JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Review

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The Jujube (*Ziziphus Jujuba* Mill.) Fruit: A Review of Current Knowledge of Fruit Composition and Health Benefits

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ABSTRACT: The nutritional jujube (*Ziziphus jujube* Mill.) fruit belonging to the Rhamnaceous family grows mostly in Europe, southern and eastern Asia, and Australia, especially the inland region of northern China. Jujube has a long history of usage as a fruit and remedy. The main biologically active components are vitamin C, phenolics, flavonoids, triterpenic acids, and polysaccharides. Recent phytochemical studies of jujube fruits have shed some light on their biological effects, such as the anticancer, anti-inflammatory, antiobesity, immunostimulating, antioxidant, hepatoprotective, and gastrointestinal protective activities and inhibition of foam cell formation in macrophages. A stronger focus on clinical studies and phytochemical definition of jujube fruits will be essential for future research efforts. This review may be useful for predicting other medicinal uses and potential drug or food interactions and may be beneficial for people living where the jujube fruits are prevalent and health care resources are scarce.

KEYWORDS: *jujube, phenolics, triterpenic acids, polysaccharides, vitamin C, health benefits*

■ INTRODUCTION

Jujube (*Zizyphus jujuba* Mill.) is recognized as the most important *Zizyphus* species for fruit production in the buckthorn family Rhamnaceae. Jujube is indigenous to China with a history of over 4000 years and is widely distributed in Europe, southern and eastern Asia, and Australia (Table 1).[1] To date, more than 700 cultivars of jujube have been found in China.[2] China is the only country known to be exporting jujube fruits,; its cultivation area has reached >1.5 million hectares.[3] The annual output of fresh jujube fruits is 400,000 tonnes. China exports about 4700 tonnes of dried jujube fruits, earning a foreign exchange of U.S. $5 million annually.[4]

Table 1. Brief Introduction of Jujube (Adapted from References 1, 6, and 43)

cultivated regions	Europe, southern Asia, eastern Asia, and Australia
required temperatures	low chill requirement
soil types	grows in different soils and is resistant to alkalinity and salinity
water supply	better adapted to arid regions
growing season	bud burst to leafing stage (stage I, early April−early May), flowering to fruit set stage (stage II, mid May−late June), fruit growth stage (stage III, late June−late July), fruit maturation stage (stage IV, early August−early September), and dormancy stage (stage V, October−March)

Jujube is generally recognized as an outstanding source of biologically active compounds related to both nutritional and nutraceutical values. Dried jujube fruits have been commonly utilized as food, food additive, and flavoring for thousands of years due to their high nutritional value.[5] Jujube fruits made into paste, puree, syrup, and confection are consumed for digestion improvement and general health maintenance.[1,6] It has also been used as a traditional Chinese medicine (TCM) for the treatment of anorexia, fatigue, and loose stools in deficiency syndromes of the spleen and of hysteria in women.[2] Previous studies have revealed that jujube contains various constituents, including triterpenic acids,[7,8] flavonoids,[9] cerebrosides,[8] amino acids,[10] phenolic acids,[11] mineral constituents,[5] and polysaccharides.[1,12] To our knowledge, there is no review published on the investigation of primary and secondary metabolites in jujube fruits. Hence, the aim of this paper is to report the state of the art related to the current knowledge of jujube composition and its health benefits.

Finally, with the aim of elucidating the importance of jujubes for human health protection, the bioactivities of fruit extracts as measured by widely adopted chemical model systems, together with the results of some in vitro and in vivo studies, are discussed. Potential values might be added to jujube fruit if extracts of the fruit were to be used for nutraceutical purposes. This review may be useful for predicting other medicinal uses and potential drug or food interactions and may be beneficial for people living where the jujube fruits are prevalent and health care resources are scarce and may encourage new research and postharvest processes to deeply explore jujube fruit in the future.

■ NUTRIENTS

Jujube fruit represents a healthy food choice. First of all, its dietary fiber[5] and fructose[13] contents may contribute to regulate blood sugar levels by slowing digestion, with its fiber content also contributing in controlling calorie intake by its satiating effect. To a lesser extent, jujubes are a source of healthy, essential fatty acids because jujube fruit is rich in unsaturated fatty acids (68.54−72.44% of the total fat in jujube fruits). There are 33 fatty acids

Received: October 30, 2012
Revised: March 12, 2013
Accepted: March 12, 2013
Published: March 12, 2013

(mainly monoenic acids) identified from the dried pulp of *Z. jujuba* Mill.[14] The chain length of those components was from 7 to 28 carbon atoms. Sixteen fatty acids, with a dominance of 16:1 (7) and 16:1 (9), are partly responsible for the fragrance of the fruit.[14] Fatty acid profiles of the fruits were influenced by their developmental stage.[15] The predominant fatty acids in jujube selections were oleic, linoleic, palmitic, and palmitoleic acids.[16] Jujube fruits were rich in lipids, especially linoleic acid (omega-6),[16] that the human body is not capable of producing.[17]

Great interest has developed in jujubes because of their high content of vitamin C, which makes them an important source of this vitamin for human nutrition. Moreover, the jujube, although to a lesser extent, is a source of several other vitamins, such as thiamin, riboflavin, niacin, vitamin B-6, and vitamin A (Table 2).

Table 2. Nutrient Composition of Fresh Jujube Fruits (Adapted from USDA National Nutrient Database, 2011)

type	nutrient (units)	content (per 100 g)
proximates	water (g)	77.86
	energy (kcal)	79
	protein (g)	1.20
	total lipid (g)	0.20
	carbohydrate (g)	20.23
minerals	calcium, Ca (mg)	21
	iron, Fe (mg)	0.48
	magnesium, Mg (mg)	10
	phosphorus, P (mg)	23
	potassium, K (mg)	250
	sodium, Na (mg)	3
	zinc, Zn (mg)	0.05
vitamins	vitamin C (mg)	69.0
	thiamin (mg)	0.02
	riboflavin (mg)	0.04
	niacin (mg)	0.9
	vitamin B-6 (mg)	0.081
	vitamin A, RAE (μg_RAE)	2
	vitamin A (IU)	40

Jujube fruit has been qualified as a good source of magnesium, phosphorus, potassium, sodium, and zinc (Table 2). Glucose, fructose, sucrose, rhamnose, and sorbitol are the major sugars for jujube fruits.[5] Different organic acids such as citric, succinic, and malic acids have been identified in jujube fruits.[18] Jujube fruits contain different types of amino acids such as L-Asn, L-Pro, L-Arg, L-Ala, 4-Abu, L-Glu, *p*-Ser, L-Asp, and L-Ser.[10,19]

