

Review Article

Recent advances on chemical constituents of *Dioscorea opposita* and their biological activities

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Abstract: *Dioscorea opposita* is a famous medicinal and edible plant that contains polysaccharides, stilbenes, diarylheptanoids, steroids, lignans, and terpenoids. It has many biological activities, such as anti-oxidation, enhancement of immunity, and hypoglycemic activity. In this paper, the research progress on the chemical constituents of *D. opposita* and their biological activities was reviewed. This review provides a scientific basis for the further development and utilization of *D. opposita*.

Keywords: *Dioscorea opposita*; chemical constituents; biological activities; research progress

1. Introduction

Chinese yam (*Dioscorea opposita* Thunb.) is a perennial twining vine of the genus *Dioscorea* in the family of Dioscoreaceae^[1]. Chinese Yam was first recorded in *Shennong's Classic of Materia Medica* and is listed as top grade. It is sweet in taste and neutral in nature. It has the functions of invigorating the spleen, replenishing Qi, nourishing Yin, and strengthening the spleen^[2]. It is one of the earliest medicinal and edible plants in China. It is widely used in the food and medical care fields. The cultivation of Chinese yam originated in China and can be traced back to the *Compilation of Four Seasons* written by E Han during the late Tang and Five Dynasties periods^[3]. Currently, it is cultivated in Henan, Shandong, Hebei, Anhui, Shanxi, Sichuan, etc.^[4] Among them, the ones produced in Wen County, Wuzhi, and other areas along the Qin River (the ancient Huaiqing Prefecture) in Jiaozuo City, Henan Province, have the best quality and are called Huaiyam^[5]. It ranks first among the four major Huai medicines and is praised as “Huai Shen (Huaiyam panax)”^[6].

Dioscorea opposita is not only rich in nutrients, such as starch, protein, amino acids, and many minerals, such as Fe, Zn, Cu, and Ca, but also contains polysaccharides, sanguinarines, allantoin, yam saponin, and other chemical components, which have a variety of pharmacological effects, such as anti-inflammatory, immunomodulatory, and anti-tumor^[7-9]. In recent years, studies on *Dioscorea opposita* mainly focused on polysaccharides and their bioactivities, and some new progress has been made in the research of the small molecule compounds of polysaccharides and their bioactivities. With the deepening of the research on the chemical composition of *Dioscorea opposita* and its biological activities, more and more active substances and biological functions of *Dioscorea opposita* have been gradually revealed. In this paper, the chemical constituents and their biological activities in Chinese yam are summarized by reviewing the relevant literature in recent years, with a view of providing a certain reference basis for the further development and utilization of *Dioscorea opposita*.

2. Chemical composition

2.1. *Dioscorea opposita* polysaccharides

Polysaccharides are the main active substance in *Dioscorea opposita*, which has a series of health effects and pharmacological activities, such as antioxidant, hypoglycemic, and immunity enhancement. The commonly used methods for extracting *Dioscorea opposita* polysaccharides include water extraction, ultrasonic-assisted extraction, ultrafiltration concentration extraction, microwave-assisted extraction, enzymatic extraction, acid-water extraction, hot water extraction, high-pressure water extraction, etc. However, due to the complex structure and composition of yam polysaccharides, their structure is not yet well-defined. Additionally, the choice of the extraction method can lead to variations in the monosaccharide composition, uronic acid content, and relative molecular weight of polysaccharides^[10].

Wang^[11] used modern analytical and biomacromolecule research techniques combined with methylation reactions to characterize the polysaccharides of Chinese yam and preliminarily postulated the structures of DOP1, DOP2, and other purified polysaccharides. In-vitro simulated gastrointestinal digestion studies revealed that DOP1 had a low degree of degradation in gastric juice, accompanied by the production of reducing sugars and free monosaccharides; it was not degraded during intestinal digestion. DOP2 may be degraded to a low degree during gastric digestion, with irregular changes in the reducing sugar content, and accompanied by the production of monosaccharides. The anti-inflammatory activity of *Dioscorea opposita* polysaccharides was investigated via a model of a swelling rat toe caused by carrageenan gum, and the results showed that DOP1 and DOP2 had an inhibitory effect on inflammatory exudates. Liu^[12] took *Dioscorea opposita* Thunb. as the research object and used the aqueous-alcoholic precipitation method, the Sevage method, and the dialysis method to isolate and purify yam to get polysaccharides, which was identified using SDS-PAGE, Molisch reaction, and infrared spectroscopy, and the content of polysaccharides in the *Dioscorea opposita* Thunb. was determined to be 91.77% via the phenol-sulfuric acid method; the study also noted that *Dioscorea opposita* polysaccharides can be obtained using further in-vivo and in-vitro anti-aging experiments. It was also found that the polysaccharides of Chinese yam could significantly increase the expression of the Klotho gene in mouse brain and kidney tissues and thus play an anti-aging role. Zhang^[6] used the bulbil of common yam as the research object to extract polysaccharides via water immersion, alkaline immersion, and enzyme immersion; the study structurally characterized the purified polysaccharide fragments and obtained a neutral polysaccharide DBP1 and an acidic polysaccharide DBP2, with carbohydrate contents of 724.73 mg/g and 777.24 mg/g, respectively, and molecular weights (Mw) of 21.9 kDa and 109.79 kDa, respectively. The monosaccharide composition of DBP1 contains nine monosaccharides, which are mainly composed of the 1,4-Galp bond on the main chain with some 1,3-Glcp, 1,6-Glcp, and 1,6-Galp bonds that may be located either in the main chain or in the side chains.

