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Research Status and Progress on the Sarcotesta of Ginkgo biloba Seeds

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Abstract

The resource distribution and main characteristics of the sarcotesta of Ginkgo biloba seeds were reviewed in this paper. It has systematically summarized its main chemical constituents, flavonoids, terpene lactones and phenolic acids, and also summarized the current research progress on the pharmacological activities of this plant, such as antibacterial, anti-inflammatory and anti-tumor activities. The pharmacological activities and safety issue of ginkgolic acid, a characteristic constituent of the sarcotesta, are especially emphasized. Its application and development in the field of biological pesticides, medicine, preservation and other fields is also discussed. This paper summarizes the existing studies and analyzes the corresponding problems, and serves as the theoretical basis for high-efficiency utilization of the resources and further research on the sarcotesta of Ginkgo biloba seeds.

Keywords

Ginkgo biloba; ginkgo seed; sarcotesta; ginkgolic acid; pharmacological effects.

1. INTRODUCTION

Ginkgo biloba L., a deciduous tree in the Ginkgoaceae family, is known as a “living fossil”. Owing to its exceptional stress tolerance and long-lived traits, it has become a research hotspot across botany, pharmacy, ecology and other disciplines. Ginkgo biloba has a long cultivation and application history in China and is of great value for both medicinal and edible purposes. Ginkgo leaf extracts have been successfully developed into pharmaceuticals for treating cardiovascular and cerebrovascular diseases, Alzheimer’s disease and other ailments, with annual sales reaching billions of US dollars. Nevertheless, the sarcotesta, a by-product of ginkgo processing, has long been discarded or simply landfilled, which not only wastes resources but also imposes environmental burdens. In recent years, with deepening research on natural products, the chemical components and biological activities of different ginkgo tissues have attracted growing research interest.

China dominates global ginkgo resources, accounting for approximately 75 % of the world’s stock and more than 90 % of global output [1][2]. As a gymnosperm, the kernel, endotesta and sclerotesta of ginkgo seeds are collectively referred to as ginkgo nuts, while the fleshy outer covering is the sarcotesta. Making up roughly two-thirds of the total seed weight, the sarcotesta has historically been treated as waste, causing resource loss and environmental pressure.

Nevertheless, studies have demonstrated that the sarcotesta is abundant in bioactive substances, especially ginkgolic acids, whose contents are markedly higher than those in ginkgo leaves, and exhibit prominent insecticidal and antimicrobial activities [3]. It contains insecticidal phenolic substances such as ginkgolic acid, ginkgol and bilobol. Crude extracts derived from it have shown broad-spectrum control efficacy against multiple agricultural pests and pathogens when developed into biopesticides [4]. Accordingly, the potential value of the

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ginkgo sarcotesta has drawn increasing research attention and become a focus for natural-product research and comprehensive resource utilization.

This paper systematically reviews research status and latest advances covering resource distribution, chemical composition, pharmacological activities, application development and safety issues of the ginkgo sarcotesta, so as to furnish scientific evidence for its high-value development and sustainable utilization.

2. RESOURCES AND CHARACTERISTICS OF THE SARCOTESTA OF GINKGO BILOBA SEEDS

2.1. Overview of Resource Distribution

Ginkgo biloba is an ancient tree species native to China, which possesses the world's richest ginkgo resources. Geographically, large-scale plantations are mainly distributed in Pizhou of Jiangsu, Tancheng of Shandong, Hanzhong of Shaanxi, Suizhou of Hubei, Guilin of Guangxi, Ya'an of Sichuan, as well as Guiding and Weng'an in Guizhou Province [5]. Pizhou in Jiangsu is reputed as "Hometown of Ginkgo in China", with a planting area exceeding 300 000 mu, an annual ginkgo-nut yield of about 15 000 tons and an annual sarcotesta output of over 30 000 tons. Large-scale ginkgo orchards and street-plant ginkgo trees supply abundant raw materials for sarcotesta research and exploitation [6].

