Herbal Medicines Journal **2023; 8(3):170-8**
DOI: 10.22087/hmj.v8i3.1077 **ISSN:** 2538-2144

Review Article

Physiological and Pharmacological Properties of the *Swertia longifolia Boiss* Plant and Its Compounds: A Mini Review

Ali Zarei[1*], Amirhossein Zarei[2]

[1]Department of Physiology, Estahban School of Paramedical Sciences, School of Nursing Hazrat Zahra (P.B.U.H) Abadeh, Shiraz University of Medical Sciences, Shiraz, Iran
[2] Department of Experimental Sciences, Saadi High School, Abadeh Education Department, Abadeh, Iran

Received: 09.11.2023; Accepted: 19.02.2024

Abstract

Swertia longifolia, from the Gentianaceae family, grows in various regions of the world and is used in traditional and modern medicine to treat many diseases. The present study aimed to systematically review the physiological-pharmacological effects of this plant and its compounds. To conduct this scoping review, articles published in PubMed, ScienceDirect, Web of Science, Google Scholar, ProQest, Cochrane, SID, and Magiran databases were searched, using the keyword *S. longifolia*, on 18th March, 2023 to find relevant articles. *S. longifolia* contains effective compounds such as xanthones, iridoid glycosides, flavonoids, and triterpenoids, which have antioxidant, anti-cholinesterase, and anti-cytotoxic properties. Moreover, the extract of this plant and its compounds have anti-diabetic, hepatoprotective, and hypolipidemic properties and can inhibit the enzyme acetylcholinesterase. Given the effects of the extract and compounds of *S. longifolia* in the treatment of various diseases, it seems that clinical trials as well as more advanced studies should be conducted on each of the compounds of the plant which will be considered as new candidates for drug development in the future.

Keywords: Physiological, Pharmacological, *Swertia longifolia Boiss*, Mini Review, Compounds

***Corresponding Authors:** Ali Zarei, Department of Physiology, Estahban School of Paramedical Sciences, School of Nursing Hazrat Zahra (P.B.U.H) Abadeh, Shiraz University of Medical Sciences, Shiraz, Iran. Email: zarei.ali40@gmail.com

Please cite this article as: Zarei A, Zarei A. Physiological and Pharmacological Properties of the Swertia longifolia Boiss Plant and Its Compounds: A Mini Review**.** Herb. Med. J. 2023;8(3):170-8.

Introduction

The plant with the scientific name *Swertia longifolia* Boiss and the English names marsh felwort, felwort, and Swertia belongs to the Gentianaceae family. This plant has a dull green color, broad and hairless leaves, a thick rhizome, and stable, herbaceous stems. Its stems lead to a long inflorescence with white or cream-white flowers and a long peduncle (1). Swertia species are widespread in East and South Asian countries, and are used in traditional medicine as antipyretic, pain reliever, and stomach and liver tonic. Among the different species, only *S. longifolia* grows in Iran (2). Swertia is mainly found in temperate, subtropical and non-mountainous tropical regions (3). It also grows in mountainous areas such as Koh-e-Safaid, the northern border of Pakistan and Afghanistan, and Northern Iran (4).

One hundred and seventy species of Swertia are widespread throughout the world, including countries in East and South Asia. The first recorded use of Swertia plants dates back to the 2nd to 3rd centuries B.C., when it was used to reduce fever and purify breast milk. In traditional Indian, Chinese and Tibetan medicine, it

has been used as a stomach tonic, antipyretic, anti-pain, anti-parasitic, and anti-inflammatory herbal medicine (2). Moreover, it is used in the treatment of malaria, liver diseases, stomach problems, diabetes, hepatitis (3).

The main compounds of Swertia species are xanthones, iridoid glycosides, flavonoids, and triterpenoids (5, 6). Among the essential xanthones of this plant, swerchirin, swertiaperenine, gentiacauleine (7), isobellidifolin, bellidin, and gentisein can be mentioned (8). These compounds have many biological and medicinal properties, including antioxidant, anti-inflammatory, antimicrobial, anti-cholinesterase, and anti-cytotoxic activities (6). The famous triterpenes of this plant include α- and β-amyrin, ursolic acid, β-sitosterol and glucoside, Daucosterol, and squiridoid sortiamarin. These compounds have antimicrobial, anti-inflammatory, anti-diabetic, antioxidant, cytotoxic, anti-wound, anti-inflammatory, and pain-relieving properties (9, 10).

