin is recognised as a very complex process, dependent on many different biochemical and physical factors, hence the permeation models usually don't take into account all of them. The possibility of penetration ability prediction of active compounds appears to be limited. The most reliable information can be obtained during laboratory experiments provided *in vivo* as well as *in vitro* [16]

Manufacturers of cosmetics have to be aware that the composition of cosmetic product should enable skin penetration of substances applied onto the skin if the active compound is required to be effective. Thus, cosmetic formulation should be elaborated very carefully, to facilitate migration of these compounds into the skin. The pH of cosmetics containing acids has to be under continuous control. To facilitate skin permeation, application of additives reported in the literature as penetration enhancers is recommended as well as employment of solvents that can enable this complicated process [17]. Substances, which are known from their weak skin penetration ability should be applied in the form of vesicles.

To sum up, many additives of plant origin possess vital influence on human skin and the problem of skin permeation process is still topical and requires further scientific investigation.

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