Chemical and pharmacological studies of cornus officinalis

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Abstract: This article reviews the chemical components and pharmacological effects of Cornus officinalis Sieb.et Zucc., a traditional Chinese medicinal herb that contains a variety of active ingredients, including iridoid glycosides, flavonoids, organic acids, and tannins. These components endow Cornus officinalis with multiple pharmacological actions, such as neuroprotection, anti-diabetes and its complications, cardioprotection, anti-tumor, and antioxidant effects. In particular, the paper discusses the impact of Cornus officinalis iridoid glycosides on learning and memory ability after cerebral ischemia, as well as their potential mechanisms in the treatment of diabetic nephropathy. Additionally, the application of Cornus officinalis methanol extract in promoting melanin synthesis and its anti-inflammatory, anti-fatigue, antibacterial, anti-osteoporotic, and hepato- and reno-protective effects are also discussed. Although progress has been made in existing research, the specific roles and mechanisms of some newly discovered compounds in Cornus officinalis still require further investigation. This paper aims to provide a reference for in-depth research and clinical application of Cornus officinalis.

Keywords: Cornus officinalis, Chemical Components, Pharmacological Effects

1. Introduction

Cornus officinalis Sieb.et Zucc., also known as Shu Zao, Shu Shi, Ji Zu, Shan Yu Rou, Shi Zao Er, Zao Pi, and Yu Rou, is a deciduous small tree of the Cornus genus. It is distributed and cultivated in various regions of China, including Zhejiang, Henan, Shandong, Anhui, Jiangsu, Shanxi, Shaanxi, and Sichuan, with the main producing areas being Western Henan and Zhejiang. The quality of its varieties significantly affects the yield and quality of the medicinal material. In clinical practice, the mature fruit, which has had its seeds removed, is commonly used as medicine. Cornus officinalis has a sour and astringent taste, is slightly warm, and is associated with the liver and kidney meridians. It has the effects of nourishing the liver and kidneys and consolidating essence to prevent leakage, primarily treating conditions such as dizziness, tinnitus, lower back and knee pain, impotence, nocturnal emission, frequent urination, metrorrhagia, excessive sweating with deficiency, and internal heat with thirst. It is one of the valuable traditional anti-aging drugs commonly used in clinical Chinese medicine. This article provides a comprehensive review of the chemical components and pharmacological actions of Cornus officinalis, aiming to offer information for further research on this medicinal plant.

2. Chemical components

2.1. Iridoid glycosides

Iridoid glycosides are not only the most abundant group in Cornus officinalis but also its characteristic components, with the majority being connected to sugars to form iridoid glycosides. The iridoid glycosides present in Cornus officinalis are shown in Table 1:

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Table 1: Iridoid Glycoside Components in Cornus officinalis

No.	Name	Formula	References
1	Loganin	$C_{17}H_{26}O_{10}$	1
2	7-dehydrologanin	$C_{17}H_{24}O_{10}$	2
3	7-O-butylmorroniside	$C_{21}H_{34}O_{11}$	3, 4
4	10-hydroxyhastatoside	$C_{18}H_{28}O_{11}$	1
5	β-dihydro-cornin	$C_{17}H_{26}O_{10}$	1
6	Cornu side I	$C_{24}H_{30}O_{14}$	2, 4

2.2. Flavonoids

The types of flavonoids in Cornus officinalis are limited and they are not present in high concentrations. The main flavonoids reported in the literature include Quercetin, Kaempferol, and Isoquercitrin, among others. See Table 2:

Table 2: Flavonoid Components in Cornus officinalis

No.	Name	Formula	References
1	Quercetin	$C_{15}H_{10}O_7$	2
2	Isoquercitrin	$C_{11}H_{11}O_{11}$	1
3	Quercetin 3-O-β-D-glucuronide	$C_{21}H_{18}O_{13}$	4
4	Quercetin 3-O-β-D-(6”-n-Butyl glucoside)	$C_{25}H_{26}O_{13}$	4
5	Kaempferol	$C_{15}H_{10}O_6$	2
5	Kaempferol-3-O-β-D-glucoside	$C_{21}H_{20}O_{11}$	2
6	Naringenin	$C_{15}H_{12}O_5$	2
7	(-)-Epicatechin-3-O-gallate	$C_{22}H_{18}O_{10}$	4