In modern medicine, laboratory studies have indicated anti-diabetic effects, liver and kidney protection, and hypolipidemic as well as antioxidant properties. By stimulating the secretion of insulin and alkaloids via inhibiting the aldose reductase enzyme, swercherin effectively treats diabetes and its complications such as neuropathy, nephropathy, and cataracts. This plant extract reduces blood fat, creatinine, urea, and liver enzymes, and shows liver protection properties against hepatotoxicity caused by acetaminophen. Thus, it is effective in treating the complications of diabetes, arteriosclerosis, and kidney failure (1, 10).

The extract of *S. longifolia Boiss* has antioxidant properties. It does not have cytotoxic effects in concentrations less than 100 micrograms per milliliter. Moreover, it is effective in treating Alzheimer's disease by inhibiting the enzyme acetylcholinesterase (2).

Therefore, the review of the literature indicates the diverse use of *S. longifolia Boiss* for medicinal purposes in the treatment of various diseases, but more studies are needed to target the compounds responsible for pharmacological effects, determine the mechanism of action of compounds and plant extracts, and also determine possible side effects. In this regard, the present study aimed to systematically review the physiological-pharmacological impacts of this plant and its compounds.

Materials and Methods

This review article was conducted by searching the *"Swertia longifolia"* in scientific databases. This keyword was searched in PubMed (5 documents), ScienceDirect (6 documents), Web of Science (9 documents), Google Scholar (15 documents), ProQuest (17 documents), and Cochrane (0 documents). Furthermore, SID (17 documents) and Magiran (4 documents) were searched to access Iranian articles. The article search was performed on 18th March, 2023. Other methods found four themes such as reviewing references in the papers. Collectively, 73 articles were found. After removing duplicates (33 records) and irrelevant (16 documents), 40 articles remained to be evaluated in this study. Out of this total (42 records), only 2 articles were removed, which were mostly about how to plant and care for the plant (Diagram 1).

Results and Discussion

Botany, and Geographical Distribution

The English names of this plant are Swertia, felwort, and marsh felwort. Swertia is a stable, matte green, erect, hairless plant with a height of 45-80 cm and a thick stem and rhizome. Its stems are grassy and lead to long inflorescences. The leaves are hairless and dull green or tending to blue, and its flowers are white, with long flower stalks and clustered flowers. Swertia usually flowers in May and June. This plant grows in humid areas. In Iran, it grows in Alborz (Kandavan) and in the West (Eshtrankoh, Rasvand, Borujerd and Alvand). Swertia L. with about 150 species worldwide is one of the most divers genera of the Gentianaceae. Diversity centers of this plant are East Himalaja, Chinese provinces of Yunnan and Sichuan (with diversity maximum of 16.3 in Nepal), and the East African Rift Valley Region (with highest diversity in Malawi (11).

Compounds

The main compounds of Swertia species are xanthones, iridoid glycosides, flavonoids, and triterpenoids (5, 6). Xanthones are secondary metabolites (12) and natural polyphenolic compounds with a simple three-ring skeleton, usually found in plants of the Gentianaceae family (13). These compounds have many biological

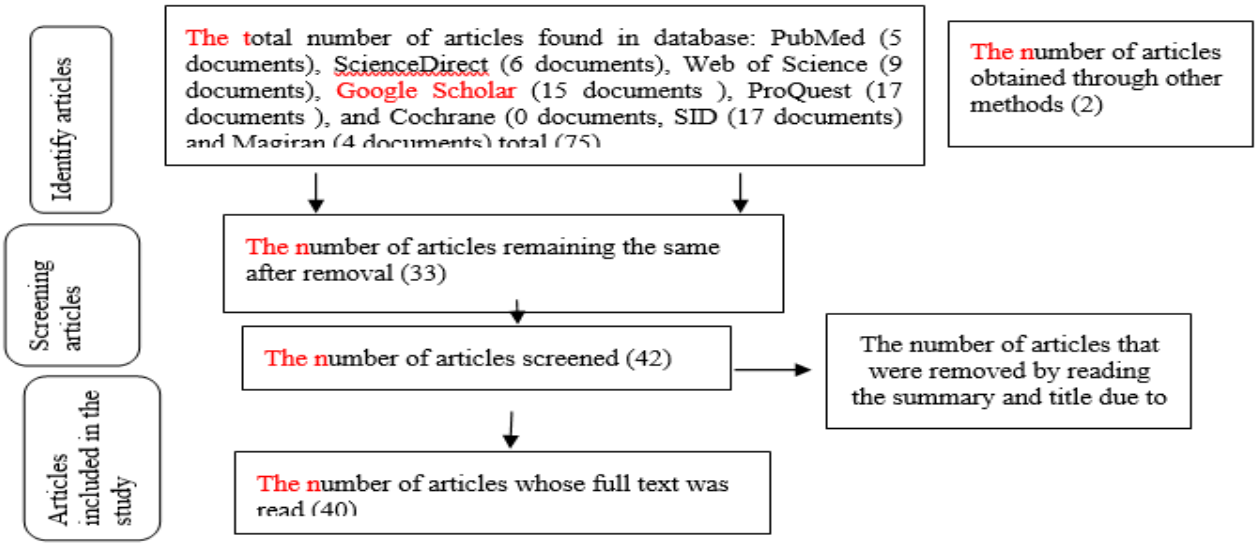

Diagram 1. Data analysis pattern of the present study.

and medicinal properties such as antioxidant, anti-inflammatory, antimicrobial, anti-cholinesterase, and anti-cytotoxic activities (Table 1) (6, 14).

