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ALOE – A UNIQUE SOURCE OF BIOLOGICALLY ACTIVE COMPOUNDS

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The review of various aloe species as potent source of biologically active compounds is presented. The general description of aloe species their morphology and characteristic features is presented. Various biologically active compounds that may be derived from aloe species are described. The ways of application of biologically active compounds as potential therapeutic agents and as additives to drugs or cosmetics have been analyzed.

Key words: *aloe, biologically active compounds, aloin*

Aloe plants are widely used in medicine for the production of medicines and additives to cosmetics due to their special biochemical composition and a wide range of biologically active compounds. Thus, the relevance of their research is associated with the rapid development of pharmacy and the need to find sources of biologically active substances with high medicinal value.

Characteristics of various aloe species

Aloe is perennial succulent xerophyte, which belongs to *Asphodelaceae* family and comprised of more than 400 species, ranging from shrubs to large trees [10]. This large and very popular genus is known and distributed all over the world. It develops water-storage tissue in the leaves to survive in dry areas. The most typical form of growth is a rosette of thick leaves with or without a main stem. However, the size of plants varies considerably: from small bulbs with thin and tender leaf-like leaves to massive 10-meter trees. Flowering is very plentiful with white to red flowers. They form small oval fruits – green berries [13, 18].

Aloe dichotoma

It is considered as the largest one, forming trees up to 10 m in height with a thick main stalk. Individual rosettes are up to 30 cm wide, with pale green cone-like tapering leaves reaching up to 20 cm long. Despite the size, flowers of this aloe are small, yellow, collected in inflorescences on flowering shoots up to 30 cm long. The plant can withstand bright sun and heat, as well as short-term frosts of up to 2 °C.

Aloe barbadensis

It is also known as *Aloe vera*. Rosettes reach 20 cm and form lateral shoots. Leaves are 5 cm wide, pale green. In early summer, yellow flowers appear, collected in inflorescences located on flower shoots up to 1 m long. The juice of this plant has medicinal properties and is widely used as a medicine, but it requires abundant watering, since the juice contained in the dry plant will be very viscous and sharply smelling. *Aloe vera* grows well in moderate sun and can withstand frosts. Propagated by seeds as well as via vegetative method, by roots.

Aloe ramosissima

This species is often confused with *A. dichotoma*, but it is a smaller plant growing on the coast. Leaves are already shorter than that of *A. dichotoma*. Inflorescences are of yellow flowers, plant reach only 2 m in height. It does not tolerate severe frosts and prefers some shading in the hot time. Propagated by seeds, sometimes by cuttings.

Aloe distans

This species with leaf stems branching from the base more than 1 m long has leaf rosettes of about 12 cm wide. Flowers are collected in inflorescences. It withstands short-term frosts and prefers a slight shade. Propagated by seeds, but some characteristic forms should be propagated by cuttings [8].

Biologically active compounds derived from aloe

Different species of aloe plants accumulate a plenty variety of various pharmacologically active substances. Thus, wide usage of aloe products is connected with diverse range of phytoconstituents. In the aloe more than 75 biologically active substances of various groups are presented like polysaccharides, anthraquinones,

anthrones, alkaloids, flavonoids, terpenoids, lectins, vitamins, enzymes, minerals (calcium, chromium, copper, iron, magnesium, manganese, potassium, phosphorus, sodium and zinc) that promote diverse biological functions [5, 9].

Main source of biologically active substances of aloe is leaf gel, however flower extract also possess valuable bioactive compounds like apigenin glycoside derivatives, that is effective against the multidrug-resistant *Pseudomonas aeruginosa* [9].

The phytochemical composition and percentage of various biologically active compounds depends on number of factors including plant species, genetic variation, growth and storage conditions, geoclimatic conditions, temperature, humidity, altitude, salinity, harvest time, the position of leaves on the stem, and method used for harvesting leaves [6, 13].

1. Anthrones

For aloe extracts, presence of various types of anthrones and their isomers is characteristic. To such compounds belong barbaloin (isomers aloin A and aloin B), homonataloin and nataloin aloinoside, aloe barbendol, aloe-emodin anthrone, chrysophanolanthrone, littoraloin, littoraloside, microdontin, and homonataloside [2].

2. Lectins

Lectins glycoproteins are characteristic for aloe extracts. Main types include aloctin A and B. They possess various physiological activities including mitogenic and immune modulating role. They are capable to stimulate cell divisions and affect the growth of B- and T-lymphocytes via activation of cell blastic transformation. In addition, they take part in destruction of cancer cells via agglutination of carcinogenic cells by binding the polysaccharide fragments of their membranes with the active center of aloctin [3].

