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Research progress on the Active Ingredients and Pharmacological Effects of Yam

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Abstract

Methods: In this paper, we conducted a literature search on the bioactivity and pharmacological effects of Yam using Web of Science, MEDLINE, PubMed, Scopus, Google Scholar, and China National Knowledge Infrastructure databases until October 2023. Results: We summarized the active bioactive compounds of Yam, including polysaccharides, starch, diosgenin, saponins, proteins, and phenolic compounds, and reviewed their bioactivities in terms of antioxidant, anti-tumor, anti-hypertensive, anti-diabetic, modulation of gut microbiota, estrogen-like effects, and immune regulation.

Conclusion: Yam and its active compounds have multiple pharmacological effects and can serve as both medicine and food, potentially becoming a supplementary and alternative therapy for various diseases in the future.

Keywords: Yam; Allantoin; Polysaccharides; Antioxidant Activity; Blood Glucose Regulation

Abbreviations: TNF-α: tumor necrosis factor alpha; IL-6: interleukin 6; IL-1β: interleukin 1β; InsR: insulin receptor; PI3K: phosphatidylinositol 3-kinase; Akt: protein kinase B; FoxO3: forkhead box O3; GLUT4: glucose transporter type 4; CYP-1: cytochrome P450 1; NF-κB: nuclear factor kappa-B; NLRP3: nucleotide-binding oligomerization domain, leucine-rich repeat and pyrin domain-containing 3; GLp-1: glucagon-like peptide-1; ALT: alanine aminotransferase; AST: aspartate aminotransferase; PGC1α: peroxisome proliferators-activated receptor γ coactivator lalpha; TFAM: transcription Factor A Mitochondrial; NRF-1: nuclear respiratory factor-1; Sirt-1: silent mating type information regulation 2 homolog- 1; Bcl-2: B-cell lymphoma-2; Bax: Bcl-2-Associated X; LDL: low-density lipoprotein; HDL: high-density lipoproteins; Mrna: messenger RNA; IRE-1α: Inositol-requiring enzyme-1α; SMMC-7721: Human Hepatocellular Carcinoma Cells; G2/M phase: gap2/mitosis phase; AOM/DSS: azoxymethane/dextran sodium sulfate; IL-12b: interleukin-12b; MMP-2: matrix metalloproteinase 2; MMP-9: matrix metalloproteinase 9; MAPK: MAP kinase; VEGF-A: vascular en-

dothelial growth factor A; LgE: Immunoglobulin E; DPPH: 1,1-diphenyl-2-picrylhydrazyl; GSH: glutathione; IκB: inhibitor of NF-κB; DPP-IV: Dipeptidyl peptidase-4; IL-5: interleukin 5; IFN-γ: interferon gamma; IgG2a: Immunoglobulin G2a; Th1/Th2: Thymus-derived helper T cell type 1/Thymus-derived helper T cell type 2; ACE: angiotensin-converting enzyme; CD4: Cluster of Differentiation Antigen 4

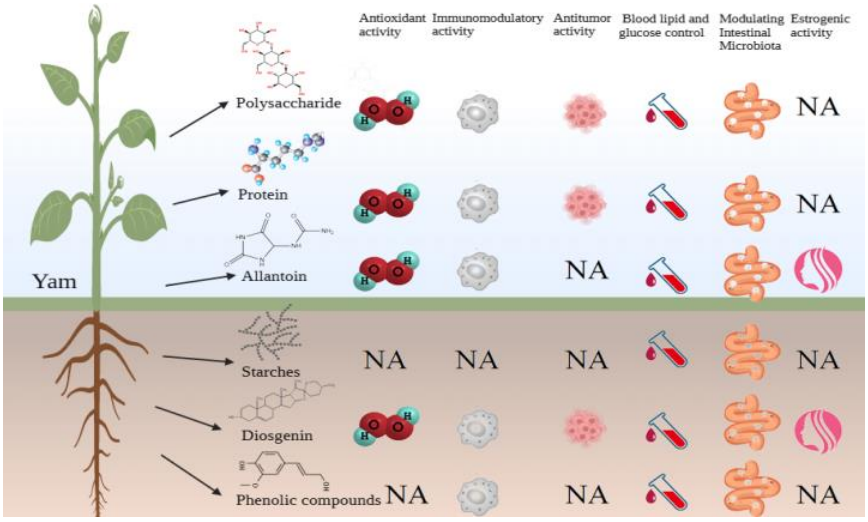


Figure 1: Graphical abstract. The active ingredients of Yam include polysaccharides, proteins,allantoin,starch, diosgenin, and phenolic compounds.. It has pharmacological effects such as antioxidant activity, immunomodulatory activity, antitumor activity, blood lipid and glucose control,modulating intestinal microbiota and estrogenic activity