BIOACTIVE COMPOUNDS

Total Phenolics. Jujube fruits contain a high amount of total phenolics measured by Folin–Ciocalteu assay (Table 3). Jujube fruits had higher total phenolics content (275.6–541.8 mg GAE/100 g)[18] than other common fruits known for their high phenolics content, such as cherries (114.6 mg GAE/100 g fresh weight (FW)), apple (74.0 mg GAE/100 g FW), guava (194.1 mg GAE/100 g FW), persimmon (112.1 mg GAE/100 g FW), sweetsop (405.4 mg GAE/100 g FW), and red grape (80.3 mg GAE/100 g FW).[20] The total phenolic content in peel was 5–6 times higher than that in the pulp of jujube fruits.[21] The phenolics contents in jujube were different with cultivar.[18] Besides the genetics, altitude and annual precipitation exert significant influences on the level of total phenolics in jujube fruit. Jujube grown in severe drought and in high-altitude areas can produce a larger amount of phenolics and exhibit higher antioxidant activities compared to fruits grown in other areas.[22]

Table 3. Summary of Total Phenolic Compounds, Flavonoids, Anthocyanins, Proanthocyanidins, Carotenes, β-Carotene, and α-Tocopherol of Jujube Fruits

fruit material	contents	reference
total phenolic content (mg gallic acid/100 g FW)	275.6–541.8	18
total flavonoids (mg rutin equiv/100 g FW)	62.0–284.9	18
total anthocyanins (c-3-gE[a]/100 g DW)	29.79–42.91	38
total proanthocyanidins (mg GSPE[b] equiv/100 g FW)	58.0–413.7	18
carotenes (mg/100 g DW)	4.12–5.98	15
β-carotene (μg/100 g FW)	35.0	16
α-tocopherol (mg/100 g FW)	0.04–0.07	16

[a]c-3-gE, cyanidin 3-glucoside equivalents. [b]GSPE, grape seed proanthocyanidin extract.

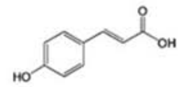
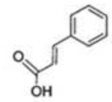
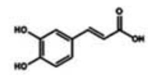
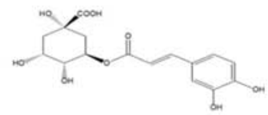
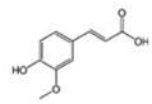
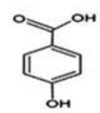
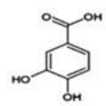
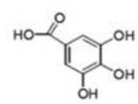
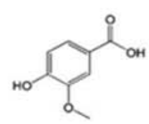
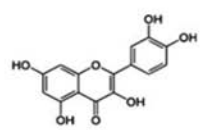
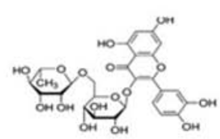
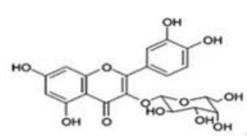
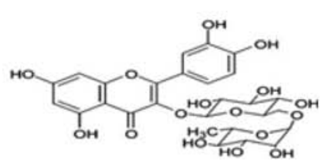
Individual Phenolic Compounds. According to the number of phenol rings that they contain and the structural elements that bind these rings to one another, phenolics are divided into several classes, including flavonoids, phenolic acids, tannins (hydrolyzable and condensed), stilbenes, and lignans.[23]

Different types of flavonoids such as flavonols[22] and flavan-3-ols[13] are found in jujube fruit (Table 4). Flavonoids may vary significantly by variety and maturity level.[18,19,24] Jujube fruits contained the following flavonoids: procyanidin B2, epicatechin, catechin, rutin, quercetin-3-*O*-rutinoside, quercetin-3-robinobioside, quercetin-3-*O*-galactoside, kaempferol-glucosyl-rhamnoside, and kaempferol-glucosyl-3″-rhamnoside.[10,18,19] Jujube seeds contained the following flavonoids: saponarin, spinosin, vitexin, swertish, 6‴-hydroxybenzoylspinosin, and 6‴-feruloylspinosin (Figure 1).[10]

Wang et al.[25] applied a liquid chromatography with electrochemical detection (LC-ECD) method for simultaneous separation and determination of six phenolic compounds, namely, gallic acid, protocatechuic acid, caffeic acid, *p*-coumaric acid, rutin, and quercetin in jujube. The content of phenolic acids in jujube fruit ranged from 751.39 μg/g dry weight (DW) in jujube peel to 143.59 μg/g DW in pulp, and the phenolic acids are mainly found in the insoluble-bound form in both jujube seed and peel, whereas in the glycosided form in the pulp.[26] Free phenolic acids constitute from 5.2% in peel to 20.7% in seed of the total phenolic acids present in jujube, whereas the phenolic acids released from soluble esters make up 6.2% in seed and 27.5% in pulp. Glycosides account for 44.7, 11.6, and 22.3% of the total phenolic acids present in jujube pulp, seed, and peel, respectively.[26] *p*-Hydroxybenzoic acid is the dominant phenolic acid in both pulp and seed of jujube, even in the whole jujube, with 51.7, 47.7, and 25.0% of the total contents in the pulp, seed, and whole jujube, respectively, whereas *p*-coumaric, cinnamic, and chlorogenic acids are present in high amount in peel. Hydroxybenzoic acids include protocatechuic and gallic acid in jujube. Caffeic, *p*-coumaric, cinnamic acid, and ferulic acid are hydroxycinnamic acids found in jujube (Table 4).[26]

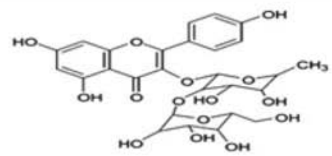
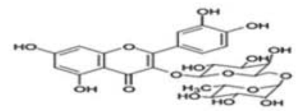
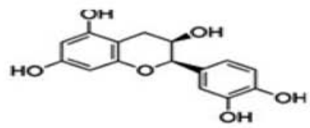
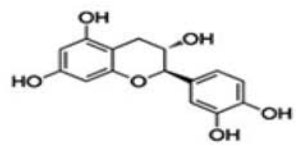
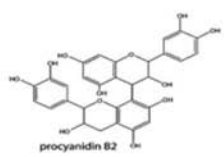
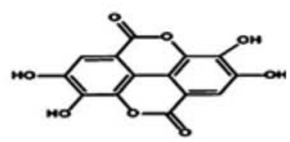
Triterpenic Acids. Triterpenic acids are widespread in plants in the form of free acids or aglycones for triterpenoid saponins,[27] which have been reported to have multiple biological effects such as anti-inflammatory,[28] antimicrobial,[29] hepatoprotective,[30] and antioxidant[31] activities. In recent years, triterpenic acids held attraction in the scientific field because of their anticarcinogenic activity,[32]