Xanthone O-Glucoside is a group of glucosides attached to an oxygen atom's three-ring body of xanthones. Two diglycosidic xanthones, namely 1,5-dihydroxy-3-methoxy-6-O-primeverosyl xanthone and 8-hydroxy-3,5-dimethoxy-1-O- primeverosyl xanthone, were isolated from the aerial parts of Swertia which grow in Northern of Iran (12). 1,8-Dihydroxy-3,5-dimethoxyxanthone (swerchirin), 1,8-Dihydroxy-2,6-dimethoxyxanthone (swertiaperenine), 2,8-Dihydroxy-l, 6-dimethoxy xanthone (gentiacauleine) (7), isobellidifolin, bellidin, gentisein, 1,5-dihydroxy-3-methoxy-6-Oprimeverosyl-xanthone and 8-hydroxy-3,5-dimethoxy-1-O-primeverosyl xanthone are among the essential xanthones of the Swertia (8). Swerchirin has significant and numerous medicinal activities, including anti-malarial, anti-hepatotoxic, and hypoglycemic effects (15). Swertiamarin also has various therapeutic activities, including liver protection, anti-inflammatory, anti-arthritic, anti-cancer, anti-diabetic, pain-relieving, antioxidant, neuroprotective, and gastric protective activities. The mechanism of the medicinal effects of swertiamarin probably includes regulating molecular targets, including growth factors, inflammatory cytokines, protein kinases, proteins related to apoptosis, receptors, transcription regulation enzymes, and their signaling pathways (16, 17). Chromatographic analysis of n-butanol extract of *S. longifolia Boiss* also indicates the presence of four compounds, i.e. an iridoid glycoside (loganic acid), a secoiridoid glycoside (gentiopicroside), a secoiridoid dilactone (gentiolactone) and a nucleoside (uridine) (18).

Uridine is a pyrimidine nucleoside that exists as an RNA base in living organisms (19). Gentiopicroside is one of the most common secoiridoid glycosides found in Gentianaceae. This compound has several medicinal properties such as anti-inflammatory (20), hepatoprotective (9, 21), protection against stomach ulcers caused by stress (22), bile secretion enhancing property (9), muscle relaxant, cell protector, and wound repair activities (9). Loganic acid, another compound of *S. longifolia*, has an iridoid glycoside structure (23). In addition to xanthones, *S. longifolia* contains the well-known triterpenes α- and β-amyrin, ursolic acid, β-sitosterol and its glucoside, daukosterol, and squiridoid sortiamarin. Some of these terpenoid compounds inhibit alpha-amylase activity. α- and β-amyrin are bioactive compounds commonly found in leaves, bark, and resin of plants, and have shown antimicrobial, anti-inflammatory, and other interesting biological activities. β-sitosterol is a steroid compound with anti-diabetic, antioxidant, cytotoxic, anti-ulcer, anti-inflammatory, and analgesic properties (9).

Table 1: Important compounds of *Swertia longifolia Boiss* and their properties.