With the development of the ginkgo industry, the utilization potential of ginkgo leaves, nuts and sarcotesta has been increasingly recognized. In regions such as Jiangsu and Shandong, preliminary industrial chains for sarcotesta collection and primary processing have taken shape, laying a foundation for subsequent high-value utilization. For instance, multiple production lines for sarcotesta drying, pulverization and crude-extraction have been built in Pizhou with an annual processing capacity above 5 000 tons. As an emerging ginkgo-planting region, Guizhou is also rapidly expanding its ginkgo industry supported by favorable climate conditions and policy incentives.

2.2. Main Morphological Characteristics

The mature seed is ovoid, elliptical or nearly spherical, 2.5–3.5 cm long and 2 cm in diameter. They are orange-yellow or yellow, and may be covered with white powder which turns into a silvery colour when touched by water. The typical aroma produced by fatty-acid oxidation is a good indicator of ripeness after abscission of the fruit. The fleshy part around the hard shell of the seed is called the sarcotesta. Its normal thickness is 2–3 mm and it is about 75 % of the fresh-seed weight. Unopened, it has yellow or light-yellow soft, juicy flesh [6]. Fresh sarcotesta contains a high amount of mucilage and lipids, making it very susceptible to spoilage and putrefaction at room temperature, with the release of an offensive fetid odor. Hence, it should be processed or dried within 24 h after harvest. All the processing methods such as natural air-drying, hot-air drying and vacuum freeze-drying have significant influence on the retention of bioactive constituents.

2.3. Ecological and Resource-Utilization Values

In addition to its wide range of bioactive chemicals, the ginkgo sarcotesta also provides ecological benefits. Extracts of it have inhibitory effect against multiple soil-borne pathogenic microorganisms and can be used as soil amendments or biofumigants. Moreover, the phenolic acids in sarcotesta are partially biodegradable in natural environment, and do not possess the ability of persistent environmental pollution, which is in line with green agriculture development orientation. Therefore the use of ginkgo sarcotesta as resource is accompanied by splendid economic and ecological benefits.

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3. CHEMICAL CONSTITUENTS AND PHARMACOLOGICAL EFFECTS OF THE SARCOTESTA OF GINKGO BILOBA SEEDS

3.1. Major Chemical Constituents

The sarcotesta possesses complex chemical profiles with numerous identified compounds including alkylphenols, flavonoids, ginkgolides, phenolic acids, sterols and stenones. Catechol, ginkgol, palmitone, amino acids, tannins and various saccharides have also been detected [7]. Quantitative analysis reveals contents of pharmacologically relevant components: terpenoid lactones 0.19 mg/g, biflavonoids 2.31 mg/g and flavonoid glycosides 0.67 mg/g. Among nutritional components, crude fat (15.97 %) and starch (14.09 %) predominate. For toxic components, ginkgolic acids reach 71.80 mg/g while cyanogenic glycosides are 0.33 μg/g [8]. These figures indicate that the sarcotesta is both a source of potential toxicity and a reservoir of high-value bioactive substances.

Recent in-depth phytochemical investigations have identified previously unreported phenolic-acid derivatives and glycosides from the sarcotesta. For example, three novel alkylphenolic-acid glycosides were isolated, exhibiting moderate inhibitory activity against Staphylococcus aureus. Discovery of these new compounds provides new clues for exploring its pharmacological properties.

3.2. Pharmacological Effects

Accumulating studies have verified multiple biological activities of sarcotesta extracts, supporting their pharmacological potential, including anti-tumor, anti-inflammatory, antibacterial and insecticidal effects [9].

3.2.1 Anti-tumor Activity

Sarcotesta extracts suppress metastasis of B16-F10 melanoma by blocking extracellular-matrix degradation and tumor-cell migration via the TGF-β1/ERK1/2/MMP-9 signaling pathway [10]. Moreover, ginkgolic acids can induce apoptosis in diverse tumor-cell lines such as breast-cancer, hepatocellular-carcinoma and colon-cancer cells, possibly through activating the mitochondrial apoptotic pathway and inhibiting NF-κB activity.