Table 4. Individual Polyphenols in Jujube Fruit

main class	sub-class	name	chemical structure	reference
phenolic acids	hydroxycinnamic acids	*p*-coumaric acid		13,25,26
		cinnamic acid		18,26
		caffeic acid		18,25,38,26
		chlorogenic acid		18,38,26
		ferulic acid		13,18,26
	benzoic acids	*p*-hydroxybenzoic acid		13,26
		protocatechuic acid		13,18,25,38,26
		gallic acid		13,18,25,38,26
		vanillic acid		13
flavonoids	flavonols	quercetin		18,25
		rutin		13,18,25
		quercetin-3-galactoside		10, 19
		quercetin-3-rutinoside		10

dx.doi.org/10.1021/jf4007032 | *J. Agric. Food Chem.* 2013, 61, 3351−3363

Table 4. continued

main class	sub-class	name	chemical structure	reference
		kaempferol-glucosyl-rhamnoside		19
		quercetin-3-robinobioside		19
	Flavan-3-ols	epicatechin		13,18
		catechin		13,18
		procyanidin B2		19
ellagic acid				18

which makes them attractive in cosmetics and health care products as functional compounds.[27]

Ten triterpenoid acids (ceanothic, alphitolic, zizyberanal, zizyberanalic, epiceanothic, ceanothenic, betulinic, oleanolic, ursonic, and zizyberenalic acids) in the dried jujube fruit were simultaneously determined by Guo et al.[8] (Figure 2). Guo et al.[33] isolated and identified two new terpenoids (2a-aldehydo-A(1)-norlup-20(29)-ene-27,28-dioic acid (zizyberanal acid) and zizyberanone) and identified two known triterpenes as zizyberanalic acid and ursolic acid from jujube fruits. Guo et al.[7] compared and evaluated the triterpenic acid profiles of the edible jujube fruits as well as their sarcocarps, hard cores, and seed by HPLC-ELSD-MS. Their results revealed that the differences in the contents of triterpenic acids depended on not only the species but also the growing conditions, such as soil, geographical, and environmental conditions.[7]

Colubrinic, alphitolic, 3-*O*-*cis*-*p*-coumaroyl alphitolic, 3-*O*-*trans*-*p*-coumaroyl alphitolic, 3-*O*-*cis*-*p*-coumaroyl maslinic, 3-*O*-*trans*-*p*-coumaroyl maslinic, betulinic, oleanolic, betulonic, oleanonic, and zizyberenalic acids of the EtOAc-soluble fraction of MeOH extract of jujube fruits were isolated by RP-HPLC.[34]

Polysaccharides. Polysaccharides from jujube fruit are subjected to hot water extraction, followed by ethanol precipitation, deproteination, dialysis, and purification in DEAE-Sepharose CL-6B anion exchange, Sepharose CL-6B, and Sephadex G-200 column chromatography.[35] The chemical structures of polysaccharides from jujube, such as the sugar composition, type of glycosyl linkage, and branch structures characterized by spectral analysis, chemical analysis, and chromatography, are shown in Table 5. Two pectic polysaccharides (Ju-B-3 and Ju-B-2) were isolated from the fruits of *Z. jujuba* Mill. cv. Jinsixiaozao. Ju-B-3 and Ju-B-2 showed $[\alpha]_D^{20}$ +151 (*c* 1.00, H_2O) and $[\alpha]_D^{20}$ +125 (*c* 1.00, H_2O), respectively. Wang et al.[36] characterized the chemical composition of the water-soluble polysaccharide from *Z. jujuba* Mill. cv. Shaanbeitanzao (ZSP) (Table 5). HPLC analysis showed that L-arabinose was the main monosaccharide component in ZSP. Several polysaccharide fractions were extracted and further purified from the fruit of jujube. Among them, a neutral polysaccharide fraction (ZJPN) and three acidic polysaccharide fractions (ZJPa1, ZJPa2, and ZJPa3) were found to be more effective in scavenging superoxide anions than hydroxyl radicals. It was shown that the acidic polysaccharides fraction had significant activity in chelating ferrous ion depending on its dose.[37]

α-Tocopherol and Carotene. San and Yildirim[16] extracted α-tocopherol and β-carotene from four promising jujube fruit samples with hexane. In their study, α-tocopherol was detected only in fruits of selections 20-ç-22 and 20-ç-52 (0.04 and 0.07 mg/100 g, respectively), and β-carotene was significantly higher in 20-ç-22 (0.035 mg/100 g of fresh weight) than in the other selections (Table 3). By contrast, Guil-Guerrero et al.[15] reported that the content of carotenes varied from 4.12 to 5.98 mg/100 g on a dry weight basis. Gao et al.[13] compared the contents of β-carotene among the fresh and properly sun-, oven-, microwave-, and freeze-dried jujubes. The results showed that β-carotene content was significantly higher in the freeze-dried samples (15.6 mg/100 g) than in the other samples.