2.3. Organic acids

The pulp of Cornus officinalis contains organic acids such as ursolic acid, 2α-hydroxyursolic acid, oleanolic acid, gallic acid, malic acid, tartaric acid, protocatechuic acid, 3,5-dihydroxybenzoic acid, vitamin A, 5-hydroxymethylfurfural, 5-methylfurfural ether, and β-sitosterol [5]. Many organic acids with phenolic acid groups produce other components through synthetic pathways, such as gallic acid combining with loganic acid to form Cornu side I, a new iridoid glycoside. The organic acid components in Cornus officinalis are shown in Table 3:

Table 3: Organic Acid Components in Cornus officinalis

No.	Name	Formula	References
1	Gallic acid	$C_7H_6O_5$	2, 4
2	Ellagic acid	$C_{14}H_6O_8$	6
3	Caffeic acid	$C_9H_8O_4$	4
4	Methyl malic acid	$C_5H_8O_5$	2
5	Butane dioic acid	$C_8H_{14}O_5$	4
6	P-hydroxycinnamic acid	$C_{11}H_{11}O_{11}$	2
7	Oleanolic acid	$C_{30}H_{48}O_3$	1, 4

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8	Ursolic acid	$C_{30}H_{48}O_3$	2
9	Maslinic acid	$C_{30}H_{48}O_4$	7
10	Corosolic acid	$C_{30}H_{48}O_4$	7

2.4. Tannins

Tannins are the components that give Cornus officinalis its astringent taste. The fruit pulp of Cornus officinalis contains 11 types of tannins, including tellimagrandin D, Cornus officinalis tannin 1 (also known as isogarcinone or trapa tannin), Cornus officinalis tannin 2 (also known as new syringin II), and Cornus officinalis tannin 3 (also known as new syringin I), which consist of 4 gallotannins and 7 ellagitannins [5]. The tannin components in Cornus officinalis are shown in Table 4:

Table 4: Tannin Components in Cornus officinalis

No.	Name	Formula	References
1	1,2,3,6-tetragalloyl-β-D-glucose	$C_{34}H_{28}O_{22}$	3
2	1,2,3,4,6-pentagalloyl-β-D-glucopyranose	$C_{41}H_{32}O_{26}$	3
3	Tellimagrandin I	$C_{34}H_{26}O_{22}$	3
4	Tellimagrandin II	$C_{41}H_{30}O_{26}$	3

2.5. Other components

In addition to the components mentioned above, Cornus officinalis also contains many other constituents, as shown in Table 5:

Table 5: Other Components in Cornus officinalis

No.	Name	Formula	References
1	Arjun glucoside II	$C_{36}H_{58}O_{10}$	2
2	Mevalo side	$C_{12}H_{20}O_8$	8
3	5-hydroxymethyl-2-furfural	$C_6H_6O_3$	8
4	β-sitosterol	$C_{29}H_{50}O$	4
5	Caftaric acid monomethyl ester	$C_{14}H_{14}O_9$	4

3. Pharmacological effects

3.1. Neuroprotective effects

Studies have shown that Cornus officinalis iridoid glycosides (CIG) promote learning and memory capabilities in ischemic gerbils and enhance the expression of BDNF protein in the hippocampal region [9]. Additionally, CIG can reduce the number of neuronal deaths in the hippocampal area of adult SD rats after transection of the fornix fimbria, and its mechanism of action may be related to upregulating apoptosis inhibitory factors and downregulating pro-apoptotic factors [10]. The active components of Cornus officinalis can also alleviate brain damage caused by ischemia-reperfusion through pathways such as inhibiting free radical damage and inflammatory responses, reducing calcium overload, and inhibiting apoptosis [11].