2.2. Stilbenes

Stilbenes are a class of naturally occurring phenolic compounds with 1,2-diphenylethylene as the backbone structure and have structural and active diversity. Zheng et al.^[13] isolated two new compounds from Chinese yam identified as dioscoposides A (**1**) and B (**2**). Sautour et al.^[14] isolated one new compound from yam rhizome identified as 3,4,6-trihydroxyphenanthrene-3-O- β -D-glucopyranoside (**3**). Yang et al.^[15] isolated 10 dibenzyl-type compounds and 3 phenanthrenes from the chloroform-soluble site of *Dioscorea opposita*, among which 3,5-dihydroxy-4-methoxybibenzyl (**4**), 3,3',5-trihydroxy-2'-methoxybibenzyl (**5**), 10,11-dihydro-dibenz[b,f]oxepin-2,4-diol (**6**), and 10,11-dihydro-4-methoxy-dibenz[b,f]oxepin-2-ol (**7**) are new compounds, while batatasin III (**8**), batatasin IV (**9**), tristin (**10**), 2',3,5-trihydroxybibenzyl (**11**), 2',4-dihydroxy-3,5-dimethoxybibenzyl (**12**), 3,4-dimethoxy-2'-hydroxybibenzyl (**13**), 3,5-dimethoxy-2,7-

phenanthrenediol (**14**), hircinol (**15**) and 9,10-dihydro-7-methoxy-2,5-phenanthrenediol (**16**) are known compounds. In addition, Ma et al.^[16] isolated a new compound from the above-ground parts of Chinese yam, identified as 6,7-dihydroxy-2-methoxy-1,4-phenanthredione (**17**). Liu^[17] isolated and identified five phenanthrene constituents from the above-ground parts of *Dioscorea opposita*, which are 7-hydroxy-2,6-dimethoxy-1,4-phenanthredione (**18**), volucrin (**19**), 6-hydroxy-2,4,7-trimethoxyphenanthrene (batatasin I, **20**), and 7-hydroxy-2,4,6-trimethoxyphenanthrene (**21**). In addition, Zhang et al.^[18] isolated two α -glucosidase inhibitors, identified as batatasin I (**20**) and 2,4-dimethoxy-6,7-dihydroxyphenanthrene (**22**), from the skin of Chinese yam using activity-directed isolation. The chemical structures of the above-mentioned stilbenes are shown in **Figure 1**.

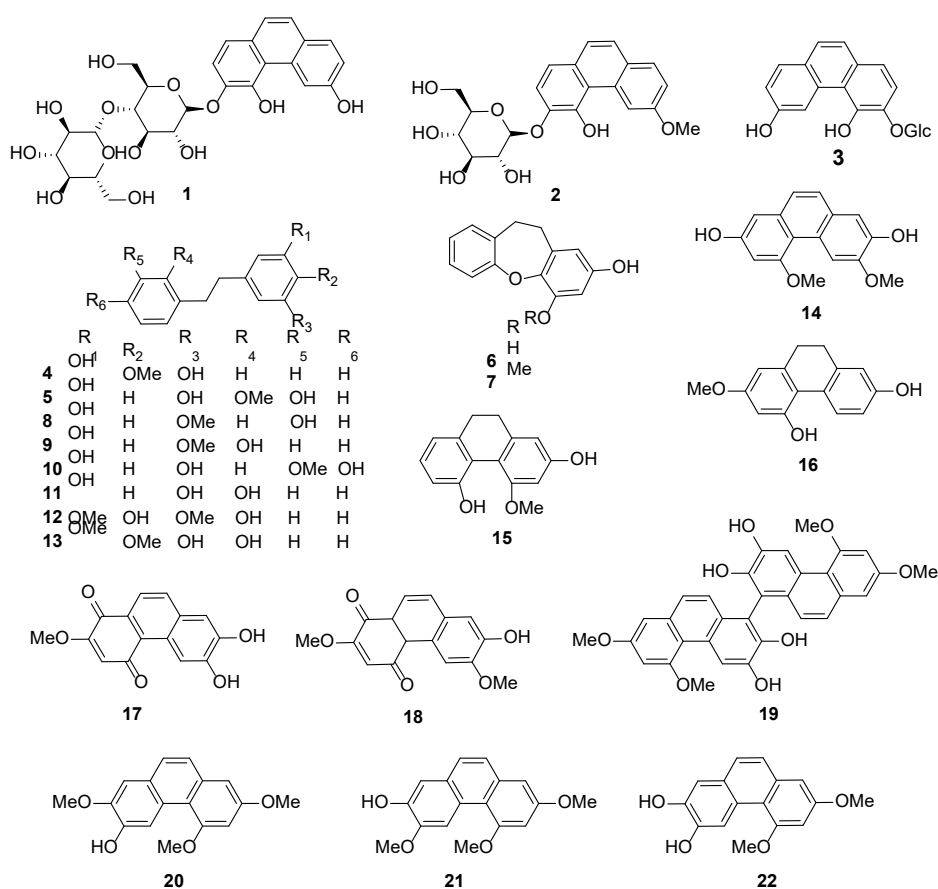


Figure 1. Stilbenes.

2.3. Diphenylheptanes

Diphenylheptanes, which can be classified into linear diphenylalkanes and cyclic diphenylheptanes^[19], possess a variety of biological and pharmacological activities, including antioxidant, anti-hepatotoxic, anti-inflammatory, antiproliferative, antiemetic, and antitumor^[20]. Studies have shown that diphenylheptanes show promising applications in the treatment of liver diseases^[21].