Vitamin C. Jujube is rich in vitamin C. Zhang et al.[38] clearly indicated that the pulps of Dongzao contained the greatest

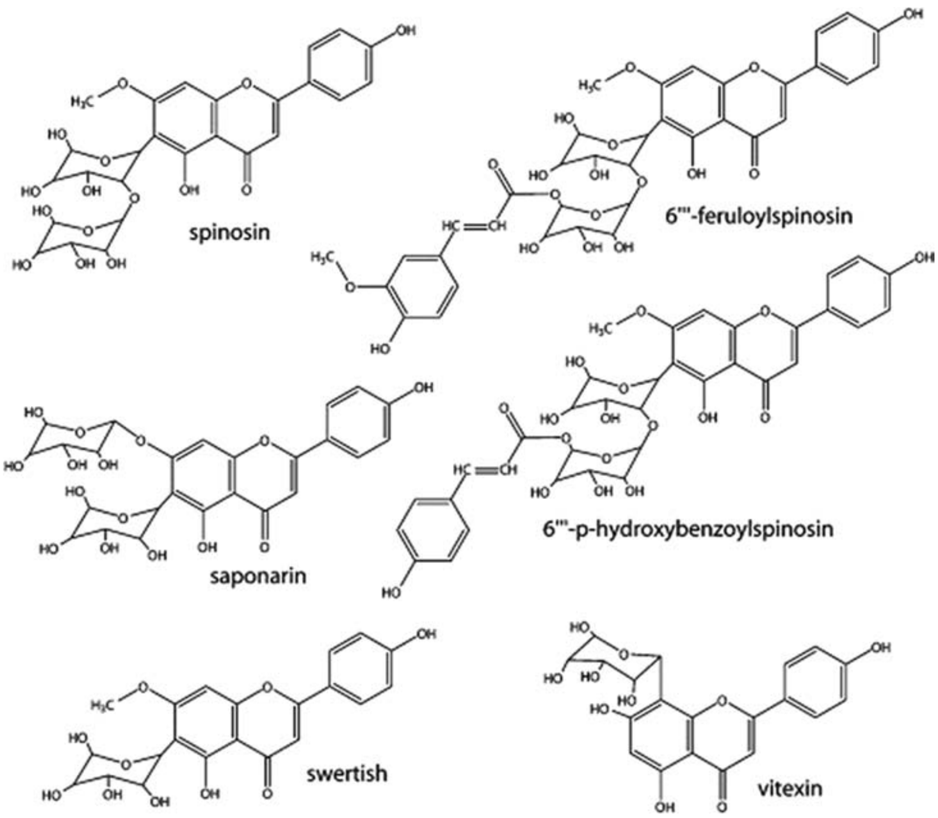


Figure 1. Structures of flavonoids in the seeds of jujube fruit.[10]

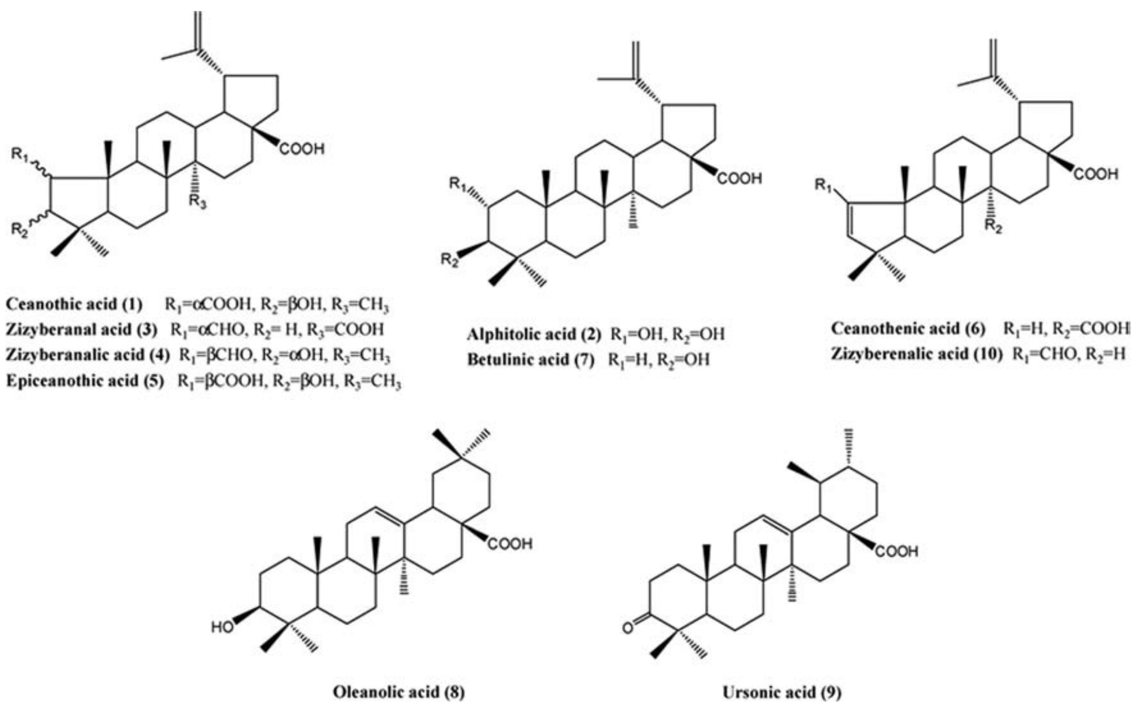


Figure 2. Chemical structures (adapted from ref 8) of 10 investigated triterpenoid acids in jujube.

concentration of ascorbic acid (534.94 mg/100 g DW). The postharvest sorting process of jujubes is important to improve quality including vitamin C during storage and marketing and increase economic benefit for food technologists and processors.

Much of the literature on vitamin C stability is contradictory because oxidation is an important pathway for degradation of vitamin C, and most studies do not control for this. In addition, oxidative enzymes (polyphenol oxidase and peroxidase) may affect vitamin C content, and these are often not evaluated.[39] Jujubes are perishable in their fresh state and may deteriorate within a few days after harvest. Therefore, postharvest treatment of fresh jujube fruits is of great importance. 1-Methylcyclopropene

