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Issue Article

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CHEMICAL COMPOSITION AND PHARMACOLOGICAL PROPERTIES OF STILBENES FROM MORUS ALBA L.

Abstract: *Stilbene derivatives from M. alba are of great importance in the pharmaceutical and medical industries. The article presents a review of important scientific literature on the chemical and pharmacological studies of stilbene derivatives from M. alba.*

Key words: *Morus alba L., Pharmacological Properties, Moraceae family.*

Language: *English*

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Introduction

Plants are an important part of nature and have irreplaceable properties for the human body. They protect the balance of the ecosystem in the environment. Due to the vitamins, minerals and antioxidants contained in plants, they strengthen the

body's immune system, reduce stress and has an important role in health protection.

In addition, some plants are able to prevent and treat diseases, being natural remedies. One of such plants is the white mulberry - *Morus alba* L.. This plant is called white mulberry not because of the color of its fruits, but because of the color of its buds when the tree blooms. *M. alba* belongs to the genus *Morus* of the *Moraceae* family. Representatives of the genus are trees and shrubs [5]. Mulberry can be grown in all regions, but this tree grows best where the necessary environmental conditions (light, temperature, water, wind) are provided.

Picture 1.

This plant, mainly of Asian origin, is grown both for ornamental purposes and for a variety of industrial and medicinal uses. In about 2,700 BCE, the Chinese Empress Xi Ling-Shi accidentally discovered that mulberry leaves were food for insects and that they formed cocoons. This discovery was believed to have been kept secret in China for about 2,000 years. In the past, mulberries were grown in Turkey and Greece not for their leaves but for their fruit [12].

The Republic of Azerbaijan, which occupies a special place in the Caucasus in terms of the richness of its flora, plays a very important role in the cultivation of mulberry. Thus, the word "mulberry", meaning "homeland" and "abode" in the ancient Turkic language, is an Azerbaijani word and is used in many countries of the world. In total, 5 species of mulberry grow in our country (*Morus alba* L., *Morus bombycis* Koidz., *Morus multicaulis* Perr., *Morus Kagayamae* Koidz., *Morus nigra* L.) and their various varieties and forms, of which the first four are species used for food purposes. In the Republic of Azerbaijan, both the underground and aboveground parts of the mulberry are used for medicinal purposes [4]. Its leaves, fruits, bark and roots have been widely used in folk medicine since ancient times (Fig. 1).

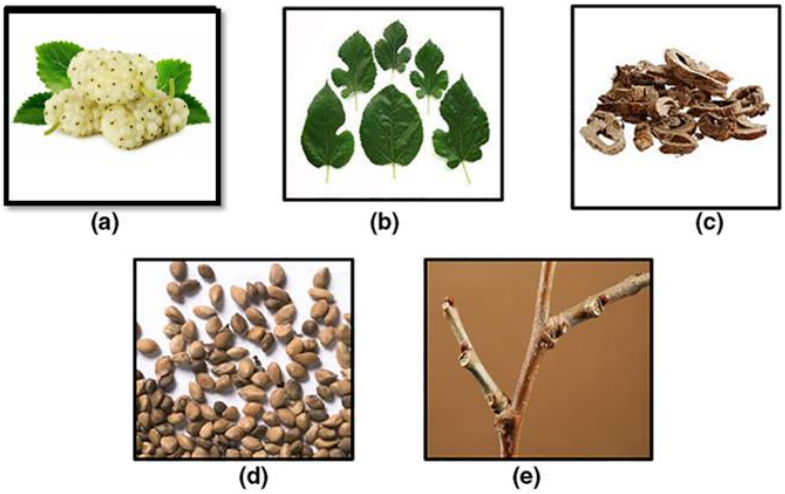

Figure 1. Fruit (a), leaves (b), bark (c), seeds (d), branch (e) of *M. alba* plant

Thus, since ancient times, the famous philosopher and great scientist in the field of medicine Ibn Sina reported that remedies prepared from the fruits and other parts of the mulberry were successfully used to treat many diseases. The main reason why sericulture in Azerbaijan occupies a special place on a global scale is that mulberry is used as feed for silkworms. White mulberry grows in all regions of Azerbaijan. Distributed mainly in the lowland zone. This plant is found in both cultivated and wild forms in Goranboy, Sheki, Zagatala, Agdash, and other regions [4].

Regarding the pharmacological study of stilbene derivatives obtained from *M. alba* plant, various parts of this plant such as fruits, leaves, roots, branches and bark are widely used in traditional medicine due to their antioxidant and other beneficial health effects. White mulberry contains many biologically active components, including stilbenes, phenolic acids, flavonoids, flavonols, anthocyanins, vitamins, macronutrients, minerals and volatile aromatic compounds. The leaves of the plant contain a large amount of quercetin, rutin and apigenin. The pharmacological effects of the listed natural biologically active substances in various diseases have been proven. These effects include antioxidant, diuretic, hypoglycemic, hypotensive, anti-cholesterol and anti-diabetic effects. The fruits of the *M. alba* plant are characterized by low lipid content and high content of proteins, carbohydrates, vitamins and minerals compared to other fruits. This also indicates its high nutritional value [13].