3. Anthraquinones

Anthraquinones are known for their strong or mild laxative properties. They possess antioxidative, bacteriostatic, antiviral, cytotoxic and peristalsis stimulating effects. Anthraquinones of various types are presented in different aloe species including aloesaponarin, chrysophanol, desoxyerythrolaccin, helminthosporin, 7-

hydroxyaloe emodin, isoxanthorin, laccaic acid-D-methyl ester, nataloe emodin, aloechryson, and aloesaponol. However aloin and aloe-emodin are the most common, applied commercially as a powder like laxatives [2, 3].

4. Enzymes

Various enzymes with diverse biological activities have been reported in aloe species. In aloe extracts the most abundant enzyme are alkaline phosphatase, superoxide dismutase, amylase, bradykinase, catalase, lipase, protease, creatine phosphokinase, carboxypeptidase, cellulase, and oxidase [3].

5. Phenolic Compounds

Aloe extracts possess a diversified content of various phenolic compounds, depending on individual morphological parts of aloe. In general, the content of phenolic compounds in aloe's leaf epidermis is higher than in flowers. For aloe leaves chromones are the most abundant phenolic compounds, namely aloeresin A and aloesin. For leaves catechin is also characteristic, while for flowers the most abundant is genistic acids [2, 3].

6. Vitamins

Extracts of various aloe plants may serve as source of various vitamins, like ascorbic acid, thiamine, riboflavin, pyridoxal phosphate, cyanocobalamin and α -tocopherol [2].

7. Alkaloids

Typical alkaloids of aloe extracts are N-methyltyramine and O,N-dimethyltyramine [2].

8. Polysaccharides

Polysaccharides constitute the most of the dry matter of the aloe parenchyma. To the primary polysaccharides of aloe belongs cellulose and pectic polysaccharides as well as acetylated mannan (or acemannan). However, a significant quantities of other polysaccharides have been reported like xylose-containing polysaccharides, arabinan, arabinorhamnogalactan, galactan, galactogalacturan, glucogalactomannan, galactoglucoarabinomannan and glucuronic acid containing polysaccharides [14].

9. Steroids

Aloe extracts are also rich in steroid compounds like cholesterol, campesterol, β sisosterol and lupeol. All of them possess anti-inflammatory action as well as may serve as antiseptics [16].

Therapeutic effects of substances derived from aloe

1. Immunomodulation effects

Aloe extracts possess immunomodulation activities due to polysaccharides presence that act via activation of macrophage cells to generate nitric oxide, secrete cytokines and present cell surface markers [14].

2. Anti-inflammatory effects

Aloe gel demonstrate anti-inflammatory effects via promotion of prostaglandin synthesis or by reducing leukocyte adhesion and pro-inflammatory cytokine production [2, 14]. Another mechanism involve anti-bradykinin activity due to bradykinase enzyme presence, which breaks down the bradykinin and reduces the inflammation. Sterols in aloe are also involved in anti-inflammatory effects due to their similarity to the anti-inflammatory steroids. Compounds like barbaloin and emodin serve as anti-inflammatory agents as they are precursors to aspirin-like compounds [8, 17].

3. Anti-oxidant effects

Anti-oxidant activity of aloe extracts is connected with antioxidants presence like α -tocopherol, carotenoids, ascorbic acid, flavonoids, tannins vitamin C and E as well as enzymes possessing glutathione peroxidase activity, superoxide dismutase enzymes [14, 17]. The possible mechanisms of action involves free radical- and superoxide radical-scavenging activities [4].

4. Wound healing effects

It is reported that aloe extracts have wound healing effects due to presence of polysaccharides that induce fibroblasts proliferation and hyaluronic acid and hydroxyproline production. The mucilage of aloe accelerates rate of wound healing via increasing amount of collagen on wound site, as well as increasing transversal connections among these bands [7].

Aloe species may be potentially used for tissue engineering applications because of its unique biological properties. Materials based on aloe may be applied as a wound dressing material, drug-eluding implant, and scaffold material in cases of damaging of tissues or organs [15].

Other possible mechanisms of aloe effects include keeping the wound moist, increase epithelial cell migration, more rapid maturation of collagen and reduction in inflammation, increasing blood supply, which increased oxygenation [2, 13, 14].

5. Anti-cancer effects

Extracts of aloe are rich in anthraquinones, barbaloin, aloe-emodin and aloesin that show cytotoxicity against cancerous cells. Emodin possess an antiproliferation activity via inhibiting both N-acetyl transferase activity and gene expression. Other possible mechanism of action may be connected with ability of aloe polysaccharides to stimulate the immune response [2, 14, 17]. Good cytotoxic activity was also demonstrated for such compounds of aloe like aloesaponarins (aloesaponarin I and II) [10].

6. Effect on gastrointestinal system

Aloe extracts are widely applied in curing of gastrointestinal disorders. Aloe has potential to prevent and cure gastric ulcers via its anti-inflammatory properties, healing effects, mucus stimulation and regulation of gastric secretions. Aloe extracts also possess potent laxative and cathartic effects due to presence of active anthraquinones, such as aloin, aloe-emodin, and emodin [2, 14].