3.2.2 Anti-inflammatory Activity

Sarcotesta extracts exert notable anti-inflammatory effects. They reduce capillary permeability in the early-stage inflammatory response and thereby alleviate inflammatory edema and exudation [11]. Animal experiments demonstrate that sarcotesta extracts markedly suppress carrageenan-induced rat paw edema and lower levels of pro-inflammatory cytokines TNF-α, IL-6 and IL-1β, showing pharmacological profiles analogous to non-steroidal anti-inflammatory drugs.

3.2.3 Antibacterial Activity

Sarcotesta extracts exhibit broad-spectrum antibacterial potency. Besides potent activity against Gram-positive bacteria, they also inhibit Gram-negative pathogens including Acinetobacter baumannii and Stenotrophomonas maltophilia. Further research indicates that the extracts interfere with the regulation of biofilm-associated genes, reduce release of extracellular DNA and cell-surface-bound proteins, and consequently restrain biofilm formation of Streptococcus haemolyticus-[12[13].

3.2.4 Fresh-keeping Effect

Sarcotesta extracts display promising fresh-keeping performance. Treatments with these extracts slow softening, restrain rising weight-loss and decay rates, and preserve fruit quality of winter jujube [14]. Such effects stem mainly from its antibacterial and antioxidant capacities, which retard postharvest senescence of fruits.

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3.2.5 Other Pharmacological Effects

Sarcotesta extracts also possess antiviral, antioxidant, hypoglycemic and neuroprotective properties. For instance, they inhibit replication of herpes simplex virus and vesicular stomatitis virus, mitigate oxidative stress, and improve blood-glucose homeostasis and insulin sensitivity in diabetic animal models.

3.3. Applied-Development Research

Zhang Kuichang et al [15]. developed an oil preparation using ginkgo sarcotesta raw materials for treating fungal skin infections, dermatitis, eczema and tinea, and filed a relevant patent application in 2018. Wang Qing et al [16]. isolated ginkgolic acids from sarcotesta and formulated cosmetic products that inhibit cutaneous tyrosinase activity, reduce melanin production and modulate keratinocyte proliferation-apoptosis for whitening, freckle fading and skin rejuvenation. In addition, sarcotesta extracts have been trialed for natural preservatives, feed additives and plant-growth regulators, demonstrating broad application prospects.

4. PROPERTIES AND RESEARCH PROGRESS OF GINKGOLIC ACID

4.1. Properties of Ginkgolic Acid

The ginkgolic acids are phenolic molecules with a salicylic-acid backbone and an aliphatic side-chain of different lengths. They are amphoteric and contain phenolic hydroxyl and carboxyl groups and are soluble in organic solvents, but not very soluble in water. This structural property makes them possess good bioactivities along with some toxic risks.

Ginkgolic acids are natural plant-derived compounds with outstanding antibacterial, insecticidal, anti-inflammatory, anti-viral and anti-tumor bioactivities[17][18]. However, there are still safety concerns: cytotoxicity, allergic reactions, non-immune toxicity and possible mutagenic and carcinogenic hazards have all been reported[19][20]. Thus, the total ginkgolic-acid content in ginkgo-leaf-extract pharmaceuticals should not be more than 5 mg/kg as stipulated in the Chinese Pharmacopoeia (2020 Edition), to ensure the safety of medicines [21].