Background

Yam (Dioscorea polystachya Turcz.) is a widely distributed medicinal and edible plant. It is the dried tuber of the yam plant, which belongs to the Dioscoreaceae family. Yam has a long history of cultivation and use in various countries due to its good taste, rich nutritional value, and convenient storage. Currently, the yield of Yam is approximately 45,000 kg per hectare, which can feed a population of 270,000. Moreover, Yam can be stored for over six months at room temperature and for more than three years at temperatures between 1 and 4 degrees Celsius. It is a highly nutritious reserve food.In recent years, research on the pharmacological properties of Yam has been conducted. Studies have shown that Yam exhibits various bioactivities, including antioxidant [1], anti-tumor [2], anti-hypertensive [3], anti-diabetic [4], modulation of gut microbiota [5], estrogen-like effects [6], and immune regulation [7]. However, the clinical application of Yam is still not comprehensive, and it remains an underutilized crop.

In this paper, we conducted a comprehensive review of the active bioactive compounds of Yam and summarized their potential therapeutic applications for various diseases. We also discussed the future research directions for Yam. Yam and its active compounds have the potential to become a supplementary and alternative therapy for various diseases in the future.

Materials and Methods

In this review, we conducted a literature search on the biological activities and pharmacological effects of Yam. We searched the Web of Science, MEDLINE, PubMed, Scopus, Google Scholar, and China National Knowledge Infrastructure databases up to October 2023 using the following keywords: "Dioscorea polystachya Turcz.", "Yam", "chemical composition", and "natural active ingredients". From the search results, we selected original papers that discussed the active ingredients and therapeutic effects of Yam.

The effective components and pharmacological effects of Yam.

The main effective components [8] in Yam are polysaccharides, starch, allantoin, diosgenin, proteins, and phenolic compounds (Figure 1).

Polysaccharides

Polysaccharides are one of the main active components in Yam and also the basis for its edible and medicinal value. The main components [1] include xylose, arabinose, mannose, galactose, and glucose. Through different extraction processes, a total of 13 polysaccharides can be isolated from Yam (Table 1), all of which have varying degrees of antioxidant, anti-aging, anti-tumor, and immune-enhancing effects.

Table 1: The names and structures of polysaccharides [9]

No.	Name	Monosaccharide composition	Structures
1	RDPS-I	Glc:Man:Gal=1:0.4:0.1	Backbone composed of α-D-(1,3)-Glcp, with a branch of α-D-(1→2)-Manp-β-D-1)-Galp
2	S1	Glc	[α-D-Glc(1→4)-]n
3	S2	Glc	[α-D-Glc(1→4)-]n
4	DFPN-1	Glc:Man:Gal = 1:1.26:2.87	1 →4,1→6,1→2 linked in a ratio of 84.3:9.0:6.7
5	DFPA-1	Glc:Man:Gal:GalA = 1:2.18:3.39:1.82	1→3,1 →2,1 →6 linked in a ratio of 84.3:9.0:6.7
6	YP-1	Glc:Man:Gal = 1:0.37:0.11	(1→3)-α-Glucopyranose as a main chain and β- galactopyranose-[(1→2)-α-mannopyranose]3-(1→2)-α-mannopyranose-(1→6)- as a side chain
7	DTA	Fru:Glc = 1:26.36	α-(1→4), β-(1→4) glycosidic bond
8	CYP	Glc:Gal = 1.52:1	β-1, 3-Glucose, α-1-galactose, α-1, 6-galactose
9	CYZ	Man:Glc:Gal:Xyl:Ara = 1:13.057 :26.56:6.07:2.22	NA
10	CYS-1	Man:Rha:GlcA:Glc:Gal:Xyl:Ara =1:0.024:0.05:0.084:2.59:0.13:0.14	β-(1→2), β-(1→4) glycosidic linkages
11	CYS-2	Man:Rha:GlcA:Glc:Gal:Xyl:Ara =1:0.82:3.86:2.68:12.88:1.29:0.54	β-(1→2), β-(1→4), β-(1→6) glycosidic linkages
12	DOTP-80	Glc:Gal:Man:Ara = 23.7:9.3:17.8:1.0	NA
13	DOM	Rha:Ara:Xyl:Man:Glc:Gal = 0.25:0.54:5.38:33.40:49.50:10.90	NA

NA: Not Avaliable

The antioxidant ability of polysaccharides is manifested in their strong ability to scavenge hydroxyl radicals [1]. Their molecular structure often consists of α-D-glucopyranosyl-(1 → 4)-glucose glycosidic bonds, and their ability to scavenge hydroxyl radicals is even comparable to that of vitamin C. In a study on endometrial epithelial cells [10], polysaccharides showed significant scavenging activity against hydroxyl radicals and superoxide radicals, promoting the proliferation of endometrial epithelial cells. From an antioxidant perspective, this provides a solution for addressing female infertility. On the other hand, a study on male infertility [11] showed that polysaccharides can enhance sperm vitality and protect sperm DNA integrity.