Cao et al.^[22] isolated two new diphenylheptanes, which are diosniponols E (**23**) and F (**24**), and seven known compounds from yam, namely, diosniponol A (**25**), diosniponol B (**26**), (1*R*,3*S*,5*R*)-1,7-bis(4-hydroxyphenyl)-1,5-epoxy-hydroxyheptane (**27**), 1,7-bis(4-hydroxyphenyl)heptane-4*E*,6*E*-heptadien-3-one (**28**), (3*R*,5*R*)-1,7-bis(4-hydroxy-3-methoxyphenyl)-3,5-heptanediol (**29**), (3*S*,5*S*)-1-(4-hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane-3,5-diol (**30**), and (3*R*,5*R*)-3,5-dihydroxy-1,7-bis(4-hydroxyphenyl)heptane (**31**). Feng et al.^[23] isolated a new natural product, which is 5-ethoxy-1,7-

diphenylheptan-3-one from yam rhizome (**32**), and six known compounds 1,7-diphenyl-4-hepten-3-one (**33**), 1,7-bis(4-hydroxyphenyl)-4-hepten-3-one (**34**), 1,7-bis(4-hydroxy-3-methoxyphenyl)-3,5-heptanediol (**35**), 1,7-bis(4-hydroxyphenyl)-1,5-epoxy-3-hydroxyheptane (**36**), 5-hydroxy-1,7-bis(4-hydroxyphenyl)-heptan-3-one (**37**), and 1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)-3,5-heptanediol (**38**), but compounds (**32**) and (**35–38**) were not stated in their absolute configuration. Yang et al.^[15] isolated six diphenylheptanes from the chloroform-soluble site of yam and identified them as (1*E*,4*E*,6*E*)-1,7-bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one (**39**), (4*E*,6*E*)-7-(4-hydroxy-3-methoxyphenyl)-1-(4-hydroxyphenyl)-4,6-heptadien-3-one (**40**), (4*E*,6*E*)-1,7-bis(4-hydroxyphenyl)-4,6-heptadien-3-one (**28**), (3*R*,5*R*)-3,5-dihydroxy-1,7-bis(4-hydroxyphenyl)-3,5-heptanediol (**31**), and (3*R*,5*R*)-1,7-bis(4-hydroxy-3-methoxyphenyl)-3,5-heptanediol (**41**) and (3*R*,5*R*)-1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)-3,5-heptanediol (**42**). Zhang et al.^[24] isolated and identified the compound of 1,7-bis(4-hydroxyphenyl)heptane-3,5-diol (**43**) from *Dioscorea opposita* by using the α -glucosidase inhibitory activity of yam as a guide. The chemical structures of the above-mentioned diphenylheptanes are shown in **Figure 2**.

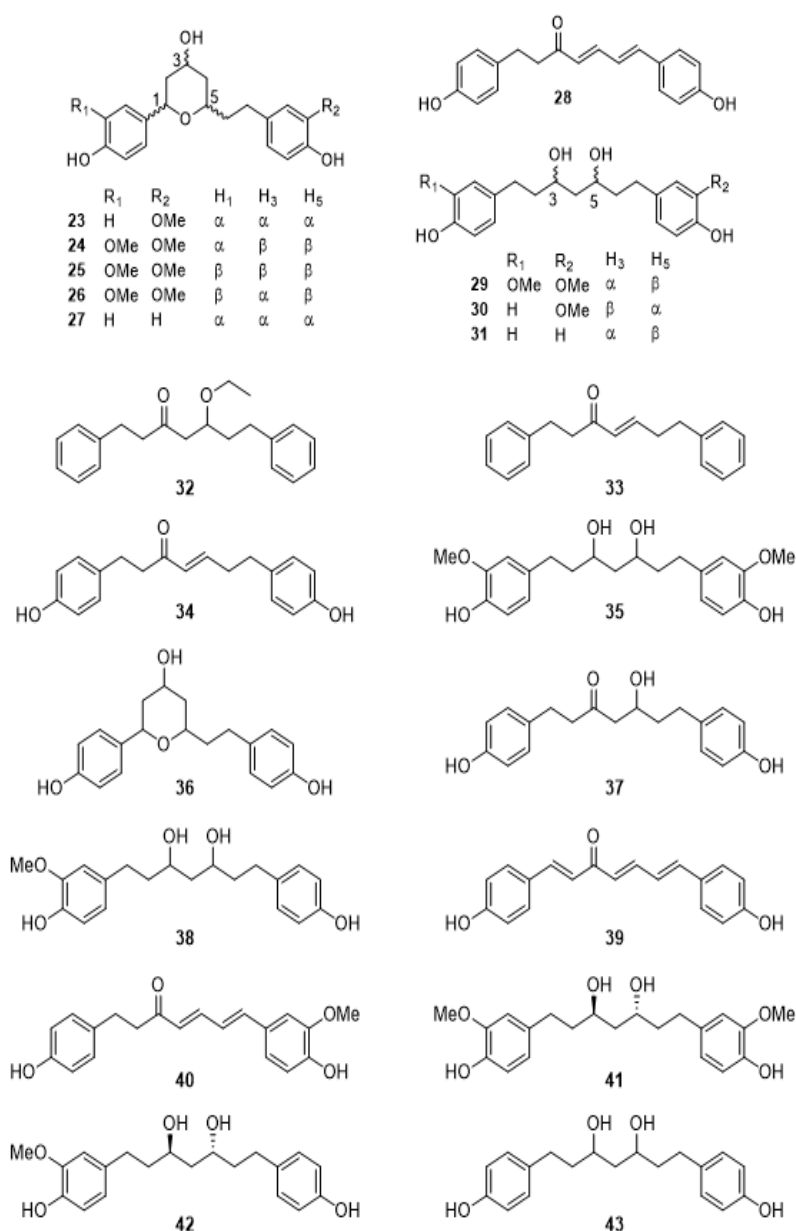


Figure 2. Diphenylheptanes.