Compounds	Properties	Type of extracts or compounds	Place of sample collection	Ref.
Swertiamarin	hepatoprotective, anti-inflammatory, anti-arthritis, anti-cancer, anti-diabetes, analgesic, antioxidant, nerve protector, and stomach protector	chloroform fraction	north of Iran, Mazandaran	(9, 16)
1,8-Dihydroxy-3,5-dimethoxy xanthone (swerchirin)	Anti-malarial, anti-hepatotoxic, and hypoglycemic effects	chloroform extract Of the Aerial parts	north of Iran, Mazandaran	(7, 15, 18)
1,8-Dihydroxy-2,6-dimethoxy xanthone (swertiaperenine)	Anti-inflammatory, hepatoprotective, protecting the stomach against ulcers caused by stress, increasing bile secretion, relaxing muscles, protecting cells, and repairing wounds.			
2,8-Dihydroxy-l,6-dimethoxy xanthone (gentiacauleine)				
Isobellidifolin and Methyl Swertian	blood sugar straw	chloroform and n-butanol	north of Iran, Mazandaran	(8)
Bellidin	not clear			
Genistein				
1,5-dihydroxy-3-methoxy-6-Oprimeverosyl-xanthone				
8-hydroxy-3,5-dimethoxy-1-O-primeverosyl xanthone				
Gentiacauleine	free radical scavenging	acetone extracts of the aerial parts	north of Iran, Mazandaran	(15, 27)
Ursolic acid	Inhibition of alpha-glucosidase and alpha-amylase	Hexane and chloroform fractions of the aerial parts	north of Iran, Mazandaran	(9)
β-amyrin	Antimicrobial, anti-inflammatory			
Daucosterol	Inhibition of alpha-glucosidase and alpha-amylase			
β-sitosterol	Anti-diabetic, antioxidant, cytotoxic, anti-ulcer, anti-inflammatory, analgesic, inhibition of alpha-amylase and human pancreatic amylase.			
α-amyrin	Antimicrobial, anti-inflammatory			
Gentiolactone	not clear	petroleum ether and ethanol of the aerial parts	north of Iran, Mazandaran	(18)
Gentiopicroside	Anti-inflammatory, hepatoprotective, protecting the stomach against ulcers caused by stress, increasing bile secretion, relaxing muscles, protecting cells, and repairing wounds.			
Loganic acid	not clear			
Uridine	One of the structural bases of RNA			
1,5-dihydroxy-3-methoxy-6-O-primeverosyl xanthone (75)	Antioxidant, anti-inflammatory, antimicrobial, anti-cholinesterase and anti-cytotoxic	aerial parts	north of Iran, Mazandaran	(6, 12)
8-hydroxy-3,5-dimethoxy-1-O-primeverosyl xanthone				

This compound inhibits the activity of alpha-amylase (IC50 300) and human pancreatic amylase (50 µg/ml) (9, 24). Ursolic acid also inhibits the activity of α-glucosidase and alpha-amylase. Daukosterol is the glycosidic form of β-sitosterol and is one of the compounds of *S. longifolia* (9), which inhibits alpha-glucosidase (25) and alpha-amylase (9, 26).

Anti-Diabetic Activity

The results of studies on the effect of the alcoholic extract of the aerial parts of *S. longifolia* on diabetes induced by streptozocin in rats indicate that oral consumption of the extract of this plant with doses of 100 mg/kg and 200 mg/kg increases the amount of insulin and body weight and also causes a decrease in

Table 2: Physiological and pharmacological effects of the *Swertia longifolia Boiss* plant and its compounds.

Effects	Extract and constituents	Model	Dose	Outcomes	Ref
Hepatoprotective Activity	Alcoholic extract of aerial parts	Diabetic rats induced by STZ	100 and 200mg/kg	reduction of GGT ،ALP, ALT, and AST	(1)
	total plant extract and swerchirin	acetaminophen-induced hepatotoxicity in Swiss mice	3, 6, 12.5, 25, 50mgkg	reduction of ALP, ALT, and AST	(10)
Anti-Diabetic Property	Alcoholic extract of aerial parts	Diabetic rats induced by STZ	100 and 200mg/kg	Increase insulin and decrease FBS	(1)
	Methyl Swertian and Bellidifolin	Diabetic rats were administered orally for one week	200mg/kg	The reduction of FBS after one week and its stability up to 4 weeks later	(37)
	Daucosterol	In vitro	10 mg/ml	α-Amylase inhibitory activity	(9, 16)
	chloroform and methanol fractions of Aerial parts	In vitro	16.8 and 18.1 mg/ml, respectively		
	α-Amyrin and β-Amyrin	In vitro	0.01and 0.02 mg/g; respectively	α-Amylase inhibitory activity	(9, 38)
Kidney protection property	Alcoholic extract of aerial parts	Diabetic rats induced by STZ	100 and 200mg/kg	Decreased creatinine and BUN	(1)
Anti-hyperlipidemic	Alcoholic extract of aerial parts	Diabetic rats induced by STZ	100 and 200mg/kg	Cholesterol and LDL reduction	(1)
	swertiamarin	Diabetic rats induced by STZ	75 mg/kg/day, i.p., for 28 days	We have reduced serum levels of triglycerides, cholesterol, LDL, non-esterified free fatty acids, fasting blood sugar, MMP-9, MMP-3, and urea, and increased insulin sensitivity index.	(39)
			15, 25, and 50 mg/kg/day, PO, 28 days	reduction in fasting blood glucose, HbA1c, total cholesterol, total glycerides, and LDL levels increase in hemoglobin, plasma insulin, complete protein, body weight, and HDL	(40)
		Diabetic rats	20 and 50 mg/kg/day, PO, for 40	-Reduction of PPARγ/GLUT-4, adiponectin mRNA,	(28)