Polysaccharides also exhibit strong immunomodulatory and anti-tumor effects. Studies [7] have shown that when polysaccharides were used in mice treated with cy-

clophosphamide immunosuppression, the splenomegaly in mice was significantly restored, and there was a noticeable proliferation of splenic lymphocytes. Further research revealed that polysaccharides effectively induced the differentiation of splenic lymphocytes into T lymphocytes. This indicates that polysaccharides have definite immunomodulatory activity. Additionally, in the serum of mice in the polysaccharide group, a significant increase in the concentration of tumor necrosis factor (TNF)-α was observed. Another experiment [12] also confirmed this point: polysaccharides effectively reduced the production of TNF-α, interleukin 6 (IL-6), and interleukin 1β (IL-1β) in the liver, decreased the levels of TNF-α and IL-6 in the plasma, and exhibited typical anti-inflammatory capabilities, thereby alleviating gastric inflammation and oxidative stress in the intestines. This demonstrates the potential of polysaccharides in anti-inflammatory and anti-tumor activities, which have not yet received widespread attention.

The hypoglycemic and hypolipidemic effects of polysaccharides have received widespread attention and research. In a study conducted by Lu L et al. [4], diabetic and hyperlipidemic rats were fed with polysaccharides, and it was found that the blood glucose levels in the diabetic rats significantly decreased, while the serum total cholesterol, triglycerides, and low-density lipoprotein levels in the hyperlipidemic rats decreased significantly. Feng X et al. [13] extracted an acidic polysaccharide with a molecular weight of 1.55 × 102 kDa from Yam, which contains various types of glycosidic bonds. Its function may be achieved by regulating the expression of insulin receptor (InsR), Phosphatidylinositol 3-kinase (PI3K), protein kinase B (Akt), Forkhead **box O3 (**FoxO3**)**, and Glucose transporter type 4 (GLUT4) proteins, accelerating glycogen synthesis, reducing gluconeogenesis, and alleviating insulin resistance.

Furthermore, polysaccharides have been found to contribute to the regulation of intestinal microbiota and exert gastrointestinal anti-inflammatory effects [14]. Some polysaccharides [15] that are difficult to digest in the stomach act on the intestinal microbiota after passing to the colon, resulting in the production of a large amount of short-chain fatty acids. This promotes the growth of beneficial bacteria such as Lactobacillus thermophiles [5], Bifidobacterium, and Prevotella [11], while inhibiting the proliferation of Desulfovibrio and Escherichia coli. Additionally, due to the presence of aldaric acid and β-glycosides in polysaccharides, they are more easily utilized to form complex helical structures with biological activity, which can significantly promote the growth of Lactobacillus thermophiles [5]. For example, Pan Li [16] extracted a polysaccharide called cytochrome P450 1 (CYP-1) from Yam and found that it can inhibit the production of TNF-α and IL-1β, thereby inhibiting the activation of colon inflammation signaling pathways such as nuclear factor kappa-B (NF-κB) and Nucleotide-binding oligomerization domain, leucine-rich repeat and pyrin domain-containing 3 (NLRP3) inflammasome, significantly alleviating colon damage and restoring the expression of tight junction proteins, thereby regulating the intestinal microbiota. Through these mechanisms,polysaccharides can achieve therapeutic effects on intestinal microbiota imbalance.

Starch

Starch is the most abundant component in Yam [8], serving as the primary source of energy stored in the tubers and bulbs. Approximately 85% of the starch is stored in the tubers [17], and its high content ensures the nutritional value of Yam. After cooking, the starch undergoes changes in its characteristics, resulting in the formation of resistant starch [18] that is difficult to digest. Resistant starch accounts for half of the starch content in the tubers [19], making Yam starch more resistant to digestive enzymes. It can be utilized by intestinal microbiota for growth and reproduction [20], thereby reducing blood glucose levels and the risk of diabetes [21-23], inhibiting fat absorption, and lowering cholesterol levels [18].