2.4. Tyramine compounds

There is a class of compounds containing structural fragments of p-hydroxyphenethylamine (also known as tyramine) in yam, which is categorized as tyramine compounds in this paper. Zhang et al.^[24] used the α -glucosidase inhibitory activity of huai yam as an orientation, from which they isolated and identified two tyramine compounds, namely, *trans*-*N*-p-coumaroyltyramine (**44**) and *cis*-*N*-p-coumaroyltyramine (**45**). Feng et al.^[23] isolated and identified compounds *trans*-*N*-feruloyltyramine (**46**) and *trans*-*N*-cinnamoyltyramine (**47**) from Chinese yam by studying its chemical composition. The chemical structures of the above-mentioned tyramine compounds are shown in **Figure 3**.

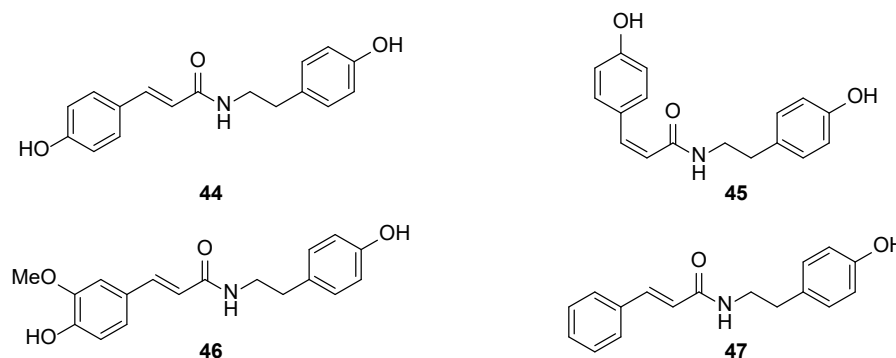


Figure 3. Tyramine compounds.

2.5. Steroids

Ma et al.^[16] isolated and identified the compound cartenoside (**48**) from the above-ground parts of Chinese yam. Bai et al. comprehensively utilized column chromatography and wave spectrometry to isolate and identify compounds β -sitosterol acetate (**49**) and 7-carbonyl- β -sitosterol (**50**) from the ethanol part of yam^[25,26]. Liu^[17] carried out a systematic study on the above-ground parts of the active parts of yam, which isolated and identified (24*S*)-24-ethylcholesta-3,5 α ,6 β -triol (**51**), stigmast-4-ene-3 α ,6 β -diol (**52**), (3 β ,7 α)-7-methoxystigmast-5-en-3-ol (**53**), (22*E*)-5 α ,8 α -epidioxyergosta-6,22-dien-3 β -ol (**54**), and other sterol components. The chemical structures of the above-mentioned steroids are shown in **Figure 4**.

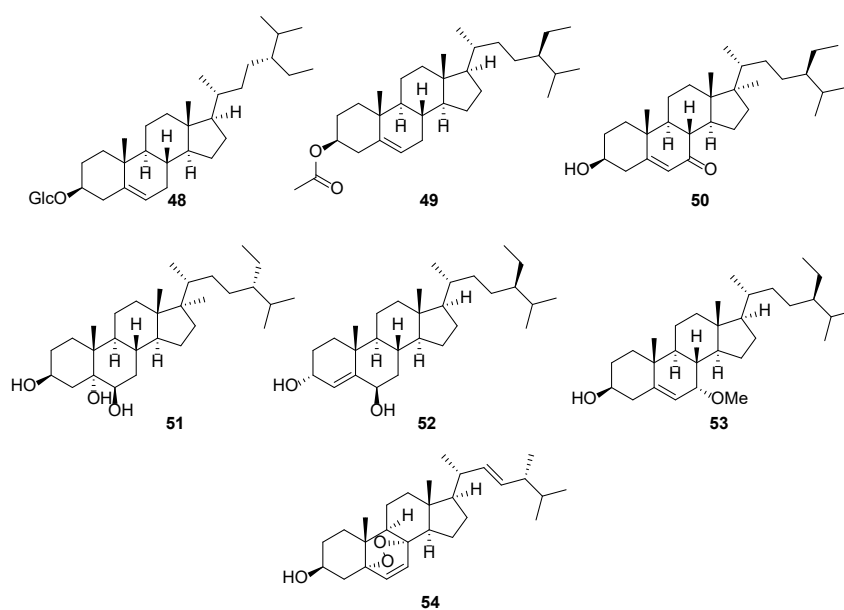


Figure 4. Steroids.

2.6. Flavonoids

Feng et al.^[27] isolated a flavonoid chemical constituent from *Dioscorea opposita*, which was identified as helichrysin A (**55**). Ma et al.^[16] isolated apigenin (**56**) from the chloroform-soluble part of yam. Ma et al.^[16] obtained several flavonoid constituents, including chrysoeriol 4'-O- β -D-glucopyranoside (**57**), chrysoeriol 7-O- β -D-glucopyranoside (**58**), and alternanthin (**59**), from the ethanol extract of the above-ground parts of Chinese yam. Liu^[17] isolated and identified six flavonoids from the above-ground parts of yam, which are 5,7,3',4'-tetrahydroxy-8-O- β -D-glucopyranoside (**60**), 6-*trans*-[2''-O-(α -rhamnopyranosyl)]ethenyl-5,7,4'-trihydroxyflavone (**61**), chrysoeriol (**62**), kaempferol-3-methyl ether (**63**), lignans (**64**), and quercetin (**65**). From the summary of the studies on the chemical composition of yam, it can be observed that flavonoids are mainly found in the above-ground parts of *Dioscorea opposita*, and only two flavonoids have been identified from the rhizome, namely, elichrysin A (**55**) and apigenin (**56**). The chemical structures of the above-mentioned flavonoids are shown in **Figure 5**.