4.2. Antibacterial Activity of Ginkgolic Acid

Laboratory assays confirm the broad-spectrum antibacterial capacity of ginkgolic acids against multiple Gram-positive and Gram-negative bacteria including Bacillus subtilis, Escherichia coli, Staphylococcus aureus, Bacillus dysenteriae and Pseudomonas aeruginosa [22][23]. Against phytopathogenic fungi such as Gibberella, Verticillium, Fusarium, Phytophthora and Rhizopus, ginkgolic acids outperform carbendazim, a commercially available fungicide [24]. Ginkgolic-acid extracts suppress growth of Colletotrichum gloeosporioides, Ralstonia solanacearum, Rhizoctonia solani, Gibberella spp [25]. and Exserohilum turcicum, reaching efficacy comparable with certain antifungal agents. They also inhibit five vegetable pathogens: Fusarium oxysporum f. sp. cucumerinum, Colletotrichum higginsianum, Alternaria brassicae, Rhizoctonia solani and Sclerotium rolfsii [26].

4.3. Insecticidal Activity of Ginkgolic Acid

Ginkgolic acids show great promise for agricultural pest management. Sarcotesta extracts exert strong contact toxicity and antifeedant activity against common agricultural pests such as aphids, spider mites, cabbage caterpillars and cotton bollworms. Their mode of action may involve disrupting insect nervous-system functions and suppressing digestive-enzyme activities [4].

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4.4. Research Progress on Ginkgolic Acid

Research on ginkgolic acids falls into two major orientations: extraction from ginkgo sarcotesta and removal from ginkgo-leaf extracts. Driven by ginkgo-industry expansion, publications on ginkgolic acids keep increasing year-by-year [27]. However, most existing research focuses on developing processes for eliminating ginkgolic acids from ginkgo-derived products. Although bioactivities and application potential of ginkgolic acids in pesticides and medicine have been preliminarily validated, field trials have provided practical evidence: a 10 % ginkgolic-acid suspension agent achieved superior control efficacy against muskmelon powdery mildew compared with 80 % carbendazim preparations [28]. In formulation development, Yang Xiaoming et al [29]. successfully prepared ginkgolic-acid microemulsions, offering new insights for practical deployment.

4.5. Toxicological and Safety Evaluation of Ginkgolic Acid

The main constraint to actual applications of ginkgolic acids is toxicity. High dose ginkgolic acids have been shown to cause hepatorenal injury, gastrointestinal irritation and hypersensitivity in the skin in animal studies. The potential toxicological mechanisms are likely to be linked to induction of oxidative stress, disturbance of mitochondrial function and activation of inflammatory pathway. Hence, during product development the dosage and administration modes have to be carefully controlled to ensure safety.

5. CONCLUSIONS AND PROSPECTS

The ginkgo sarcotesta is an abundant agricultural by-product with a high capacity of bioactive compounds including flavonoids, lactones and phenolic acids that have potent antibacterial, anti-inflammatory, anti-tumor and other pharmacological properties. Ginkgolic acid is its typical component and has a huge potential for exploitation as botanical pesticides and functional ingredients. This is reflected in an increasing number of publications related to ginkgolic acids, mostly dealing with extraction and removal technologies.

Firstly it is important to reconcile the bioactivity and toxicity of the ginkgolic acids for practical translation. Further investigation is needed to elucidate structure-activity relationships and safe-dose ranges. Systematic structural modification and toxicological evaluation is suggested to screen high efficiency and low toxicity derivatives.

Secondly, the studies that are currently available are mainly laboratory scale. Breakthroughs are needed for industrial scale extraction-purification technologies that are high efficiency, environmentally friendly and low cost. Some new extraction methods, such as green-solvent (e.g. deep-eutectic-solvent) extraction, membrane separation and continuous counter-current extraction can be adapted to improve the extraction yield and reduce the organic-solvent residues.

Third, the synergism of more than one active component from sarcotesta has not been fully understood and systematic pharmacodynamic studies are inadequate. Multi-component synergism should be studied by modern analytical methods such as metabolomics and network pharmacology to elucidate the molecular mechanisms of multi-component synergism.