Allantoin

Allantoin is an imidazole heterocyclic compound, with the chemical name 2,5-dioxy-4-imidazolylalkylurea. It is one of the active ingredients in Yam that has the function of reducing blood glucose levels. Research [24] has found that allantoin has anti-diabetic effects in a streptozotocin-induced diabetic rat model. In the case of high blood glucose, oxidative stress occurs in pancreatic beta cells, impairing their function and leading to insulin resistance. Allantoin has antioxidant effects on pancreatic beta cells, effectively promoting their regeneration and insulin production. This

mechanism is similar to that of a pancreatic-associated protein called glucagon-like peptide-1 (GLP-1) and the mechanism of GLP-1 receptor agonist treatment for diabetes. In the same experiment, electrolyte imbalance and acid-base imbalance caused by diabetes were improved after the application of allantoin, and it effectively inhibited the elevation of HCO3−. This indicates that the antioxidant effects of allantoin can act on the kidneys, helping to restore renal failure caused by excessive loss of ions in the urine and electrolyte imbalance, and preventing the occurrence of diabetic ketoacidosis. It also suppressed the elevation of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), demonstrating effective antioxidant capacity in the liver and inhibition of liver toxicity. In addition, Ning Zhou's study [25] confirmed that allantoin can treat septic myocarditis by promoting amino acid, arachidonic acid, sphingolipid, glycerophospholipid, and ethylene glycol metabolism. It corrects metabolic disorders in septic myocarditis through its antioxidant ability. This indicates that allantoin has great potential in treating metabolic diseases such as liver failure, kidney failure, and myocarditis.

In addition, allantoin can enhance muscle function [26]. By activating mitochondrial transcription factors peroxisome proliferators-activated receptor γ coactivator lalpha (PGC1α), Transcription Factor A, Mitochondrial (TFAM), nuclear respiratory factor-1 (NRF-1), and silent mating type information regulation 2 homolog- 1 (Sirt-1), it promotes the differentiation of myoblasts into myotubes and stimulates mitochondrial synthesis, leading to energy generation. This allows allantoin to effectively alleviate the progression of conditions such as myasthenia gravis.

Allantoin can also effectively reduce body weight and control blood lipids [27]. After administering a high dose of allantoin to mice fed a high-fat diet, the total cholesterol and triglycerides in their plasma significantly decreased, and the accumulation of fat in the liver was significantly inhibited. This demonstrates the potential application of allantoin in obesity, a characteristic that is currently not receiving much attention and still has significant room for development.

In research [28] on the treatment of lower extremity venous ulcers, it was found that allantoin has a role in promoting ulcer healing, which has expanded the application of Yam in surgery.

Diosgenin

Diosgenin is a plant steroidal saponin that exhibits multiple active effects.It can effectively regulate endocrine function in the human body, particularly in the metabolism of blood glucose and blood lipids, as well as in the complications of diabetic retinopathy. Experimental findings [18,29] have shown that the fasting blood glucose levels and pancreatic sensitivity of the test models improved after the application of diosgenin. This improvement can be attributed to the inhibition of α-glucosidase and α-amylase activities by diosgenin, which is similar to the mechanism of action of acarbose. Diosgenin also effectively regulates the gut microbiota by promoting the growth of beneficial bacteria such as Lactobacillus and Bifidobacterium [30,31], and inhibiting the growth of pathogenic bacteria. This helps in regulating the gut microbiota and improving blood glucose levels. Additionally, diosgenin has been found to be effective in treating diabetic retinopathy. Studies [32] have shown that the use of diosgenin significantly increases retinal thickness and the number of retinal ganglion cells, while reducing retinal cell apoptosis. This is likely due to the improvement of decreased B-cell lymphoma-2 (Bcl-2) expression and increased Bcl-2-Associated X (Bax) and cleaved caspase-3 expression induced by high glucose levels in retinal pigment epithelial cells [33], as well as the regulation of Bax and Bcl-2 protein expression, and significant reduction of caspase-3 protein expression in high glucose-induced cardiomyocytes, which significantly inhibits cell apoptosis [34]. This clearly demonstrates the therapeutic effect of diosgenin on diabetic retinopathy. In addition, it was found in the experiment that the use of diosgenin significantly reduced the content of low-density lipoproteins (LDL) and increased the level of high-density lipoproteins (HDL) in mouse plasma, and the body weight of the mice decreased in long-term observations. This may be due to the upregulation of messenger RNA (mRNA) levels of lipoprotein lipase and peroxisome proliferator-activated receptor gamma coactivator-1α in the liver by diosgenin [35]. In this mechanism, the liver can more effectively prevent hepatic fat accumulation, reduce the size of fat cells, and thus prevent and treat non-alcoholic fatty liver disease [18].