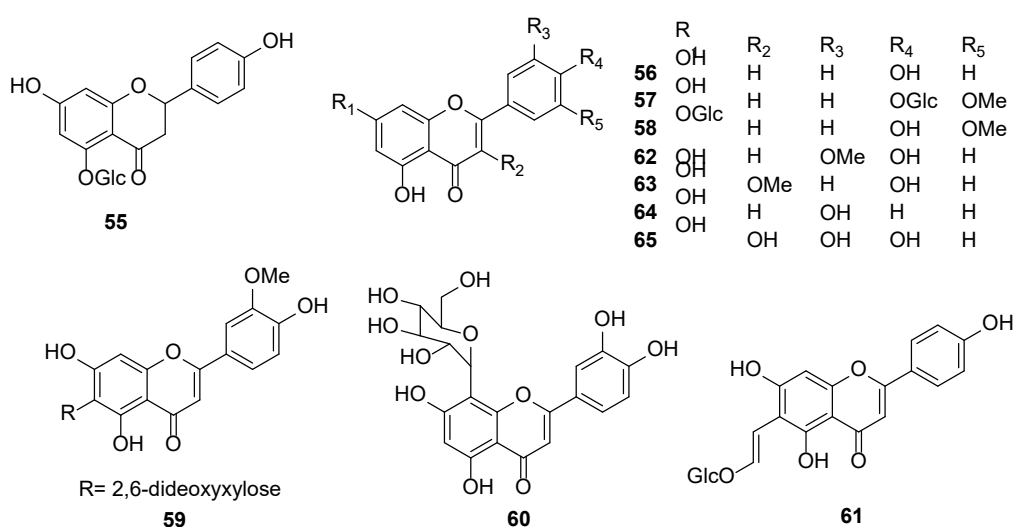


Figure 5. Flavonoids.

2.7. Terpenoids

Liu^[17] studied the above-ground parts of the active site of Chinese yam and identified several monoterpenoids, such as (*S*)-dehydrovomifoliol (**66**), blumenol A (**67**), (3*R*)-4(2*R*,4*S*)-2-hydroxy-2,6,6-trimethylcyclohexylidenej-3-buten-2-oneol (**68**), pubinernoid A (**69**); 3 triterpenoids 9,19-cyclolart-25-en-3*R*,24*R*-diol (**70**), cycloeucaenol (**71**), and epi corkyol (**72**). The chemical structures of the above-mentioned terpenoids are shown in **Figure 6**.

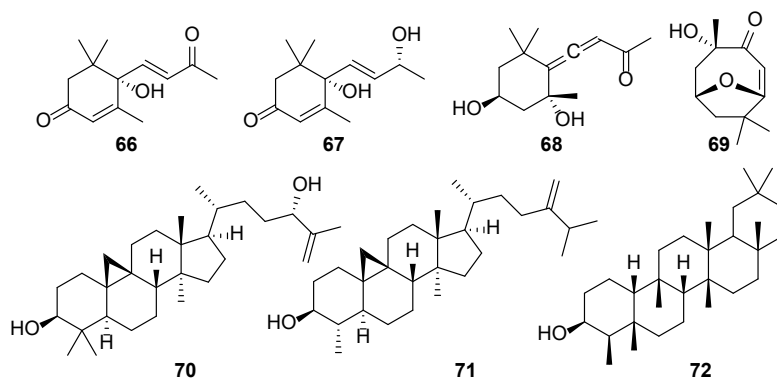


Figure 6. Terpenoids.

2.8. Lignans

Liu^[17] isolated and purified constituents from the above-ground parts of yam and identified (+)-syringaresinol (**73**). Ren et al.^[28] used chromatographic separation to isolate and purify paulownin (**74**) and (+)-8-hydroxypineol (**75**) from the acetone extract of the stem and leaves of Chinese yam, both of which were isolated from yam for the first time. The chemical structures of the above-mentioned lignans are shown in Figure 7.

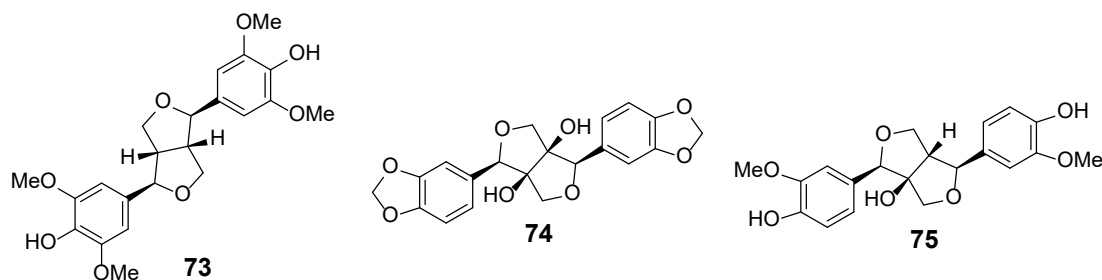


Figure 7. Lignans.