			days	Oxidative stress, and insulin resistance -Upregulation of GLUT-2 -Decrease of the PEPCK -α-Glucosidase inhibitor ↓urea and creatinine	
Antioxidant	Methanolic extract of different Swertia genera	In vitro (Determination of antioxidant activity via DPPH free radical scavenging assay)	30–270 µg/ml	A significant correlation was observed between the polyphenol content and antioxidant values.	(36)
		thin layer chromatography	0.01-0.16 mg/g	Different genera of Swertia contain three main compounds, i.e. amarogentin, swertiamarin, and mangiferin.	
	Aqueous, alcoholic, and hydroalcoholic extracts of aerial and root parts	In vitro (Determination of antioxidant activity via DPPH free radical scavenging assay)	1, 1.5, 2, 2.5, 3 µg/ml	Scavenger of free radicals by various extracts, especially root aqueous extract	(2)
Acetylcholinesterase inhibitory activity	Aqueous, alcoholic, and hydroalcoholic extracts of aerial and root parts	In vitro (Ellman's reagent)	300 µg/ml	Inhibition of acetylcholinesterase activity by chloroform, ethyl acetate, methanol, and hydroalcoholic extracts	(2)
Cytotoxic activity	Aqueous, alcoholic, and hydroalcoholic extracts of aerial and root parts	In vitro on cell lines (HepG2, MCF7, HT29, A549 and MDBK)	100 µg/ml	No Cytotoxic activity	(2)

Properties of *s. longifolia Boiss*: AST: aspartate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, GGT: gamma-glutamyl trans-peptidase, FBS: fasting blood sugar test, BUN: Blood urea nitrogen, GLUT: Glucose transporter, LDL: low-density lipoprotein, HDL: high-density lipoprotein, PEPCK: phosphoenolpyruvate carboxykinase, PPARγ: Peroxisomeproliferator–activated receptors, MMP: Matrix metalloproteinase, HepG2: human hepatocellular liver carcinoma, MCF7: human breast adenocarcinoma, HT29: human colon adenocarcinoma, A549: human lung adenocarcinoma and MDBK: bovine kidney cells.

fasting blood sugar (1). In traditional medicine, Swertia is widely used in the treatment of diabetes. This plant contains compounds such as bitter secoiridoids, triterpenes, xanthans, swercherin, a furanocoumarin, flavonoids, and alkaloids (2). Swercherin (50 mg/kg) reduces blood sugar by stimulating insulin secretion from the islets of Langerhans (1, 28). Moreover, alkaloids inhibit the aldose reductase enzyme. Aldose reductase is a critical enzyme in the polyol pathway that decreases the conversion of glucose to sorbitol. Accumulation of sorbitol in the body causes severe disorders such as neuropathy, nephropathy, and cataracts (29). Administration of the extract of another species of Swertia named S. chirayita (250 mg/kg) in normal rats also increased insulin and decreased blood sugar (28). Methylsurtian and bledifolin that could decrease blood sugar after one week of oral administration (200 mg/kg) are also among the essential compounds of this plant (1). Swertiamarin and Daucosterol are the primary and anti-diabetic compounds of *S. longifolia Boiss* (10, 16). Swertiamarin is probably metabolized to gentianine. This active metabolite improves adipogenesis and diabetes by increasing mRNA levels of PPAR-γ, GLUT-4, and adiponectin (16). Daucosterol also has alpha-amylase inhibitory activity (Table 2) (9, 30).

Hepatic and Renal Protective Functions

Zarei et al. (2017) studied the impacts of the alcoholic extract of the aerial parts of *S. longifolia Boiss* with doses of 100mg/kg and 200mg/kg on liver and kidney function tests in diabetic rats induced by streptozocin. This plant extract could reduce creatinine, urea, and liver enzymes (1). Moreover, the hepatoprotective properties of the extract of the aerial parts of this plant (50-6 mg/kg) and swerchirin (50-6 mg/kg) against hepatotoxicity caused by paracetamol (acetaminophen) were confirmed in Swiss mice. They significantly decreased biochemical parameters, AST (aspartate aminotransferase), ALT (alanine aminotransferase), and ALP (alkaline phosphatase) (10). Sweroside, an iridoid glycoside derived from the flower buds of Swertia, has traditionally been used in the treatment of liver diseases, and is has a hepatoprotective role in chemical models of liver injury (31). However, a preliminary study by *Liu et al*. (1994) showed that Sweroside could not have a protective role against some liver toxins (Table 2) (32, 33).