Diosgenin has significant anticancer effects and is effective in treating various cancers such as leukemia, gastric cancer, colorectal cancer, and breast cancer [36]. Its anticancer mechanisms are diverse. Meng X's research [37] found that diosgenin can enter liver cancer cells and distribute in the endoplasmic reticulum, mitochondria, and lysosomes of liver cancer cells, causing swelling of the endoplasmic reticulum and damaging the mitochondria. At the same time, it upregulates inositol-requiring enzyme-1α (IRE-1α) to induce autophagy and apoptosis, triggering endoplasmic reticulum stress and mitochondria-mediated apoptosis. Tsukayama I [38] discovered that diosgenin can downregulate and inhibit cyclooxygenase-2 and microsomal prostaglandin E synthase-1 in lipopolysaccharide-induced acute liver injury macrophages through glucocorticoid receptors, thereby inhibiting hepatitis and liver cancer. Cruz, M.S et al. [39] found that diosgenin has significant cytotoxicity and genotoxicity on HepG2 liver cancer cells. Li Y [36] confirmed through experiments that diosgenin can inhibit the activity of SMMC-7721 cells, thus having a clear inhibitory effect on the proliferation of liver cancer cells and inducing gap2/mitosis (G2/M) phase cell cycle arrest and apoptosis in liver cancer. Diosgenin is also effective against colorectal cancer [2]. Research has found that diosgenin can inhibit the occurrence of colon cancer induced by azoxymethane/dextran sodium sulfate (AOM/DSS) in mice, which is related to its induction of cell cycle arrest and apoptosis. It changes the expression of pro-apoptotic genes and anti-apoptotic genes [40], such as P32, P5, Bcl-2, caspase-3 in colon cancer cells [41,42], and significantly increases the levels of IL-1β, IL-6, interleukin-12b (IL-12b), and TNF-α. Diosgenin can also induce an increase in apoptosis-related protein Bax and a decrease in anti-apoptotic protein Bcl-2 [43], reduce the expression of matrix metalloproteinase-2 and matrix metalloproteinase-9, thereby inhibiting the growth of C6 and T98G cell lines and showing anti-glioblastoma effects. Additionally, diosgenin can serve as a carrier for anticancer drugs due to its ability to change the affinity of biological membranes [44]. It can be combined with other anticancer substances to prevent the degradation and clearance of other anticancer substances.

Diosgenin has antioxidant effects. Studies [45] have shown that it can significantly increase the activity of total superoxide dismutase, glutathione peroxidase in red blood cells, and hydrogen peroxide in red blood cells and liver, thereby enhancing the expression of peroxidase and exerting antioxidant effects. At the same time, it can achieve antioxidant and anti-inflammatory effects by inhibiting NF-κB and myeloperoxidase activity [46], providing protection against alcohol-induced gastric injury and gastric damage caused by excessive gastric acid. In addition, oxidative stress is considered a major risk factor for the development of atherosclerosis. Through its antioxidant effects, diosgenin can significantly reduce the risk of atherosclerosis [47].

Diosgenin has estrogen-like effects. Postmenopausal women exhibit a range of clinical syndromes due to decreased estrogen levels. Cardiomyocytes can activate mitochondria-dependent cytotoxicity and apoptosis, causing damage to the heart muscle. Chang,C.C. [48] demonstrated through experiments that diosgenin can regulate the activity of matrix metalloproteinase 2 (MMP-2) and matrix metalloproteinase 9 (MMP-9), thereby increasing hormone levels. Additionally, it can protect cardiomyocytes by activating the estrogen receptor and the PI3K/Akt and extracellular signal-regulated kinase pathways to reduce oxidative stress [49]. It can also induce angiogenesis in osteoblast-like cells by activating the estrogen receptor, src kinase, p38 MAP kinase (MAPK), and Akt signaling pathways and upregulating vascular endothelial growth factor A (VEGF-A) through a factor-1α-dependent mechanism [50], thus counteracting postmenopausal osteoporosis. Therefore, diosgenin in Yam is a potential hormone replacement therapy for postmenopausal women.

In addition, studies have found that diosgenin has a certain effect in improving memory impairment and repairing axonal atrophy and synaptic degeneration [51]. Diosgenin has immunomodulatory effects [52,53], as it can promote the expression of CXCR3, CCL3, and CxCL10 in the intestine while inhibiting the production of ovalbumin-specific immunoglobulin E (IgE) and total IgE, thus achieving an anti-allergic effect. Diosgenin can also increase the synthesis of bone matrix proteins and bone-specific transcription factor Runx2 in osteoblastic cells MC3T3-E1, thereby promoting bone formation [54]. Man, S [55] discovered through experiments that it can reduce the mechanical withdrawal threshold by inhibiting oxidative stress, glial fibrillary acidic protein, and pro-inflammatory cytokines in

the brain, thus achieving analgesic effects

Proteins

Yam contains a large amount of storage proteins [8], which are mainly divided into dioscorin, DOI protein, and galactose-binding lectin in current research.