3.2. Effects on diabetes and its complications

Formulas containing Cornus officinalis that lower blood sugar and benefit the kidneys can significantly reduce the expression levels of IRS-1 and PI-3K proteins in the glomeruli of MKR rats on a high-fat diet, decreasing the proliferation of mesangial cells in diabetic nephropathy [12]. Huang et al. [13] replicated a diabetic rat model, dividing the rats into normal, model, and treatment groups (with high, medium, and low

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doses of Cornus officinalis granules and valsartan), and observed the kidney function and 24-hour urinary protein levels of the rats. Immunohistochemical detection of TGF-β1 and Smad7 protein expression in renal tissue indicated that Cornus officinalis granules can be used to treat early diabetic nephropathy, and the mechanism may be related to its ability to inhibit the activation of the TGF-β1/S mads signaling pathway in the kidneys of diabetic rats. When different polarity extracts of Cornus officinalis were applied to streptozotocin-induced diabetic model mice, it was found that both the ethanol extract and the ethyl acetate extract of Cornus officinalis could reduce the levels of triglycerides in the mouse serum, and the ethanol extract could also increase the level of serum insulin [14].

3.3. Cardioprotective effects

The application of Panax no to ginseng saponins/total glycosides of Cornus officinalis (PNS/TGCO) in dogs with acute myocardial ischemic infarction caused by coronary artery ligation can significantly reduce the degree of myocardial ischemia after coronary ligation, constrict the scope of myocardial ischemia, and notably decrease the activity of serum creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) [15]. In the primary culture of neonatal mouse myocardial cells with ischemia and hypoxia established by liquid paraffin seal method, after treatment with a drug concentration of 10g/L of total glycosides of Cornus officinalis, it was found that compared with the control group, the apoptosis rate at various time points in the treatment group decreased, indicating that the total glycosides of Cornus officinalis can inhibit myocardial cell apoptosis [16].

3.4. Antitumor effects

The polysaccharides from Cornus officinalis exhibit significant tumor suppression effects in S180 sarcoma mice, capable of increasing the number of peripheral blood CD4+ T cells, decreasing the number of CD8+ T cells, and elevating the levels of IL-2 while reducing IL-4 levels, showing a positive correlation with dosage and concentration [17].

3.5. Antioxidant effects

Using 70% ethanol as a solvent and an ultrasonic cell disruptor for drug extraction, a spectrophotometer was employed to measure the DPPH free radical scavenging ability and FRAP values of ethanol extracts from 41 kinds of traditional Chinese medicinal herbs. It was found that at a concentration of 10mg/ml, Cornus officinalis showed a DPPH free radical clearance rate of over 70%, with a total antioxidant capacity FRAP value greater than 200, indicating that Cornus officinalis has strong antioxidant capabilities.

3.6. Other effects

The methanol extract of Cornus officinalis promotes the synthesis of melanin, which can be appropriately used to treat white hair; moreover, Cornus officinalis is also rich in polyphenols and has good anti-inflammatory effects, as well as properties such as anti-fatigue, antibacterial, anti-osteoporotic, hepato- and reno-protective, and immune-modulating capabilities.

4. Outlook

Cornus officinalis is one of the world's three most precious woody medicinal materials and is also one of the top 25 most frequently used botanical drugs in China, Japan, and Korea. To date, research on the bioactive components of Cornus officinalis has yielded fruitful results, providing a basis for the study of Cornus officinalis as a single medicinal material and in compound traditional Chinese medicine formulas, and showing promising prospects for the development of treatments for diseases such as diabetes. However, the roles and mechanisms of many newly discovered compounds in Cornus officinalis are still unclear, necessitating further research into the various components of Cornus officinalis.

5. Conclusion

Although existing research has provided a scientific basis for the application of Cornus officinalis, further exploration of the mechanisms of action of its newly discovered compounds is still needed. Future research should focus on the separation, identification, and elucidation of the mechanisms of action of these

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active components to facilitate the maximization of Cornus officinalis in drug development and clinical applications. With the continuous accumulation of a deeper understanding of Cornus officinalis, its prospects for application in modern medicine will be broader, making a greater contribution to human health.

6. References

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