Hypolipidemic activity

It has been shown that the administration of *S. longifolia* plant extract with doses of 100 mg/kg and 200 mg/kg in diabetic rats leads to a decrease in cholesterol levels and low-density lipoproteins (LDL) (1). Administration of Swertiamarin in dyslipidemia caused by type 2 diabetes reduced the serum level of triglyceride, cholesterol, LDL, non-esterified free fatty acids, fasting blood sugar, MMP-9, MMP-3, and urea, and increased insulin sensitivity index. Therefore, it is effective in treating the complications of diabetes, arteriosclerosis, and kidney failure (Table 2) (34, 35).

Antioxidant and Cytotoxic Activity

An investigation of the antioxidant activities of chloroform, ethyl acetate, and methanolic, hydroalcoholic, as well as aqueous extracts of the roots and aerial parts of *S. longifolia* showed that the aerial parts and origins of this plant could significantly induce radical reduction activity compared with vitamin C as a standard. Thus, among the mentioned extracts, the aqueous root extract has a greater degree of radical scavenging activity than the others (2). The highest concentration of different Swertia species methanol extract is related to its phenolic content. These compounds, along with flavonoids, are central to the inhibition of free radicals (2,2-diphenyl-1-picrylhydrazyl) DPPH. Moreover, there is a substantial relationship between the polyphenol content and antioxidant values. Different genera of Swertia contain alkaloids, resins, phenols, flavonoids, glycosides, diterpenes, tannins, and phytosterol, but their three main compounds are amarogentin, swertiamarin, and mangiferin (36). Xanthone is one of the main phenolic compounds of *S. longifolia*, which has antioxidant, anti-inflammatory, anti-microbial, anti-cholinesterase, and anti-cytotoxic properties (6).

Researchers cultured HepG2 (human hepatocellular carcinoma), MCF7 (human breast adenocarcinoma), HT29 (human colon adenocarcinoma), A549 (human lung adenocarcinoma), and MDBK (bovine kidney cells) cell lines. After investigating the cytotoxic effects of chloroform extracts, Ethyl acetate, methanolic and hydroalcoholic roots, and aerial parts (100 µg/ml) on these cell lines, they found that concentrations less than 100 µg/ml of *S. longifolia* plant extracts had no cytotoxicity on MDBK, MCF7, HepG2, A549, and HT29 cell lines. (Table 2) (2).

Acetylcholinesterase Inhibitory Activity

Bioactive substances such as in steroidal-piperidine-alkaloids, furanocoumarins, xanthones, flavonoids, and diterpenes often inhibit the acetylcholinesterase enzyme. Since *S. longifolia* contains xanthone (7, 8), researchers studied the effect of the root extract and aerial parts of *S. longifolia* at a dose of 300mg/kg on the activity of acetylcholinesterase enzyme isolated from red blood cells of cows in a laboratory environment. It was found that chloroform, ethyl acetate, methanolic and hydroalcoholic extracts of roots, and aerial parts inhibit enzyme activity. The inhibitory activity of the root extract was more potent than those of the aerial parts. However, the aqueous extract of this plant did not have inhibitory effects on the activity of the acetylcholinesterase enzyme. Nevertheless, other sections of this plant can be used to treat Alzheimer's disease because Alzheimer's treatment is primarily based on acetylcholinesterase inhibitors, and sometimes chemical drugs have severe peripheral and central side effects (Table 2) (2).

Conclusion

Swertia longifolia Boiss contains effective compounds such as xanthones, iridoid glycosides, flavonoids, and

triterpenoids, which have antioxidant, anti-inflammatory, antimicrobial, anti-cholinesterase and anti-cytotoxic properties. Furthermore, the extract of this plant and its compounds have anti-diabetic, hepatoprotective, and hypolipidemic properties and inhibit the enzyme acetylcholinesterase. Thus, it effectively treats diabetes, arteriosclerosis, renal as well as kidney failure, and Alzheimer's. Given the effects of S. longifolia extract and compounds, clinical trials and more advanced studies should be performed on each plant compound, and each should be investigated as a new candidate for future drug development. It may have the potential to be used in the treatment of Alzheimer and help produce anti-cancer as well as anti-fat drugs in the future.

Acknowledgment

We would like to thank the Vice Chancellor of Research at Shiraz University of Medical Sciences, who helped us to approve and implement the present research.

Conflict of Interest

The authors declare that they have no conflict of interest.

Funding

We are grateful to the research vice-chancellor of Shiraz University of Medical Sciences who helped us in carrying out this project.