Dioscorin

Dioscorin is the main soluble storage protein in Yam, which is a glycosylated form of carbonic anhydrase. It has bioactivities such as antioxidant, immune modulation, regulation of blood glucose and lipids, anti-allergic, and anti-hypertensive effects.

Hou, W.C [56] found that dioscorin can scavenge 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals and capture hydroxyl radicals, thereby exhibiting antioxidant bioactivity. Nagai, T [57] also discovered that dioscorin has the ability to scavenge hydroxyl radicals and superoxide anion radicals. Additionally, Han, C.H [58] conducted a study on mice with induced oxidative stress and found that the use of dioscorin significantly increased the level of glutathione (GSH) in the brain, improved the antioxidant capacity against oxygen radicals, and decreased plasma malondialdehyde and inducible nitric oxide synthase levels. Another experiment by Han [59] involved the hydrolysis of dioscorin with pepsin, resulting in five cysteine-containing peptide products: KTCGNGME, PPCSE, CDDRVIRTPLT, KTCGY, and PPCTE. After testing for oxygen radical scavenging and anti-low-density lipoprotein peroxidation activities, it was found that all five products exhibited antioxidant activity, with KTCGY being the most potent. Furthermore, the dipeptides in the hydrolysis products demonstrated an inhibitory effect on methylglyoxal-induced apoptosis in human umbilical vein endothelial cells. Moreover, due to the antioxidant properties of dioscorin, it has a clear inhibitory effect on inflammatory reactions induced by strong oxidizing agents such as hydrogen peroxide, as it activates inhibitor of NF-κB (IκB) and inactivates NF-κB, thereby attenuating the impact of hydrogen peroxide on G2/M cell cycle arrest [60]. Additionally, studies suggest that dioscorin can confer reducing and antioxidant activity through disulfide-thiol exchange [59,61,62]. These studies indicate the potential value of dioscorin in terms of antioxidant and anti-aging properties.

Dioscorin has immunomodulatory effects.Liu, Y.W [63] found that treatment with dioscorin in RAW264.7 cells and human monocytes promotes the production of IL-6, IL-1β, and TNF-α, as well as proliferation of splenocytes, achieving immunomodulation. Further studies [64] have shown that after oral administration of dioscorin for 21 days, natural killer cell subsets and B cell subsets increase in mice, enhancing phagocytic activity of monocytes, natural killer cells, and polymorphonuclear cells. Dioscorin also promotes proliferation of splenocytes in response to bacterial lipopolysaccharide and phytohemagglutinin, providing insight into the underlying mechanisms of dioscorin's immunomodulatory effects.

Dioscorin glycosides can lower total cholesterol and low-density lipoprotein levels, while improving impaired glucose tolerance. Wu, G.C [65] found through experiments that mice intervened with dioscorin glycosides showed significant reductions in total cholesterol and low--density lipoprotein, as well as decreased overall visceral lipid content. Furthermore, in an oral glucose tolerance test, mice treated with dioscorin glycosides had significantly lower blood glucose levels compared to the control group. Shih, S.L [3] conducted more detailed experiments and discovered that the hypoglycemic mechanism of dioscorin glycosides is through the inhibition of Dipeptidyl peptidase-4 (DPP-IV), similar to sitagliptin phosphate. Sitagliptin phosphate belongs to DPP-IV inhibitors, which can promote insulin secretion and improve glucose tolerance by inhibiting DPP-IV activity and prolonging the bioactivity of GLP-1.

Dioscorin glycosides can inhibit allergic reactions. In experiments [66] on ovalbumin-sensitized mice, dioscorin glycosides significantly suppressed the mice's allergic reactions. Further studies on the mice's lymphocytes revealed that the levels of interleukin 5 (IL-5) in the cells decreased to normal levels, while the levels of interferon gamma (IFN-γ) and Immunoglobulin G2a (IgG2a) increased, resulting in a decrease in IgE and histamine levels. This indicates that dioscorin glycosides inhibit allergic reactions caused by ovalbumin, possibly by regulating, Thymus-derived helper T cell type 1/Thymus-derived helper T cell type 2 (Th1/Th2) immune responses. Additionally,

when A549 human airway epithelial cells were stimulated by dust mites to induce allergic reactions and then intervened with dioscorin glycosides, it was found that dioscorin glycosides could restore the normal function of the cells without damaging them and inhibit allergic reactions [67]. The underlying reason is that dust mites have pancreatic protease activity, while dioscorin glycosides have anti-pancreatic protease activity, thereby protecting airway epithelial cells.