2.9. Other compounds

Feng et al. identified bungein A, hydroquinone, vanillin, arbutin, methyl butyrate-4-O- β -D-glucopyranoside, phenylalanine, 1,2-benzenedicarboxylic acid, 1,2-bis[2-(2-hydroxyethoxy) ethyl]ester, thymine, and 5'-deoxy-5'-sulfinyladenosine, etc. Moreover, a new pyrazine derivative was isolated from Chinese yam and identified as 2-(1',2', 3'-trihydroxybutyl-4'-O- α -D-glucosidyl)-6-(2'',3'',4'''-trihydroxybutyl)-pyrazine^[27,29]. Li et al.^[30] isolated a compound containing bound water from yam, which was identified as 1,5-dimethylcitrate monohydrate. Sautour^[14] isolated several known compounds from yam rhizome, including palmitic acid, palmitoylcholine, and others. Wang^[31] used UC, IR, MS, and NMR to identify several chemical constituents in yam drinking tablets, such as monomethyl citrate, dimethyl citrate, trimethyl citrate, cyclo-(Phe-Tyr), and several other compounds. Liu^[17] identified the compounds of n-butyl- β -D-fructopyranoside, p-hydroxybenzaldehyde, 3,4-dihydroxybenzaldehyde, 4-hydroxy-3-methoxybenzaldehyde, 1-n-hexadecanoic acid glycerol ester, eicosatetraic acid, hexadecanoic acid, indole-3-carboxaldehyde, and allantoin in the above-ground portion of Chinese yam. Ren et al.^[28] isolated 1H-indazole, amarantholidoside IV, and 3-indolecarboxylic acid for the first time from the acetone extract of the stem and leaves of Chinese yam.

3. Biological activities

Dioscorea opposita polysaccharides have good effects in the treatment of chronic kidney disease, diabetes mellitus, coronary heart disease, atherosclerosis, etc., and are most widely studied by scholars^[1]. Yam saponins, phenols, and other small molecules also have potential exploitation values. The following summarizes the biological activities related to the chemical constituents of yam, with a view of providing a reference for the research and development, as well as the utilization, of yam.

3.1. Antioxidant activity

Yang et al.^[15] isolated 19 compounds from the chloroform fraction of yam and conducted antioxidant activity analysis on some of these compounds by assessing their ability to scavenge DPPH and superoxide radicals. Among these compounds, tristin, 2',4-dihydroxy-3,5-dimethoxybibenzyl, hircinol, 9,10-dihydro-7-methoxy-2,5-phenanthrenediol, (4*E*,6*E*)-7-(4-hydroxy-3-methoxyphenyl)-1-(4-hydroxyphenyl)-4,6-heptadien-3-one, and (3*R*,5*R*)-1,7-bis(4-hydroxy-3-methoxyphenyl)-3,5-heptanediol exhibited significant

antioxidant activity. Nagai et al.^[32] found that the mucilage water extract of Chinese yam tubers showed no inhibitory activity against angiotensin-converting enzymes but exhibited high scavenging activity against DPPH, superoxide radicals, and hydroxyl radicals. Liu et al.^[33] conducted antioxidant activity studies on ethanol extracts of yam peel and yam flesh separately. The results indicated that the yam peel extract had significantly better DPPH and hydroxyl radical scavenging activity compared with the yam flesh extract. Ma et al.^[16] screened multiple compounds from ethanol extracts of the aerial parts of yam for antioxidant activity. The results showed that compounds, such as 6,7-dihydroxy-2-methoxy-1,4-phenanthrenedione, chrysoeriol 4'-O- β -D-glucopyranoside, chrysoeriol 7-O- β -D-glucopyranoside, and alternanthin, exhibited moderate to strong antioxidant activity.

3.2. Blood glucose lowering activity

Cao et al.^[22] conducted α -glucosidase inhibition activity screening on 10 compounds isolated and identified from Chinese yam. Among them, (2*R*,4*R*)-6-(4-hydroxy-3-methoxyphenyl)-hexane-1,2,4-triol and 1,7-bis(4-hydroxyphenyl)heptane-4*E*,6*E*-heptadien-3-one showed inhibitory effects on α -glucosidase, with IC₅₀ values of 16.2 ± 2.2 and 8.7 ± 1.6 μ M, respectively. Zhang et al.^[18] found that yamogenin I and 2,4-dimethoxy-6,7-dihydroxyphenanthrene, selectively extracted and identified from yam peel extracts, exhibited significant α -glucosidase inhibition activity with IC₅₀ values of 2.55 mM and 0.40 mM, respectively, significantly higher than the positive control.

Yu et al.^[34] discovered that feeding diabetic rats with nano-yam polysaccharides at concentrations of 50 mg/mL and 100 mg/mL for 12 and 30 days significantly reduced blood glucose levels, improved glucose tolerance, and increased glycogen and C-peptide content. Furthermore, the “three highs and one low” symptoms of diabetic rats were improved.

3.3. Blood lipid-lowering activity

Nishimura et al.^[35] studied the effects of *Dioscorea opposita* on lipid metabolism and cecal fermentation in rats. The results showed that yam has the ability to reduce plasma cholesterol levels and may be associated with the inhibition of the release of very low-density lipoprotein (VLDL). Yang et al.^[36] discovered that the butanol fraction of yam and its isolates exhibited significant lipase inhibition activity. Further research on the lipid-lowering mechanism of yamogenin I revealed that at a concentration of 20 μ M in 3T3-L1 adipocytes, yamogenin I can inhibit fat production by increasing p-AMPK and CPT-1, indicating that yamogenin I may exert its lipid-lowering effects through the inhibition of PPAR γ and C/EBP α activation of p-AMPK and CPT-1.