Stilbenes are a group of natural chemicals with unique properties that can affect various physiological processes. The anti-inflammatory, antioxidant, and antimicrobial effects of stilbenes have been confirmed by many scientific studies. However, the mechanisms of action of stilbenes present in *M. alba* are still not fully understood. This requires large-scale studies to further explore their medical and pharmacological potential. Stilbenes, such as resveratrol, found in particular in the *M. alba* plant, are of great importance for health. Their protective functions at the cellular level, as well as their potential use in the prevention and treatment of diseases, will be among the main areas of extensive research in the future. As a result of these studies, the medicinal value of white mulberry chemical structure of resveratrol consists of two phenolic rings linked by an ethylene bridge [1]. There are two isomers of resveratrol in nature: cis- and trans- . The trans-isomer of resveratrol is more stable than can be studied in more depth and its use can be expanded [15].

Stilbenes are phenolic compounds with a broad spectrum of antibiotic and pharmacological activity. In nature, this group of compounds is present in a small number of plant species, such as grapes (*Vitis* sp.), mulberries (*Morus* sp.), and peanuts (*Arachis hypogaea*) [14]. These plants synthesize stilbenes as an adaptive mechanism in response to stress. One of the main properties of stilbenes found in plants is that they have phytoalexin (protection against infection) properties. The most active derivative of stilbenes is resveratrol. In the literature data, particular attention is paid to trans-resveratrol and trans-oxyresveratrol [17].

These substances are naturally synthesized in various plant families. For example, resveratrol itself has been isolated from 34 plant families and 100 different species, such as grapes, blueberries, mulberries, cranberries, peanuts, etc. [16]. Stilbenes help protect cells from oxidative stress by reducing the effects of free radicals on the body, thereby slowing down the aging process and reducing the risk of chronic diseases. They have a positive effect on strengthening the immune system, improving blood circulation and preventing cardiovascular diseases [10].

Stilbenes are widely used in various fields. They play an important role in photophysical, biomedical and photochemical research. Stilbenes are widely used in the production of lasers, optical illuminators, phosphors and dyes. In recent years, the demand for stilbenes in the pharmaceutical, food and cosmetic industries has increased [16].

The most well-known stilbenes derived from white mulberry are resveratrol. The main representatives of stilbenes are phosphestrol (1), diethylstilbestrol (2) and dienestrol (3), which are synthetic derivatives of resveratrol and have found application in the production of estrogens from non-steroids. Due to its low price and few side effects, resveratrol is also widely used in the food industry. Today, there are more than 400 food products containing resveratrol on the world market. In addition, products containing resveratrol have been included in the human diet due to their anti-aging effect and reduced risk of vascular problems [16]. The the cis-isomer and also has higher biological and antioxidant activity [8]. The chemical formula and structure of resveratrol are shown in Figure 2 [1].

The chemical formula of $C_{14}H_{12}O_3$

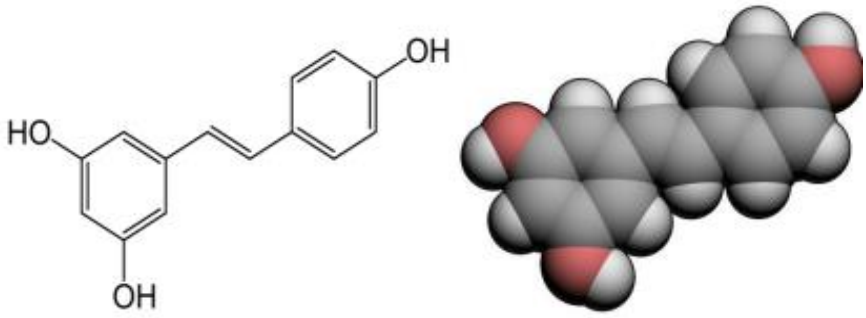

Figure 2. Structure of resveratrol
International nomenclature: 3,4-5- trihydrostilbene

Resveratrol has many positive effects on the human body. For example, resveratrol normalizes heart rhythm and blood pressure, reduces cholesterol and triglyceride levels in blood plasma, and ultimately reduces the risk of cardiovascular disease [1]. Another effect of resveratrol is its antibacterial action and natural protective effect against pneumonia [11].