Dioscorin glycosides can lower blood pressure. In the renin-angiotensin system, if angiotensin-converting enzyme (ACE) hydrolyzes angiotensin I to produce angiotensin II, it will lead to an increase in blood pressure [68]. It has been confirmed through experiments [3] that dioscorin glycosides and their hydrolysates have the ability to inhibit ACE activity. This process may be due to the fact that oxidative stress in vascular smooth muscle cells is increased under hypertension, leading to an increase in the content of malondialdehyde. The antioxidant properties of dioscorin glycosides inhibit this reaction, thereby exhibiting vasorelaxant and ACE inhibitory activities. Hsu, F.L [69] and Nagai, T [57] further discovered that dioscorin glycosides exhibit a mixed non-competitive inhibitory effect on ACE, thus achieving ACE inhibition activity.

DOI Protein

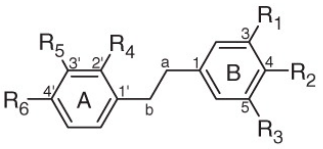
The DOI protein belongs to the chitinase-like superfamily [8]. It can promote the synthesis of estrogen [70]. Estrogen is produced by aromatase catalysis in granulosa cells of the ovary [71]. The DOI protein cans upregulate the expression of aromatase and follicle-stimulating hormone through the follicle-stimulating hormone-aromatase pathway, thereby promoting the synthesis of estrogen. During menopause, the level of estrogen decreases in the body, while the levels of pro-inflammatory serum markers increase, Cluster of Differentiation Antigen 4 (CD4) T lymphocytes and B lymphocytes decrease, and natural killer cell cytotoxic activity decreases [72,73]. DOI, by promoting the synthesis of estrogen and stimulating the activity of splenic cells, can treat the immune decline during menopause.

Lectin

Currently,various lectins, including those from Dioscorea alata, D. cayenesis, D. polygonoides, D. rotundata, and D. batatas, can be extracted from Yam. These proteins have been proven to inhibit cancer cell growth [74]. Experiments have shown that lectins exhibit anti-proliferative activity against various cancer cells, including breast cancer MCF7 cells, liver cancer HepG2 cells, and nasopharyngeal carcinoma CNE2 cells. The mechanism behind this activity is related to lectins inducing apoptosis in tumor cells through their carbohydrate-binding ability [75-80]. Therefore, lectins may serve as a clue for the development of new anticancer drugs.

Phenolic Compounds

Yang, M.H [81] isolated and extracted 23 phenolic compounds from Yam using bioactivity-guided method (Figure 2), among which 15 showed clear pancreatic lipase inhibitory activity. The compound with the strongest activity was 3,3',5-trihydroxy-2'-methoxybibenzyl. Zhang.L [82] found that the phenolic compounds in Yam can prevent diabetes by accelerating lipid metabolism.



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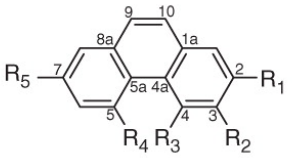
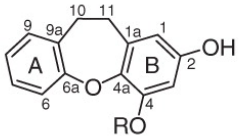
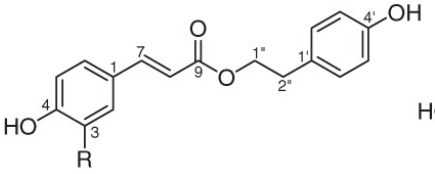


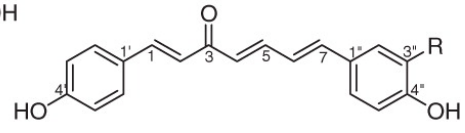


11 R_1=OH, R_2=OCH_3, R_3=H, R_4=OCH_3, R_5=OH
12 R_1=OCH_3, R_2=OH, R_3=H, R_4=OCH_3, R_5=OCH_3
13 9, 10-dihydro, R_1=H, R_2=H, R_3=OH, R_4=OCH_3, R_5=OH
14 9, 10-dihydro, R_1=OH, R_2=H, R_3=H, R_4=OH, R_5=OCH_3

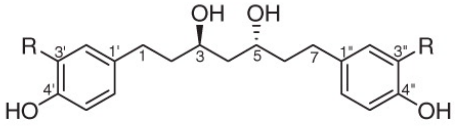
15 R=H
16 R=CH_3



17 R=H
18 R=OCH_3



19 R=H
20 1,2-dihydro, R=H
21 1,2-dihydro, R=OCH_3



22 R=H
23 R=OCH_3

Figure 2: Chemical structures of phenolic compounds.