Table 5. Polysaccharides Isolated from Jujube

no.	compd name	monosaccharide composition	mol wt (Da)	structures	pharmacological properties	ref
1	Ju-B-2	rhamnose, arabinose, galactose, and galacturonic acid at a molar ratio of 2:1:1:10.5	2.0×10^4	polygalacturonan interspersed with rhamnogalacturonan in the main chain; 10.47% D-galacturonic acid; existed as methoxylation and *O*-acetyl groups amounted to 2.5% branched side chains composed of 1,5-linked arabinofuranosyl residues and 1,6-linked galactopyranose residues attached to O-4 of rhamnose residues	immunomodulating	63
2	Ju-B-3		2.0×10^4	polygalacturonan with 7.49% methoxylation		63
3	ZSP3c	rhamnose, arabinose, and galactose at a molar ratio of 1:2:8	1.4×10^5	backbone composed of (1→4)-D-galacturonopyranosyl residues interspersed with (1→2)-L-rhamnopyranosyl residues residues and (1→2,4)-L-rhamnopyranosyl residues; branches composed of arabinofuranosyl residues and galactopyranosyl residues attached to the O-4 position of rhamnopyranosyl residues		35
4	ZSP	mannose, ribose, rhamnose, glucuronic acid, galacturonic acid, glucose, xylose, galactose, and arabinose in 2.8, 1.8, 6.6, 2.6, 10.9, 5.3, 3.4, 16.5, and 50.2 mol %			antioxidative and hepatoprotective effects	36
5	ZJPN	arabinose, xylose, mannose, glucose, and galactose at a molar ratio of 0.3:0.2:0.2:1:0.7	4.7×10^4		antioxidant activity	37
6	ZJPa1	rhamnose, arabinose, xylose, mannose, glucose, and galactose at a molar ratio of 0.3:9.6:0.1:0.4:1:12.1	5.6×10^4		antioxidant activity	37
7	ZJPa2	rhamnose, arabinose, xylose, mannose, glucose, and galactose with at a molar ratio of 3:16.8:1.2:0.2:1:12.2	6.0×10^4		antioxidant activity	37
8	ZJPa3	rhamnose, arabinose, xylose, glucose, and galactose at a molar ratio of 21:24:2:1:20	5.2×10^4		antioxidant activity	37
9	deproteinized polysaccharide (DPP)	rhamnose, arabinose, xylose, mannose, glucose, and galactose at a molar ratio of 2.2:7.8:1.2:0.2:1.4:3.8	two fractions, with average MWs of 14.3×10^4 and 6.8×10^4		antiproliferation effect	58

(1-MCP)-treated jujube fruit maintained a much higher level of vitamin C than untreated fruit stored at both 25 and 0 °C.[40] Zhang et al.[40] suggested that 1-MCP may be related to the enzyme activities of catalase (CAT) and superoxide dismutase (SOD), which are associated with reactive oxygen species (ROS) scavenging, phenylalanine ammonia-lyase (PAL), and polyphenol oxidase (PPO). Nanopacking was also beneficial in preserving the ascorbic acid content of jujube fruits.[41] Wang et al.[42] observed that the combination of marine yeast *Rhodosporidium paludigenum* and CMC-Na did not affect the fruit quality, but rather preserved ascorbic acid in Dongzao.

Jujubes grown under deficit irrigation showed increased concentrations of vitamin C.[43] High vitamin C content may serve as a protective strategy against drought injury. Therefore, from a nutritional point of view, jujube crops grown under deficit irrigation may be preferred due to the high content of vitamin C.

Nucleosides and Nucleobases. It is well-known that nucleosides and their bases are involved in the regulation and modulation of various physiological processes in the body[44,45] and exhibit multiple bioactivities, such as antiplatelet aggregation,[46] antiarrhythmic,[47] antioxidant,[48] antiseizure,[49] and antitumor effects.[50] With these benefits for human health, recently, these compounds have held attraction in the scientific field, and many of them have been selected as quality control markers for several TCMs and foods.[51−53] Guo et al.[2] simultaneously determined nine common nucleosides and nucleobases with an ultraperformance liquid chromatograph coupled with a photodiode array detector and electrospray ionization−mass spectrometer method (UPLC-DAD-MS) in 49 jujube samples, which comprised 43 cultivars from 26 cultivation regions. Their results showed that almost all of these jujube samples were rich in nucleosides and nucleobases (287.79−1239.23 μg/g). Their results also revealed that in the different cultivars from various cultivation regions, the contents of these nucleosides and nucleobases were different, and the variation could be attributed to many factors, including genetic variation, plant origin, and climate or geography (soil or minerals).

HEALTH BENEFITS

Jujubes have long been studied for their biological activity using in vitro and animal model studies,[54−56] but evidence from human epidemiologic and interventional studies is lacking. The hypothesized health benefits related to jujube consumption include their role in anticancer, anti-inflammatory, antiobesity, immunostimulating, antioxidant, hepatoprotective, and gastrointestinal protective activities and in the inhibition of foam cell formation in macrophages (Table 6; Figure 3).

Anticancer Property. An Italian group found that jujube extracts inhibited the growth of selected cancer cell lines. The group indicated that triterpenic acids resulted the from bioactive compounds present in the most effective extracts and showed that they inhibited the growth and induced apoptosis in MCF-7 and SKBR3 breast cancer cell lines.[57] Related literature also demonstrated that induction of apoptosis is one of the mechanisms for the anticancer activities of jujube extracts in different cell lines.[54] Huang et al.[55] investigated the anticancer activity of *Z. jujuba* Mill and its underlying mechanisms of action in human hepatoma cells (HepG2) and found that the extract of jujube decreased the viability of the cells. Choi et al.[19] found that jujube extracts from eight growth stages (S1−8) inhibited HeLa cervical cancer cells dose-dependently, whereas the inhibition of Hel299 normal lung and A549 lung cancer cells decreased as the fruit matured and was well correlated with the content of fruit flavonoid and antioxidative activity. U937 lymphoma cells were unaffected by the jujube extracts. Hung et al.[58] isolated polysaccharides from jujube by boiling water extraction, ethanol precipitation, deproteinization, and dialysis. Two fractions of polysaccharides possessed antiproliferation capability on melanoma cells that followed a dose- and time-dependent course. In vitro studies revealed that deproteinized polysaccharide arrested melanoma cells at the G2/M phase during the cell cycle, accompanied by the formation of an apoptotic body and increases of caspase-3 and caspase-9 activities.

Anti-inflammatory Property. Excess generation of free radicals generated from activated inflammatory leukocytes, especially under conditions of chronic inflammation, is highly deleterious and aggravates arthritis, diabetes, etc.[59] Therefore, for better health and vitality, it is extremely important to control inflammation. As a famous folk medicine, jujube is used as an antidote in the traditional Chinese formula, Shi Zao Decoction, to relieve the drastic inflammatory irritant nature of *Euphorbia* species. The irritant activities may cause serious adverse effects in clinical practices. The anti-inflammatory action of jujube was described by Yu et al.[60] Their study demonstrated that the triterpene acids fraction was the most active part of jujube through the inhibitory effects on the inflammatory cells activated by *Euphorbia kansui* and prostratin, a phorbol ester isolated from *Euphorbia fischeriana*. Goyal et al.[61] suggested that *Z. jujuba* fruits play a protective role against experimental acute and chronic inflammatory reactions in rat, possibly by attenuating NOS activity.