Further research is required to investigate the synergism between sarcotesta bioactive compounds and to form high-value products like eco-friendly biopesticides, fruit-and-vegetable preservatives, specific dermatological drugs and natural antioxidants. Considering China's dominance in the global ginkgo resource, there is practical importance in setting up integrated systems for sarcotesta collection and comprehensive utilization to expand the ginkgo industrial chain, and to maximize the sustainability of ginkgo resources.

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Furthermore, systematic collection of ginkgolic-acid toxicological information is recommended to establish safety-evaluation standards and promote the use of ginkgolic-acid in medicine and agriculture in compliance with these standards. The multidisciplinary integration and industry-university-research collaboration can be used to turn the ginkgo sarcotesta from waste into a valuable resource and to make contributions to green development and circular-economy goals.

REFERENCES

[1] Zhang, X., Yu, W., Cai, J., & others. (2020). Effects of Ginkgo biloba exocarp extract on mulberry leaf growth, physiological indexes and cocoon quality. Chinese Agricultural Science Bulletin, 36(10), 47–52.

[2] Tang, S., Song, J., Gu, S., & others. (2020). Separation of ginkgolic acids from Ginkgo biloba exocarp by macroporous resin combined with high-speed counter-current chromatography. Food Science and Technology, 45(1), 280–293. https://doi.org/10.1590/fst.37719

[3] Pan, H., Wu, C., Cao, F., & others. (2011). Extraction and component study of ginkgolic acids in ginkgo seed kernel. Journal of Nanjing Forestry University (Natural Sciences Edition), 35(6), 29–33.

[4] Shi, Q. (2004). Study on prevention and control of agricultural pests with ginkgolic acid substances. Chemistry and Industry of Forest Products, (2), 84–87.

[5] Tian, L. (2015). Study on extraction technology of ginkgolic acid from Ginkgo biloba exocarp [Master's thesis]. Southeast University.

[6] Huang, L. (2023). Study on separation, purification technology and bacteriostatic effect of ginkgolic acid from ginkgo sarcotesta [Master's thesis]. Guizhou University.

[7] Ni, X., & Wu, M. (2001). Study on extraction and application of ginkgolic acid from Ginkgo biloba exocarp. Journal of Hubei University of Chinese Medicine, (4), 22–24+3.

[8] Luo, K. (2019). Chemical basis of medicinal and health-care effects of ginkgo seed and Ginkgo biloba exocarp [Doctoral dissertation]. Wuhan University of Technology.

[9] Zhu, M., Ren, J., Shen, N., Xin, H., Liu, Y., Li, W., & Cui, Y. (2022). Research progress on chemical constituents, biological activities and resource utilization of Ginkgo biloba exocarp. West China Journal of Pharmaceutical Sciences, 37(5), 587–593.

[10] Luo, C., Wang, M., Gao, Y., & others. (2019). Ginkgo biloba exocarp extracts inhibits metastasis and its effects on TGF-β1/ERK1/2/MMP-9 signaling pathway in B16-F10 melanoma. In Abstracts of the 15th National Academic Conference of Chinese Pharmacological Society (p. 2).

[11] Liu, G. (2016). Pharmacological effects and clinical application of Ginkgo biloba preparations. Shanghai Medical & Pharmaceutical Journal, 37(3), 8–22.

[12] Shen, N., Liu, Y., Cui, Y., & Xin, H. (2022). Large-scale targetedly isolation of biflavonoids with high purity from industrial waste Ginkgo biloba exocarp using two-dimensional chromatography coupled with macroporous adsorption resin enrichment. Industrial Crops & Products, 175, 114264. https://doi.org/10.1016/j.indcrop.2021.114264

[13] Wang, C., Wei, P., Song, C., Wang, X., Zhu, G., Yang, Y., Xu, G., Hu, Z., Tang, L., Liu, H., & Wang, B. (2022). Evaluation of the antimicrobial function of Ginkgo biloba exocarp extract against clinical bacteria and its effect on Staphylococcus haemolyticus by disrupting biofilms. Journal of Ethnopharmacology, 298, 115602. https://doi.org/10.1016/j.jep.2022.115602

[14] Zhang, J., Wang, W., & Wang, G. (2018). Study on fresh-keeping effects of Ginkgo biloba exocarp and ginkgo leaf extracts on winter jujube. Ningxia Journal of Agriculture and Forestry Science and Technology, 59(7), 55–57.