7. Effect on skin

Aloe has been traditionally used to treat various skin disorders, like psoriasis, sunburn or radiation-related dermatitis, nappy dermatitis, mucositis or lichen planus. It is also applied in cases of skin dryness, it increases a level of skin hydration and reduces wrinkle depth. Mucopolysaccharides assist in keeping skin moist via humectant mechanism [11, 13]. Aloe extract also possess anti-age properties by stimulating fibroblast to produce the collagen and elastin, making skin more elastic and less wrinkled [13, 16].

8. Hepatoprotective activities

Hepatoprotective effects of aloe are connected with anthraquinones presence that are capable to protect against hepatocyte death and lipid peroxidation. Phytosterols of aloe, could impact on fatty acid oxidation upregulation in the liver, resulting in intra-abdominal fat reduction. The hepatoprotective action may be connected also with preserving the metabolizing enzymes of the liver through an antioxidant activity [2, 14].

Advantages of application of medicines based on natural products, like aloe include the good efficacy of bioactive molecules, biodegradability, biocompatibility, hydrophilicity, lower side effects [15].

Ways of application of biologically active compounds originated from aloe

As aloe contains a plenty variety of biologically active substances, thus it is widely applied in various industries. Nowadays product containing aloe additives are of great interest in food industry. Also medicines based only on aloe extracts as well those containing aloe as additional product are well developed especially in cosmetic industry and for wound healing.

In general, aloe active ingredients are extracted and undergo certain processing to obtain target formulations. Basic types of aloe formulations include juice, gels, liquid extracts, dry powder and concentrates.

Juice preparation involves such stages as crushing, grinding, of aloe leaves, followed by filtration and stabilization by means of addition of certain preservatives to restore the unique properties of aloe juice. To avoid sedimentation of juice upon storage such preservatives as sulphited polysaccharides isolated from the red microalgae, guar gum may be added [1]. Further processing of aloe juice may be carried out in order to obtain concentrate of aloe biologically active compounds. In addition, the drying procedure may be carried out for dry powder obtaining or vice versa addition of polymers to give the extract of gel structure [1].

Juices of aloe are applied for functional food production or certain other beverages, like tea, diet drinks, laxative drinks, hangover drink with vitamins and aminoacids and various juice mixes. Powder of aloe may be applied as additives to ice

cream, curd, yoghurts. Gels in food industry may be used in production of candies, bar, munch, chewing.

In the pharmaceutical industry, aloe extracts are mainly used for father production of topical formulations like cream, gel, facial solution, moisturizer ointments, but also they find application in form of tablets and capsules. Drinking of aloe juices is considered to have the therapeutic effects on arthritis, ulcers, diabetes, and other health conditions. Creams and gels based on aloe are mainly used in cases of serious thermal injuries, such as burns and frostbite. Dentists also employ aloe gels to reduce swelling and inflammation of the gums. Dermatologists apply topical aloe formulations to clear acne, due to fact that aloe extracts have ability to improve the bioavailability of co-administered vitamins via absorption enhancing effects. Aloe products could also be used in soothing eye inflammations [12].

Dry aloe powder could be used to manufacture matrix type tablets that are capable to slowly released a model compound over an extended period of time [5, 12].

CONCLUSIONS

Aloe is a unique source of biologically active compounds that are widely applied in various spheres. Number of aloe investigations quickly increases due to its specific properties. The main phytochemical constituents of aloe include polysaccharides, anthraquinones, anthrones, alkaloids, flavonoids, terpenoids, lectins, vitamins, enzymes, minerals. Such biologically active compounds are widely applied in food industry for functional food production as well as additives to traditional food. Medicinal application of aloe extracts is also very diverse due to its anti-inflammatory, antioxidant, anticancer, immunomodulation properties.

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АЛОЕ – УНІКАЛЬНЕ ДЖЕРЕЛО БІОЛОГІЧНО АКТИВНИХ СПОЛУК

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Наведено огляд різних видів алое – потужного джерела біологічно активних сполук. Наведено загальний опис видів алое, їх морфології та характерних особливостей. Описано різні біологічно активні сполуки, які можуть бути отримані з алое. Проаналізовано шляхи застосування біологічно активних сполук як потенційних терапевтичних засобів і як добавок до лікарських засобів або косметики.

Ключові слова: алое, біологічно активні сполуки, алоїн

АЛОЭ – УНИКАЛЬНЫЙ ИСТОЧНИК БИОЛОГИЧЕСКИ АКТИВНЫХ СОЕДИНЕНИЙ

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Приведен обзор различных видов алоэ – мощного источника биологически активных соединений. Представлено общее описание видов алоэ, их морфологии и характерных особенностей. Описаны различные биологически активные соединения, которые могут быть получены из алоэ. Проанализированы пути применения биологически активных соединений в качестве потенциальных терапевтических средств и в качестве добавок к лекарственным средствам или косметике.

Ключевые слова: алоэ, биологически активные соединения, алоин