(1) tristin. (2) 2′,3,5-trihydroxybibenzyl. (3) 3,3′,5-trihydroxy-2′-methoxybibenzyl. (4) batatasin III. (5) batatasin IV. (6) 2′,4-dihydroxy-3,5-dihydroxy-4-methoxybibenzyl. (7) 3,5-dimethoxy-2′-hydroxybibenzyl. (8) 3,5-dimethoxybibenzyl. (9) 3,4-dimethoxy-2′,5-dihydroxybibenzyl. (10) batatasin V. (11) 3,5-dimethoxy-2,7-phenanthrenediol. (12) batatasin I. (13) hircinol. (14) 2,5-dihydroxy-7-methoxy-9,10-dihydrophenanthrene. (15) 9,10-dihydro-dibenzoxepin-2,4-diol. (16) 9,10-dihydro-4-methoxy-dibenzoxepin-2-ol. (17) *p*-hydroxyphenylethyl *p*-coumarate. (18) *p*-hydroxyphenethyl *trans*-ferulate. (19) (1*E*,4*E*,6*E*)-1,7-*bis*(4-hydroxyphenyl)-1,4,6-heptatrien-3-one. (20) (4*E*,6*E*)-1,7-*bis*(4-hydroxyphenyl)-4,6-heptadien-3-one. (21) (4*E*,6*E*)-7-(4-hydroxy-3-methoxyphenyl)-1-(4-hydroxyphenyl)-4,6-heptadien-3-one. (22) two *p*-hydroxyphenylethyl-*p*-hydroxyphenyl propenoic acids, (3*R*,5*R*)-3,5-dihydroxy-1,7-*bis*(4-hydroxyphenyl)-3,5-heptanediol. (23) (3*R*,5*R*)-1,7-*bis*(4-hydroxy-3-methoxyphenyl)-3,5-heptanediol [81].

Clinical Research on Yam

Due to its high safety, nutritional value, and medicinal value, clinical research on Yam has been ongoing. Zhao, Y.L [83] conducted a controlled trial on 49 patients with stable moderate or severe chronic obstructive pulmonary disease. In the experiment, the patients were orally administered a mixture of Yam and Epimedium. It was found

that after three months of use, the patients' symptoms of respiratory difficulty improved significantly, and their exercise capacity as well as quality of life also significantly improved. Matsuoka, T [84] conducted a controlled experiment on healthy individuals to examine the blood sugar changes after consuming white rice with mixed Yam sauce. Within 15 minutes after oral intake of the corresponding rice, the blood sugar and insulin concentrations of the participants were monitored. It was found that the participants who consumed white rice with mixed Yam sauce had relatively lower blood sugar and insulin concentrations, indicating that Yam can lower postprandial blood sugar levels and reduce insulin secretion. Zhao, W. [85] obtained similar results in a similar experiment, administering rice noodles containing 10g of Yam sauce to healthy participants and observing their blood glucose levels within 60 minutes. Ultimately, it was demonstrated that Yam can inhibit the absorption of rice noodles and reduce the peak blood glucose levels. In a study conducted by Wu, W.H. [6], 24 healthy postmenopausal women were asked to replace their staple food with Yam. These women consumed a total of 390g Yam daily and the experiment lasted for 30 days. It was found that after 30 days, there was a significant increase in the levels of estrone, sex hormone-binding globulin, and estradiol. Additionally, the plasma cholesterol concentration and the levels of urinary 8-isoprostane were significantly decreased. The lag time of low-density lipoprotein oxidation was also prolonged. These findings indicate that Yam has the potential to improve hormone secretion, lipid metabolism, and act as an antioxidant. Tohda, C. [51] conducted a study in which healthy adults were given a capsule formulation containing 8 mg of diosgenin daily for a duration of 12 weeks. The study showed that Yam can improve cognitive function in healthy adults. It is worth noting that no adverse reactions were reported in the clinical trial mentioned above. While Yam has been the subject of many pharmacological studies, clinical research on its potential is still relatively limited, and further exploration is needed to fully understand its clinical potential.

Conclusions

The active ingredients of Yam include polysaccharides, starch, allantoin, diosgenin, proteins, and phenolic compounds. It has pharmacological effects such as antioxidant, anti-tumor, anti-hypertensive, anti-hyperglycemic, regulation of intestinal flora, estrogen-like effects, and immune modulation. It is also safe to consume, making it a potential supplementary and alternative therapy for various diseases.

Declarations

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Availability of Data and Materials

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

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Author Contributions

QD searched the literature and searched the manuscript. MXZ and XYZ searched the literature and categorized the information. BW searched the literature and revised the article.LQG determined the main research direction and reviewed the article. All authors read and approved the final manuscript.

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