Antiobesity Property. Jujube extract has been shown to prevent obesity on adipocyte differentiation of 3T3-L1 preadiocytes. The results showed that treatment with jujube extract could suppress lipid accumulation and glycerol-3-phosphate dehydrogenase activity without affecting cell viability, and the chloroform fraction of jujube extract with organic solvents revealed the most inhibitory effect.[62]

Immunostimulating Property. Li et al.[56] studied the immunological activity of the polysaccharides fractions from *Z. jujuba* cv. Jinsixiaozao (ZSP). They found that the crude ZSP dramatically increased thymus and spleen indices in mice and enhanced the proliferation of splenocytes and peritoneal macrophages. Two fractions of ZSP (ZSP3c and ZSP4b) were the main active components. The ZSP3c fraction was rich in pectin with a degree of esterification of 49%.[56] Zhao et al.[63] previously isolated two pectic polysaccharides (Ju-B-3 and Ju-B-2) from the fruits of *Z. jujuba* Mill. cv. Jinsixiaozao. Ju-B-2 had significant ($P < 0.01$) activity in enhancing the effect of spleen cells proliferation at a higher dose (>30 μg/mL), whereas Ju-B-3 did not show any proliferation activity compared with the control. According to their structures, rhamnogalacturonan and side chains were proposed as the major contributors in stimulating the immune responses.[63]

Antioxidant Activity. The antioxidant capacity of fruit is closely correlated to the presence of efficient oxygen radical scavengers, such as phenolic compounds and vitamin C.[64] A Chinese group[65] compared the antioxidant capacities of extracts from five cultivars of Chinese jujube and found that the antioxidant capacity differed with cultivar. No correlation was seen between the total phenolics content and antioxidant capacities of extracts from five cultivars of Chinese jujube. Later, another group[38] evaluated the antioxidant capacities of various tissues of jujube. They found that the peel of all cultivars has the highest antioxidant capacities, reflecting the highest content of total phenolics, flavonoids, and anthocyanins in this part. They also found that the predominant phenolic acids in jujube were protocatechuic acid, followed by gallic, chlorogenic, and caffeic acids.

Table 6. Pharmacological Properties of Jujube Fruits

no.	pharmacological property	subject	jujube sample	observation	ref
1	anticancer activity	MCF-7 and SKBR3 breast cancer cells	lyophilized fruits extracted with *n*-hexane (ZE1), chloroform (ZE2), 80% ethanol, followed by evaporation, the remaining water mixture with AcOEt (ZE3) defatted lyophilized fruits (100 g) extracted with MeOH (4 × 200 mL) to yield 50 g of residue, which was dissolved in water and partitioned with AcOEt (ZE4) and *n*-BuOH (ZE5)	ZE1, ZE2, and ZE4 exerted significant antiproliferative effects on estrogen receptor MCF-7 (IC_{50} values of 14.42, 7.64, 1.69 μg/mL) and SKBR3 (IC_{50} values of 14.06, 6.21, 3.70 μg/mL)	57
		HeLa (human cervical carcinoma cell line), HEp-2 (human larynx carcinoma cell line), and Jurkat (T cell leukemia)	water extract of dried jujube fruit at different concentrations (0−1 mg/mL)	induction of apoptosis on human tumor cell lines, HEp-2, HeLa, and Jurkat cell lines; jurkat leukemic line was found the most sensitive with IC_{50} of 0.1 μg/mL	54
		HepG2 cells	jujube extract with different solvents (water, chloroform, ethyl acetate, and *n*-butanol)	chloroform fraction ($CHCl_3$−F) was the most effective; $CHCl_3$−F induced G1 arrest at 100 μg/mL with an increase in phosphorylation of Rb and $p27^{Kip1}$, and a decrease of phosphorylated Rb induced G2/M arrest at 200 μg/mL correlated with a decrease of the $p27^{Kip1}$ levels and generation of the phosphorylation of $p27^{Kip1}$; the hypophosphorylation of Rb remained	55
		human cervical carcinoma (HeLa), histiocytic lymphoma (U937), lung cancer (A549), and normal human liver (Chang) and lung cell lines (Hel299)	treated with four concentrations (1, 10, 50, 100 μg/mL) of extract of phenolic compounds for 48 h	inhibit HeLa cervical cancer cells, Hel299 normal lung, and A549 lung cancer cells by (S1−8 jujube extracts); inhibited Chang normal liver cells by only the S5 jujube extract	19
		melanoma cells	DPP	50% inhibitory concentration of DPP at 3.99 mg/mL after 24 h of treatment, decreased significantly to 3.36 mg/mL after 48 h	58
2	anti-inflammatory activity	male ICR mice (20−22 g);	fraction A, crude polysaccharides fraction, 1.63%, w/w	inhibitory effects on the inflammatory cells activated by *Euphorbia kansui* and prostratin, a phorbol ester isolated from *Euphorbia fischeriana* fraction F to be the most active part	60
		SD rats (200−240 g)	fraction B, deproteinized polysaccharides fraction, 0.9%, w/w		
			fraction C, oligosaccharide fraction, 22.7%, w/w		
			fraction D, ammonia−water fraction, 2%, w/w		
			fraction E, flavonoids fraction, 0.057%, w/w		
			fraction F, triterpene acids fraction, 0.04%, w/w		
		Wistar albino rats (180−240 g)	dried coarse powder extracted with 60% ethanol to yield jujube extract (17.4% w/w)	significantly attenuated the effect of carrageenan in rat paw and extended to 2 and 3 h at 100, 200, and 400 mg/kg; inhibited granuloma formation at 200 and 400 mg/kg; markedly decreased serum nitrite/nitrate at 200 and 400 mg/kg	61
3	antiobesity activity	mouse embryo 3T3-L1 cells	jujube extract with different solvents (chloroform, ethyl acetate, *n*-butanol, and water)	$CHCl_3$−F efficiently suppresses adipogenesis in 3T3-L1 preadipocytes	62
4	immunostimulating activity	3-month-old Kunming mice (males and females, 20 ± 2 g)	water-soluble crude polysaccharides fractioned by DEAE-Sepharose CL-6B anion-exchange column (4.5 cm × 50 cm), Sepharose CL-6B (2.6 cm ×160 cm)	CZSP dramatically increased thymus and spleen indices, and peritoneal macrophages CZSP, ZSP3, ZSP3c, ZSP4, and ZSP4b induced the proliferation of spleen lymphocyte	56
5	antioxidant activity	diphenyl-1-picrylhydrazyl (DPPH), ferric-reducing antioxidant power (FRAP), reducing power and antioxidant activity in a linoleic acid system	five jujube cultivars were extracted with different solvents	Jinsixiaozao with the highest antioxidant activities	65