3.4. Blood pressure lowering activity

Amat et al.^[37] investigated the mechanism of Chinese yam water extract in lowering blood pressure using a two-kidney one-clip (2K1C) renal hypertensive Wistar rat model. The 2K1C group was treated with captopril, low-dose yam water extract, and high-dose yam water extract for six weeks. Blood pressure, heart mass index (heart weight/body weight), and the levels of angiotensin II (Ang-II), endothelin-1 (ET-1), superoxide dismutase (SOD), and malondialdehyde (MDA) in plasma were measured. The results showed that yam water extract significantly reduced average systolic and diastolic blood pressure, significantly increased plasma SOD activity, and decreased plasma MDA concentration after treatment. Yam water extract improved renal function, reduced plasma Ang-II activity and ET levels, and significantly reduced left ventricular hypertrophy and heart mass index.

3.5. Anti-inflammatory activity

Sun^[38] isolated and extracted aloin from *Dioscorea opposita* and investigated its anti-inflammatory mechanism, providing new insights for the clinical prevention and treatment of allergic contact dermatitis (ACD) and the use of aloin to treat ACD. Yang et al.^[15] conducted anti-inflammatory activity screening on monomeric compounds isolated and identified from the chloroform fraction of yam. The results showed that 3,3',5-trihydroxy-2'-methoxybibenzyl, 10,11-dihydro-dibenz[b,f]oxepin-2,4-diol, 2',3,5-trihydroxybibenzyl, 9,10-dihydro-7-methoxy-2,5-phenanthrenediol, (4*E*,6*E*)-7-(4-hydroxy-3-methoxyphenyl)-1-(4-hydroxyphenyl)-4,6-heptadien-3-one, and (4*E*,6*E*)-1,7-bis(4-hydroxyphenyl)-4,6-heptadien-3-one exhibited selective inhibition activity against COX-2. Zheng et al.^[13] performed anti-inflammatory activity screening on compounds dioscorosides A and B using mouse macrophage RAW 264.7 cells, resulting in IC₅₀ values of 5.8 μM and 7.2 μM, respectively.

3.6. Immune modulation

Huang et al.^[39] obtained sulfated yam polysaccharides from non-starch yam polysaccharides using the chlorosulfonic acid-pyridine method. Sulfation modification altered the physicochemical properties of yam polysaccharides. Compared with the model group, mice in the polysaccharide group showed increased body weight and thymus index compared with mice in the cyclophosphamide-induced immunosuppressive model group. It also restored splenomegaly function. Furthermore, it was indicated that sulfated yam polysaccharides enhanced the immunomodulatory activity of splenic lymphocytes, as they increased splenic lymphocyte proliferation and effectively induced the differentiation of splenic lymphocytes into T lymphocytes in cooperation with ConA. The numbers of CD3⁺CD4⁺ and CD3⁺CD8⁺ T lymphocytes increased and the CD4⁺/CD8⁺ ratio was restored in the polysaccharide group. Sulfated yam polysaccharides significantly elevated the levels of cytokines (IL-1β, TNF-α) and immunoglobulins (IgG and IgM) in the spleen.

Currently, research on the immunomodulatory effects of yam mainly focuses on yam polysaccharides and yam glycoproteins, with limited reports on the immunostimulatory activity of yam small molecules. Hu et al.^[40] investigated the impact of Chinese yam peel on the immunity of the fish *Carassius auratus*. The results showed that adding Chinese yam peel to the diet upregulated the mRNA expression levels of anti-inflammatory factors (IL-10), tight junction protein gene (Claudin-1), antioxidant genes (CAT and GST), and TLR pathway genes (TLR4). This suggests that adding yam peel to the diet can enhance the immune response of the fish to some extent.

3.7. Gastrointestinal regulation and protection

In terms of the nature and efficacy of Chinese yam, yam is considered neutral in nature and has a sweet taste. It is known for its properties of invigorating the spleen and replenishing Qi, as well as regulating the spleen and stomach. It is commonly used in clinical practice to treat conditions such as spleen deficiency with chronic diarrhea and chronic gastritis. For example, it can be found in formulations, such as stomach-invigorating and digestive tablets. Additionally, yam is widely used in dietary therapy, such as in dishes of yam and red date porridge^[7]. Zhang et al.^[41], by establishing an antibiotic-associated diarrhea (AAD) mouse model induced by ampicillin, administered low, medium, and high doses of yam containing uracil (4.35 mg/g) and polysaccharides (85.51 mg/g) continuously for 10 days. The results showed that yam helped restore intestinal microbiota dysbiosis induced by ampicillin, enriching the populations of *Bacteroides* and *Clostridium* species. Furthermore, the addition of yam also increased the production of short-chain fatty acids (SCFAs).

Li et al.^[42] investigated the protective effect and molecular mechanism of the active component 6,7-dihydroxy-2,4-dimethoxyphenanthrene from yam on the intestinal mucosa of mice. BALB/c mice were given

yam phenol extract and 6,7-dihydroxy-2,4-dimethoxyphenanthrene before treatment with dextran sulfate sodium (DSS). The results showed that after drug intervention, the disease activity index (DAIs), histological damage score (HDS), and survival rate of DSS-treated mice significantly improved, and the effect was better than the positive control of berberine. The compound 6,7-dihydroxy-2,4-dimethoxyphenanthrene downregulated oxidative stress-related factors MPO and NO, improved tight junction protein closure, significantly downregulated the expression of caspase-3 in intestinal epithelial cells, and decreased the apoptosis rate. It also improved the production of colitis-related cytokines, including TNF- α , IFN- γ , IL-10, and IL-23. Compared with the model control, the 6,7-dihydroxy-2,4-dimethoxyphenanthrene-treated group exhibited inhibition of the protein expression of ERK1/2, NF- κ B p65, pNF- κ B, and COX-2. This suggests that this compound effectively inhibited the activation of NF- κ B/COX-2 in a mouse intestinal mucosal injury model, indicating that yam phenol extract and 6,7-dihydroxy-2,4-dimethoxyphenanthrene had a protective effect on mouse intestinal mucosal injury and can prevent DSS-induced colitis.