References

1. Zarei A, Malekirad AA, Abdollahi M, Vaezi G, Changizi-Ashtiyani S. Swertia longifolia Boiss has beneficial effects on hepatic and renal functions in diabetic rats. Physiology and Pharmacology. 2017;21(2):163-71.
2. Hajimehdipoor H, Esmaeili S, Shekarchi M, Emrarian T, Naghibi F. Investigation of some biologic activities of Swertia longifolia Boiss. Research in pharmaceutical sciences. 2012;8(4):253-9.
3. Kshirsagar P, Jagtap U, Gaikwad N, Bapat V. Ethanopharmacology, phytochemistry and pharmacology of medicinally potent genus Swertia: An update. South African Journal of Botany. 2019;124:444-83.
4. Hussain W, Badshah L, Hussain F, Ali A. Floristic configuration and ecological characteristics of plants of Koh-e-Safaid range, northern Pakistani-afghan borders. Acta Ecologica Sinica. 2020;40(3):221-36.
5. Cao T-W, Geng C-A, Jiang F-Q, Ma Y-B, He K, Zhou N-J, et al. Chemical constituents of Swertia yunnanensis and their anti-hepatitis B virus activity. Fitoterapia. 2013;89:175-82.
6. Jia Y, Xiong C. Assessing the biological activities of xanthone derivatives from Swertia macrosperma CB Clark. Natural product research. 2017;31(6):704-6.
7. Hajimehdipour H, Amanzadeh Y, Sadat Ebrahimi S, Mozaffarian V. Three tetraoxygenated xanthones from Swertia longifolia. Pharmaceutical biology. 2003;41(7):497-9.
8. Hajimehdipoor H, Dijoux-Franca M-G, Mariotte A-M, Amanzadeh Y, Sadat-Ebrahimi S-E, Ghazi-Khansari M. Two new xanthone diglycosides from Swertia longifolia Boiss. Natural Product Research. 2006;20(13):1251-7.
9. Saeidnia S, Ara L, Hajimehdipoor H, Read RW, Arshadi S, Nikan M. Chemical constituents of Swertia longifolia Boiss. with α-amylase inhibitory activity. Research in pharmaceutical sciences. 2016;11(1):23.
10. Sadeghi Z, Elmi S, Elmi A, Ghazi-Khansari M, Hajimehdipoor H, Amanzadeh Y, Sadat-Ebrahimi S-E. Protective effects of Swertia longifolia Boiss. and its active compound, swerchirin, on paracetamol-induced hepatotoxicity in mice. Journal of pharmacy and pharmacology. 2006;58(2):277-80.
11. Mészáros S, Höhn M. Species diversity and advancement of Swertia (Gentianaceae): ecological and morphological correlates. Acta Botanica Hungarica. 2002;44(3-4):317-34.
12. Huang Q, Wang Y, Wu H, Yuan M, Zheng C, Xu H. Xanthone glucosides: Isolation, bioactivity and synthesis. Molecules. 2021;26(18):5575.
13. Le Pogam P, Boustie J. Xanthones of lichen source: A 2016 update. Molecules. 2016;21(3):294.
14. Tovilovic-Kovacevic G, Zogovic N, Krstic-Milosevic D. Secondary metabolites from endangered Gentiana, Gentianella, Centaurium, and Swertia species (Gentianaceae): promising natural biotherapeutics. Biodiversity and Biomedicine: Elsevier; 2020. p. 335-84.
15. Shekarchi M, Hajimehdipoor H, Khanavi M, Adib N, Bozorgi M, Akbari-Adergani B. A validated method for analysis of Swerchirin in Swertia longifolia Boiss. by high performance liquid chromatography. Pharmacognosy Magazine. 2010;6(21):13.
16. Muhamad Fadzil NS, Sekar M, Gan SH, Bonam SR, Wu YS, Vaijanathappa J, et al. Chemistry, pharmacology and therapeutic potential of swertiamarin–A promising natural lead for new drug discovery and development. Drug Design, Development and Therapy. 2021:2721-46.
17. He Q-Y, Wang R, Sun X-C. Cytotoxicity of methanolic extract of Swertia petiolata against gastric cancer cell line SNU-5 is via induction of apoptosis. South African Journal of Botany. 2017;109:196-202.
18. HAJI MH, DIJOUX FM, Mariotte A, Amanzadeh Y, SADAT ES, GHAZI KM, MOZAFARIAN V. Phytochemical study of Swertia longifolia. 2008.
19. Mouffok S, Haba H, Lavaud C, Long C, Benkhaled M. Chemical constituents of Centaurea omphalotricha Coss. & Durieu ex Batt. & Trab. Rec Nat Prod. 2012;6(3):292-5.
20. Gohari AR, Saeidnia S, Shahverdi AR, Yassa N, Malmir M, Mollazade K, Naghinejad AR. Phytochemistry and antimicrobial compounds of Hymenocrater calycinus. Eur Asia J Bio Sci. 2009;3(9):64-8.
21. Chowdhury S, Islam M, Jung H, Choi J. In vitro antidiabetic potential of the fruits of Crataegus pinnatifida. Research in pharmaceutical sciences. 2014;9(1):11.
22. Nagmoti DM, Juvekar AR. In vitro inhibitory effects of Pithecellobium dulce (Roxb.) Benth. seeds on intestinal α-glucosidase and pancreatic α-amylase. Journal of Biochemical Technology. 2013;4(3):616-21.
23. Saraswathy A, Ariyanathan S. 1, 5, 8-Trihydroxy-3-methoxyxanthone from Swertia corymbosa (Griseb.) Wight ex. CB Clarke. International Journal of Pharmacy & Life Sciences. 2011;2(8).
24. Rathinavelusamy P, Mazumder PM, Sasmal D, Jayaprakash V. Evaluation of in silico, in vitro α-amylase inhibition potential and antidiabetic activity of Pterospermum acerifolium bark.