Resveratrol has strong antioxidant properties and prevents cell damage by reducing the impact of free radicals on the body. One of its main benefits is strengthening and increasing the elasticity of the walls of blood vessels. This has a positive effect on improving blood circulation and normalizing blood pressure. But the benefits of resveratrol do not end there, it also attracts attention with such effects as slowing down the aging process, preventing cardiovascular diseases and reducing the risk of cancer. Studies show that this substance regulates the energy metabolism of cells, reduces inflammation and strengthens the immune system. In addition, resveratrol can reduce the risk of neurodegenerative diseases such as Alzheimer's and Parkinson's by protecting nerve cells. Studies have also shown that resveratrol derivatives significantly reduce lung metastases [2]. Due to these properties, resveratrol is widely used not only for medical purposes, but also as part of dietary supplements for a healthy lifestyle. A deeper study of its mechanisms of action may open up new opportunities for fully exploiting the potential of this substance. Thus, resveratrol is of great importance both from a health perspective and in the field of scientific research [9]. People around the world consume mulberry fruits for their nutritional value, taste, safety, and numerous health benefits. Currently, products such as syrups, jams, fruit cakes, jellies, teas, wines, and liqueurs are produced from the fruits of the *M. alba* plant [13].

Studies have shown that *M. alba* leaves are rich in proteins, carbohydrates and vitamins, especially ascorbic acid and β-carotene, as well as calcium (Ca), potassium (K), magnesium (Mg), zinc (Zn) and other important minerals.

The leaves of the *M. alba* plant have better antidiabetic and hypolipidemic properties compared to the fruits. Mulberry leaves are as important as its fruits. They are used not only to feed silkworms, but also because they have a number of beneficial properties. It was found that white mulberry leaf extract reduces the activity of α-glucosidase and α-amylase enzymes significantly. This effect may be useful in regulating blood sugar levels [13].

Studies on mice have shown that *M. alba* leaves significantly reduce cholesterol, triglyceride, and lipid peroxidation levels in blood plasma. In a study of Alzheimer's disease, one of the most common diseases in the world, it was found that when administered orally 100 mg/kg of an ethanol extract of *M. alba* leaves for 28 days improved memory function in rats with impaired spatial memory. The extract at doses of 200 mg/kg and 400 mg/kg completely prevented memory impairment [13].

In toxicity studies of *M. alba* leaves, male and female rats were orally administered medium (1%) and high (5%) concentrations for 4 weeks. During this period, their general health, biochemical parameters, and other toxicity-related parameters were monitored. The studies revealed no significant effects on growth, organ size, weight, biochemical composition, or pathological and hematological test results. Accordingly, the use of *M. alba* leaves is considered safe. In addition, intraperitoneal administration of the leaf extract resulted in a median lethal dose (LD_{50}) of approximately 4 g/kg in mice and 5 g/kg in Wistar rats. In the studies an ethanol extract obtained from the leaves of *M. alba* was administered to mice at doses of 300 and 2000 mg/kg for 14 days and then observed. No death or other changes were observed. Although the extract administered at a dose of 2000 mg/kg showed mild toxicity to mice, the extract at a dose of 300 mg/kg altered the balance of hemocyte

cells but did not harm any cells. In addition, in a toxicity study of the fruits of the plant, it was found that consumption of polysaccharides from the fruits at a dose of 1000 mg/kg did not cause any adverse effects such as respiratory distress, weight loss or death [3].

Regarding the antimicrobial properties of M. alba, it was found that its leaves inhibit the growth of *Staphylococcus aureus*, *Bacillus cereus*, and *Pseudomonas fluorescens* [13]. The seeds of the *M. alba* plant are rich in carbohydrates, fatty acids, and proteins. It was studied that the seed oil of the plant is rich in linolenic (75.83–81.1%), palmitic (7.96-9.51%), oleic (5.64-10.38%), stearic (3.45-5.01%), and many fatty acids [13].

White mulberry branches contain substances such as arabinose, glucose, fructose, maltose and tannins, which are widely used in medicine. The benefits of these substances in the treatment of some serious diseases of the human body are known from literary data [13].

The roots, bark, leaves and branches of the mulberry are used medicinally to treat conditions such as fever, inflammation, cancer, diabetes, diarrhea, upset stomach and hypertension [7]. In addition to the above, it is also used to improve vision, lower blood pressure, protect the liver and facilitate urination [3].

The branches of the plant (*Mori Ramulus*), leaves (*Mori Folium*), roots and bark (*Mori Cortex*), and fruits (*Mori Fructus*) are rich in alkaloids, flavonoids, anthocyanins, benzofurans, stilbenes, and many other chemical compounds [18]. The substances contained in the plant have antitumor, antimicrobial, hepatoprotective, immunomodulatory, hypolipidemic, and diuretic properties. The *M. alba* plant also has antianginal, antidysenteric, antianemic, and other pharmacological properties [6].

Thus, it is known from scientific literature that *M. alba* is one of the most important medicinal plants.

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