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[15] Zhang, J., Wang, W., & Wang, G. (2018). Study on fresh-keeping effects of Ginkgo biloba exocarp and ginkgo leaf extracts on winter jujube. Ningxia Journal of Agriculture and Forestry Science and Technology, 59(7), 55–57.

[16] Zhang, J., Wang, W., & Wang, G. (2018). Study on fresh-keeping effects of Ginkgo biloba exocarp and ginkgo leaf extracts on winter jujube. Ningxia Journal of Agriculture and Forestry Science and Technology, 59(7), 55–57.

[17] Zang, L., Li, Y., Ni, L., & Zhang, L. (2000). Research overview of ginkgolic acid. Chinese Journal of Pharmaceuticals, (7), 45–48.

[18] Xiao, Y., Li, F., & Tao, Z. (2020). Research progress on the anti-tumor effect of ginkgolic acid. Chinese Pharmacological Bulletin, 36(11), 1486–1489.

[19] Pan, H., Wu, C., Cao, F., Fan, G., Yang, J., Jia, S., & Li, T. (2011). Extraction and component study of ginkgolic acids in ginkgo seed kernel. Journal of Nanjing Forestry University (Natural Sciences Edition), 35(6), 29–33.

[20] Baron-Ruppert, G., & Luepke, N.-P. (2001). Evidence for toxic effects of alkylphenols from Ginkgo biloba in the hen's egg test (HET). Phytomedicine, 8(2), 133–138. https://doi.org/10.1078/09447110130032245

[21] Chinese Pharmacopoeia Commission. (2020). Pharmacopoeia of the People's Republic of China (Volume I). China Medical Science Press.

[22] Liang, L. (2003). Research status and development and utilization prospect of Ginkgo biloba exocarp. China Resources Comprehensive Utilization, 21(10), 12–14.

[23] Zhao, C. (1997). Extraction of acidic constituents from Ginkgo biloba exocarp and discussion on its medicinal value. Chinese Traditional and Herbal Drugs, 28(4), 250–251.

[24] Lou, F., Wang, G., & Guo, Y. (1998). Study on chemical constituents of Ginkgo biloba exocarp. Journal of China Pharmaceutical University, (4), 76–78.

[25] Ji, Y. (2005). Preliminary study on inhibitory effect of Ginkgo biloba exocarp extract on crop pathogenic bacteria. Journal of Anhui Agricultural Sciences, 33(9), 1598–1603.

[26] Lin, Q., Li, J., Lin, Z., Huang, Y., Xu, W., & Lin, G. (2014). Inhibitory effect of Ginkgo biloba exocarp extracts against several vegetable pathogenic bacteria. Subtropical Plant Science, 43(3), 242–245.

[27] Xiao, S., Cao, C., Liu, H., Gao, X., Sun, Y., Zhao, J., Li, X., Guo, Y., Zhu, C., Chen, X., Wang, J., Li, S., Peng, Y., Wang, Y., Wang, X., Hu, Y., Guo, H., Yang, W., Cai, T., & Chen, G. (2022). Pharmaceutical research progress of Ginkgo biloba leaf extract. China Pharmaceutical Affairs, 36(4), 429–443.

[28] Zhang, S., Tian, F., Liu, Y., Leng, P., Rui, W., Su, G., Cui, A., & Lü, X. (2018). Control efficacy of ginkgolic acid suspension agent against muskmelon powdery mildew. China Fruits and Vegetables, 38(11), 44–46.

[29] Yang, X., Xia, L., Liu, W., & Liu, F. (2008). Development of 1.5 % ginkgolic acid microemulsion. Pesticides, (5), 330–332.