Table 6. continued

no.	pharmacological property	subject	jujube sample	observation	ref
		DPPH, superoxide anion, hydroxyl radical-scavenging activity, and reducing power	four water-soluble polysaccharide fractions (ZSP1b, ZSP2, ZSP3c, and ZSP4b) isolated and purified by DEAE-Sepharose CL-6B and Sepharose CL-6B column chromatography	ZSP3c and ZSP4b containing more uronic acid had the stronger free radical scavenging activities	66
		DPPH, FRAP, and trolox equivalent antioxidant capacity (TEAC)	jujube peel and pulp samples extracted with 70% methanol	total phenolic content in peel was 5−6-fold higher than that in the pulp; high levels of total polyphenolics result in antioxidant capacity	21
		DNA damage protective activity, DPPH, FRAP, reducing power, inhibition of lipid peroxidation, bleaching ability of β-carotene in linoleic acid system,	dried jujube powder extracted with 75% ethanol for 30 min in an ultrasonic bath	jujube fruits from Ningxia, Gansu, and Shaanbei grown in the semiarid regions of loess plateaus showed fairly higher antioxidant activities	22
		DPPH and FRAP	free, esterified, glycosided, insoluble-bound phenolic acid fractions in jujube pulp, seed, and peel	glycosided and insoluble-bound phenolic acid fractions in pulp represent the strongest antioxidant activity	26
6	hepatoprotective activity	Kunming male mice (18−22 g)	dried jujube fruit powder soaked in water (1:20, w/v) at 80 °C for 160 min after three cycles, solutions filtered and concentrated, then precipitated with 95% ethanol at 4 °C for 24 h; refined pellets dialyzed with water for 4 days (cutoff M_w 0.8 × 10^4 Da); retentate deproteinized by freeze−thaw process repeated 10 times followed by filtration; supernatant was lyophilized	reduced activities of CCl_4-elevated ALT, AST, and LDH in serum, and hepatic MDA level at 400 mg/kg; better profile of HI, normal GSH-Px, and SOD activities in liver	36
		male ICR mice (25−28 g)	dried jujube powder (5 kg) extracted three times with 70% EtOH under reflux for 3 h each time; concentrated crude 70% EtOH extract of 328 g with a yield of 6.56% (w/w, to dried material)	decreased ALT and AST, attenuated histopathology of hepatic injury, and ameliorated the oxidative stress in hepatic tissue at 200 mg/kg	68
7	gastrointestinal protective activity	*Bacillus cereus* BCRC 10603, *Escherichia coli* BCRC 13086, *Listeria monocytogenes* BCRC 14848, *Salmonella choleraesuis* BCRC 12948, and *Staphylococcus aureus* BCRC 15211; 32 male Golden Syrian hamsters (6 weeks old) weighing 105 ± 2.0 g	dried jujube distilled with boiled water for 2 h, then filtered and dried by lyophilization	water-soluble carbohydrate concentrate (5.0 and 15 g/kg diet) shortened gastrointestinal transit time (by 34.2−57.3%), reduced cecal ammonia (by 58.1−60.3%), elevated total short-chain fatty acid concentrations in cecum (3−4-fold), increased fecal moisture (147−170%), reduced daily fecal ammonia output (by 31.9−75.8%), and decreased the activities of β-D-glucuronidase (by 73.0−73.8%), β-D-glucosidase (by 58.2−85.7%), mucinase (by 46.2−72.6%), and urease (by 31.9−48.7%) in feces	1
		32 rabbits	jujube powder (200 g) extracted three times with boiled water (1500 mL) for 5 h each time; the concentrated extract precipitated with 70% ethanol for 12 h; the precipitates lyophilized to obtain polysaccharides	reduced intestine MDA level and increased antioxidant enzyme activities in rabbits with ischemia/reperfusion (I/R) of the small intestine	69
8	inhibit foam cell formation in macrophages	human peripheral mononuclear cells	crude plant extracts; isolated triterpenoid compounds	*Zizyphi fructus* and *Zizyphi semen* extracts inhibited foam cell formation induced by acetylated LDL; oleanonic acid, pomolic acid, and pomonic acid were the major active compounds	70

dx.doi.org/10.1021/jf4007032 | J. Agric. Food Chem. 2013, 61, 3351−3363

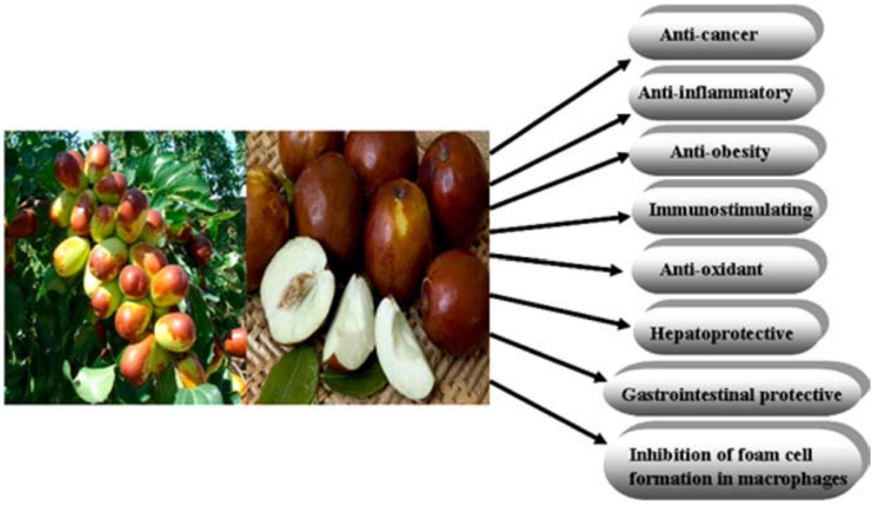


Figure 3. Pharmacological activities of jujube fruit.