Li et al.^[43] isolated a mannoglucan from yam and found that it can inhibit the excessive production of pro-inflammatory cytokines (such as TNF- α and IL-1 β) induced by LPS in RAW 264.7 cells and in a DSS-induced colitis mouse model. Oral administration of mannoglucan significantly alleviated colonic pathological damage, suppressed the activation of colitis-related signaling pathways (such as TNF- α and IL-1 β) and the colonic inflammation signaling pathway (such as NF- κ B and NLRP3 inflammasome), restored the mRNA expression of tight junction proteins (such as ZO-1, claudin-1, occludin, and connexin-43), and modulated gut microbiota by reducing microbial abundance.

3.8. Cytotoxic activity

Ren et al.^[28] identified 20 monomeric compounds from the aerial part of Chinese yam and conducted an initial screening for cytotoxic activity against MCF-7 cells and HepG2 cells at a concentration of 25 μ M. The results showed that at this concentration, the isolated and identified monomeric compounds did not exhibit significant cytotoxic activity. Liu et al.^[33] conducted a comparative study of the cytotoxic activity of yam peel extract and yam flesh extract against Ehrlich ascites carcinoma (EAC) cells and H22 liver cancer cells. They found that the cytotoxic activity of yam peel extract was significantly higher than that of yam flesh extract.

3.9. Estrogen-like activity

Zeng et al.^[44] studied the estrogen-like activity of yam extract through experiments on mouse uterine weight and proliferation of breast cancer cell lines (MCF-7 cells). The results revealed that the mechanism by which yam exerted estrogen-like effects was mainly mediated by estrogen receptors ER α , ER β , and GPR30. Additionally, the active components in yam that exhibited estrogen-like activity were adenosine and diosgenin. Adenosine's estrogen-like activity was primarily mediated through estrogen receptors ER α and ER β , while diosgenin primarily acted through estrogen receptors ER β and GPR30.

3.10. Antibacterial activity

Wang et al.^[45] discovered biodegradable films prepared using carboxymethyl cellulose, glycerol, yam mucilage, and silver nanoparticles. These films exhibited significant antibacterial effects against both *Staphylococcus aureus* (golden staph) and *Escherichia coli*. Li et al.^[46] used a casting method to prepare edible films composed of carboxymethyl cellulose, glycerol, yam mucilage, and zinc oxide nanoparticles (ZnO-NPs). Films containing 2.0 g of ZnO-NPs showed antibacterial properties against both *Staphylococcus aureus* and *Escherichia coli*.

3.11. Antibacterial activity

Lim et al.^[47] investigated the anti-neuroinflammatory activity of 6,7-dihydroxy-2,4-dimethoxyphenanthrene and found that it significantly reduced the production of pro-inflammatory mediators, such as NO, TNF- α , IL-6, i-NOS, and COX-2 in BV2 cells. In addition, the compound strongly inhibited the nuclear translocation of NF- κ B and the phosphorylation of p38 mitogen-activated protein kinase (MAPK) in BV2 cells but did not affect the levels and phosphorylation of ERK and JNK. Also, the compound was able to increase the expression of heme oxidase-1 (HO-1) in HT22 cells. The results showed that 6,7-dihydroxy-2,4-dimethoxyphenanthrene effectively suppressed the LPS-mediated inflammatory response in BV2 cells and promoted the survival of HT22 neuronal cells by inhibiting the transcription factor activity of NF- κ B and its downstream mediators.

Yang et al.^[48] found that an emergency treatment (200 mg/kg body weight, orally) and 10 days of daily administration (50 mg/kg body weight, orally) of yam chloroform extract to mice significantly improved spatial learning and memory abilities through ex-vivo experimental studies. Moreover, the extract was neuroprotective against glutamate and hydrogen-peroxide-induced neurotoxicity in primary-cultured rat cortical neurons.

4. Conclusions and outlook

Dioscorea opposita, a well-known medicinal and edible herb in traditional Chinese medicine, has a huge market demand in both medicinal materials and food industries. So far, over 150 compounds have been isolated and identified from *Dioscorea opposita*, and the diversity of its chemical components inevitably leads to a variety of pharmacological activities. However, there is still no direct and comprehensive link established between the diversity of chemical structures in yam and its pharmacological activities. Due to the lack of characteristic marker compounds and clearly defined active substances in yam, the 2020 edition of the Chinese Pharmacopoeia did not include content determination items for yam. Currently, Chinese yam can only be subjected to low-level quality control through thin-layer identification, making it difficult to achieve precise quality control for yam raw materials and products. Therefore, the quality standards for yam still need further improvement. In addition, the secondary resources of yam, such as the aerial parts of yam, the bulbil of common yam, and endophytic fungi, require further in-depth research to fully exploit and utilize yam resources.

Funding

This research was funded by the NSFC-Henan Joint Fund (grant number U1604169), the Key Scientific Research Fund of Henan Provincial Natural Science Foundation (grant number 232300421127), and the “Young Talent” Startup Fund of Henan Agricultural University (grant number 30500662).

Conflict of interest

The authors declare no conflict of interest.

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