Pharmaceutical Biology. 2014;52(2):199-207.
25. Sheng Z, Dai H, Pan S, Wang H, Hu Y, Ma W. Isolation and characterization of an α-glucosidase inhibitor from Musa spp.(Baxijiao) flowers. Molecules. 2014;19(7):10563-73.
26. Dumandan NG, Kagaoan ACT, Acda RD, Tumambing CR, Pham LJ. Extraction, Profiling, and Characterization of Phytosterols and Triterpenoids from Pili (Canarium ovatum Engl.) Pulp Oil Exhibiting Antioxidant and Antibacterial Properties. Biochemistry Research International. 2022;2022.
27. Negi JS, Singh P, Rawat B. Chemical constituents and biological importance of Swertia: a review. Current Research in Chemistry. 2010;3(1):1-15.
28. Patel D, Prasad SK, Kumar R, Hemalatha S. An overview on antidiabetic medicinal plants having insulin mimetic property. Asian Pacific journal of tropical biomedicine. 2012;2(4):320-30.
29. Kawanishi K, Ueda H, Moriyasu M. Aldose reductase inhibitors from the nature. Current Medicinal Chemistry. 2003;10(15):1353-74.
30. El Omari N, Jaouadi I, Lahyaoui M, Benali T, Taha D, Bakrim S, et al. Natural Sources, Pharmacological Properties, and Health Benefits of Daucosterol: Versatility of Actions. Applied Sciences. 2022;12(12):5779.
31. Luo Y-D, Chen J, Cao J, Wen X-D, Li P. Determination of sweroside in rat plasma and bile for oral bioavailability and hepatobiliary excretion. Chemical and Pharmaceutical Bulletin. 2009;57(1):79-83.
32. Jie L, Yaping L, Klaassen CD. The effect of Chinese hepatoprotective medicines on experimental liver injury in mice. Journal of ethnopharmacology. 1994;42(3):183-91.
33. Subramanya SB, Venkataraman B, Meeran MFN, Goyal SN, Patil CR, Ojha S. Therapeutic potential of plants and plant derived phytochemicals against acetaminophen-induced liver injury. International journal of molecular sciences. 2018;19(12):3776.
34. Ahamad J, Uthirapathy S, T Anwer E, S Mohammed Ameen M, Samad A. A Critical Review on Potential Pharmacological Activity and Pharmacokinetic Perspective of Swertiamarin. Research Journal of Phytochemistry. 2021;15(1):1-13.
35. Leong XY, Thanikachalam PV, Pandey M, Ramamurthy S. A systematic review of the protective role of swertiamarin in cardiac and metabolic diseases. Biomedicine & Pharmacotherapy. 2016;84:1051-60.
36. Khanal S, Shakya N, Thapa K, Pant DR. Phytochemical investigation of crude methanol extracts of different species of Swertia from Nepal. BMC research notes. 2015;8(1):1-9.
37. UPendra Rao M SM, Chengaiah B, Jaganmohan Reddy MC. A review herbal medicines for diabetes mellitus. . IntJ PharmTech Res. 2010;2:1883.
38. Quan NV, Xuan TD, Tran H-D, Thuy NTD, Trang LT, Huong CT, et al. Antioxidant, α-amylase and α-glucosidase inhibitory activities and potential constituents of Canarium tramdenum bark. Molecules. 2019;24(3):605.
39. Vaidya H, Giri S, Jain M, Goyal R. Decrease in serum matrix metalloproteinase-9 and matrix metalloproteinase-3 levels in Zucker fa/fa obese rats after treatment with swertiamarin. Experimental & Clinical Cardiology. 2012;17(1):12.
40. Dhanavathy G. Immunohistochemistry, histopathology, and biomarker studies of swertiamarin, a secoiridoid glycoside, prevents and protects streptozotocin-induced β-cell damage in Wistar rat pancreas. Journal of endocrinological investigation. 2015;38:669-84.