In a paper prepared by Li et al.,[66] the antioxidant activity of the four water-soluble polysaccharides fractions (ZSP1b, ZSP2, ZSP3c, and ZSP4b) of the jujube fruit was determined, and it was suggested that ZSP3c and ZSP4b, containing more uronic acid, had stronger free radical scavenging activities than ZSP1b, containing no uronic acid. The work carried out by Sun et al.[22] indicated that the jujube fruits from Ningxia, Gansu, and Shaanbei grown in the semiarid regions of loess plateaus showed fairly higher antioxidant activities. The same group also concluded that the fruits in arid harsh and high-altitude areas can accumulate higher levels of natural antioxidants and display stronger antioxidant activities. Wang et al.[26] investigated free, esterified, glycosided, and insoluble-bound forms of eight phenolic acids in the pulp, seed, and peel of jujube by HPLC-ECD. *p*-Hydroxybenzoic and cinnamic acids were the most abundant phenolic acids in the whole jujube. Phenolic acids in seed and peel are present in the insoluble-bound form, whereas in pulp, in the glycosided form, the glycosided and insoluble-bound phenolic acid fractions in jujube pulp represent the highest total phenolic content and the strongest antioxidant activity.

Although jujube fruit is a potential source of natural antioxidant for the food industry, we should be aware of the essential metabolic functions of the ROS. The removal of too many ROS can upset cell signaling pathways and actually increase the risk of chronic disease.[67]

Hepatoprotective Property. To make a good recognition of the hepatoprotective activity of the jujube fruit, the effect of jujube fruit on carbon tetrachloride (CCl_4)-induced liver injury was examined.[68] Male ICR mice were administered by subcutaneous injection (ip) with CCl_4 2 days prior to jujube fruit administration. Serum liver enzyme levels, histology, and expression of antioxidant enzymes were subsequently estimated. The results suggested that jujube fruit effectively prevented liver injury, mainly through down-regulation of oxidative stress and inflammatory response. Wang et al.[36] also analyzed the effects of polysaccharide from jujube fruits on liver function. The data showed that jujube fruit treatment reduced the activities of CCl_4-elevated alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactic dehydrogenase (LDH) in serum and the hepatic malondialdehyde (MDA) level. Mice treated with polysaccharide from jujube fruits showed a better profile of hepatosomatic index (HI) and antioxidant system with normal glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) activities in the liver.

Gastrointestinal Protective Property. The water-soluble carbohydrate concentrate extracts of jujube fruits including glucose, fructose, pectin polysaccharide, and hemicellulose, were observed to be effective in maintaining intestinal health via reducing the exposure of intestinal mucosa to toxic ammonia and other harmful substances in a hamster model.[1]

Chinese jujube polysaccharides are anecdotally reputed to be useful in ameliorating intestine oxidative injury resulting from ischemia and reperfusion in rabbits. The jujube polysaccharides composed of glucose (23%), xylose (31.3%), mannose (12.9%), and fructose (21.6%) possess antioxidant effects, and this may have contributed to the observed effects.[69]

Inhibition of Foam Cell Formation in Macrophages. Fujiwara et al.[70] reported triterpenoids from *Z. jujuba* could inhibit the formation of foam cells in macrophages. The authors investigated the inhibitory effect of 50 crude plant extracts on foam cell formation. Their results showed that *Zizyphi fructus* and *Zizyphi semen* extracts significantly inhibited the foam cell formation induced by acetylated LDL among the 50 crude extracts. The major active compounds were triterpenoids, such as oleanonic acid, pomolic acid, and pomonic acid. Fujiwara et al.[70] also demonstrated triterpenoids containing a carboxylic acid at C-28 play an important role in the inhibitory effect on foam cell formation in human macrophages.

Other Health Benefits. Lee et al.[34] found that oleanane-type triterpenes 3-*O*-*cis*-*p*-coumaroyl maslinic, 3-*O*-*trans*-*p*-coumaroyl maslinic, and oleanolic acids exhibited significant anticomplement activity with IC_{50} values of 101.4, 143.9, and 163.4 μM, respectively, whereas the ceanothane-type and the lupane-type triterpenes were inactive. Their results suggested that the oleanane structure plays an important role in inhibiting the hemolytic activity of human serum against erythrocytes.[34] Lee et al.[71] reported that the lupine-type triterpenes, such as 3-*O*-*cis*-*p*-coumaroyl alphitolic, 3-*O*-*trans*-*p*-coumaroyl alphitolic, betulinic, and betulonic acids, showed high cytotoxic activities, and the cytotoxic activities of 3-*O*+*p*-coumaroyl alphitolic acids were better than those of noncoumaroic triterpenenoids. Their results suggested that the coumaroyl moiety at the C-3 position of the lupine-type triterpene may play an important role in enhancing cytotoxic activity.

dx.doi.org/10.1021/jf4007032 | *J. Agric. Food Chem.* 2013, 61, 3351−3363

DISCUSSION AND PERSPECTIVE

Phytochemical data combined with biological activity information confirm that jujube fruits have potential medicinal and dietary values for humans. However, other unidentified phenolics or other compounds, including saponins and nonpolar constituents, should also be investigated in these fruits for their biological effects. This review demonstrates that compiling ethnobotanical and nutritional compositions of jujube fruits information, to interpret data from phytochemical investigations, is useful for predicting the biological activities of under-researched natural foods or medicines, such as jujube fruits. Research on jujube fruits may be especially important to people in areas where such natural resources may be prevalent but proper health care is scarce. Furthermore, this review provides information that may be useful for predicting other medical uses and drug or food interactions of jujube fruits. The information about phenolics, triterpene acids, and polysacchrides may also serve as a springboard for research studies on their bioavailability and the mechanisms of anti-inflammatory and immunostimulating activities.

Finally, to better understand the effect of jujube metabolites on human health, in vivo studies on animals and, when possible, on humans should be introduced, because the effect of the compound on human cells and tissues measured by in vitro tests cannot represent the actual evaluation of the in vivo effect.

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Notes

The authors declare no competing financial interest.

ABBREVIATIONS USED

cAMP, adenosine 3′,5′-cyclic monophosphate; cGMP, guanosine 3′,5′-cyclic monophosphate; TCM, traditional Chinese medicine; UPLC-DAD-MS, photodiode array detector and electrospray ionization−mass spectrometer method; GAE, gallic acid equivalent; DW, dry weight; DPPH, 1,1′-diphenyl-2-picrylhydrazyl; 1-MCP, 1-methylcyclopropene; CAT, catalase; SOD, superoxide dismutase; PAL, phenylalanine ammonia-lyase; PPO, polyphenol oxidase; ROS, reactive oxygen species; HI, hepatosomatic index; GSH-Px, glutathione peroxidase

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