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## Review Article

# Phytochemical and Ethnomedicinal Uses of Family Gentianaceae

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## Abstract

Cognitive capacity of human beings has placed natural products in the core of our lives. It has redefined role of science in establishment of its values for society. Evolution of sciences along with various inductivist views and epistemological evidences has changed shape and state of affairs in the world of natural products. As a matter of fact importance of these constituents growing rapidly in our lives. Volatile constituents of Swertia hold many idiosyncratic qualifications, enough to consider them as a promising candidate for their medicinal exploitation. Claim of this genus for a reliable alternative in the present remedial system seems to be acceptable. Many other therapeutic activities have been reported which endorse belief that this genus is going to revolutionize state of affairs in the world of essential oil. This study is devoted to the comprehensive review of recent research work on the genus and is bolstered by epistemic achievements and evidences collected by research community in recent times. The discussion in this study has been devoted to captivating and bewitching role of essential oil of the genus Swertia for various therapeutic purposes. This study gives a core idea of contemporary state of affairs and recent scientific developments.

Key words: Swertia, therapeutic, natural products, scientific, volatile constituents

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

## INTRODUCTION

Gentianaceae is a family of flowering plants comprising approximately 70-80 genera and 900-1200 species. The plants of the family are annual and perennial herbs or shrubs. They are native to Northern temperate areas of the world[1]. Plants belonging to genus Gentiana are very well-known for their pharmacological properties. They are intensely bitter and once upon a time were valuable remedy for digestive system ailments. The medicinal value is due to presence of bitter glycosides[2].

The family Gentianaceae is characterized by the presence of a group of rare yellow pigments (xanthones) in most of its members[3]. The plants species of genus Swertia are diverse and large genus populated with 170 species The plants species of genus Swertia are diverse and large genus populated with 170 species[4,5] distributed at the mountainous region of tropical Asia, Europe, America and Africa. Himalayan regions houses most of the *Swertia* species[6,7]. *Swertia chirayita* is known to contain various active principles including xanthones, secoirioid glycosides, flavonoids, alkaloids, phenolics[4,6].

Among the plants often used in traditional medicine, *Swertia* species, which belong to the Gentianaceae family play a vital role. A variety of Swertia plants are used as crude drugs in the Indian pharmacopoeia. *Swertia chirata*, commonly known as chirayata, demands special attention in this regard because of its multidirectional use as a bitter stomachic, febrifuge, anthelmintic, antimalarial and antidiarrheal[8]. In Chinese traditional medicine, 20 species of this genus are being used for the treatment of hepatic, choleric and inflammatory diseases[9]. Other traditionally important *Swertia* species substitute for the traditional healing. The *S. davidi* is used as remedy for acute bacillary dysentery, *S. alata* as an appetite tonic and febrifuge, *S. minor* in the treatment of malarial and fever, *S. petvolata* and *S. thomsonii* finds its applications in the amchies system of medicine[4]. Other important plants species includes *S. angustifolia*, *S. corymbosa*, *S. decussta*, *S. hookeri*, *S. macrosperma*, *S. petiolata*, *S. lawii*, *S. paniculata*, *S. punctata*, *S. calycina*, *S. purpurasencs*, *S. bimaculata*, *S. ciliata*, *S. densifolia*, *S. japonica* and *S. frachetiana* that are used in folklore medicine and as substitutes for *S. chirayita* in various countries for treatment of liver disorders, fever, dysentery, diarrhea, stomach problems and other ailments[4,6,10].

The main aim of this study is to collect all the possible information regarding the chemical constituents and ethnomedicinal uses of the family Gentinanceae, thus will help to the researchers and scientists to take action for future study in this displine.

## CHEMICAL CONSTITUENTS

The phytochemical investigation of the genus Swertia as carried out so far, has afforded some 200 compounds with varying structural patterns. Among these constituents, xanthonoids, terpenoids, flavonoids and alkaloids were presented from the major classes, together with other compounds, according to the following classification[4].

**Xanthonoids:** Xanthones are secondary metabolites commonly occurring in higher plant families, fungi and lichen[11] . Their pharmacological properties have raised great interest. Structures of xanthones are related to that of flavonoids and their chromatographic behaviors are also similar. Flavonoids are frequently encountered in nature, whereas xanthones are found in limited number of families. Xanthones always occur in the family Gentianaceae, Guttiferae, Moraceae, Clusiaceae and Polygalaceae. Xanthones are sometimes found as the parent polyhydroxylated compounds but most are mono or polymethyl ethers or are found as glycoside[12]. Xanthones are class of tricyclic compounds characterized by a dibenzo-γ-pyrone nucleus. The prefix 'Xanth' means 'Yellow' color of these compounds and '-one' is from their 'Keto' nature. The xanthones bear a close structural relationship to the other naturally occurring γ-pyrone derivatives like flavonoids and chromones. Xanthones can be classified into six major groups depending upon oxygenation pattern[13,14] (Fig. 1-3).

Xanthones and their glycosides have been isolated from *Swertia* species. Mangiferin is the most common C-glycosides

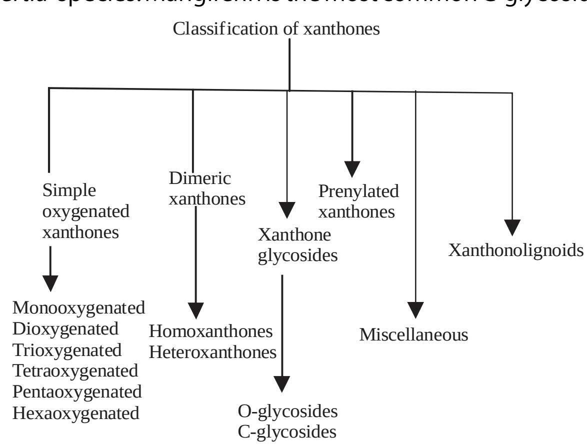


Fig. 1: Pictorial representation of the classification of xanthones

in *S. chirayita*, *S. mussotii*, *S. cordata*, *S. macrosperma* and *S. connata*. Xanthone O-glycosides (swertianolin) from *S. japonica* and *S. ciliata*[15] have been reported. The first xanthone O-glycoside, norswertianin-1-O-glucosyl-3-O-glucoside has been isolated from *S. perennis*[16]. The xanthones isolated and characterized from various *Swertia* species so far are listed in Table 1.

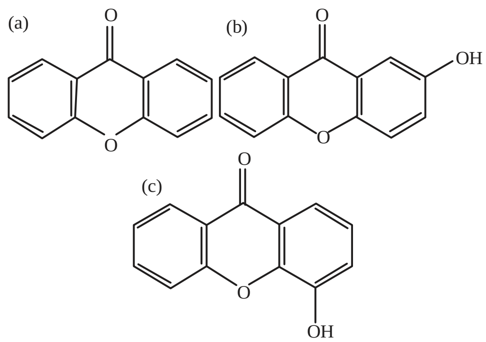

Fig. 2(a-c): Structure of mono oxygenated (a) Xanthone, (b) 2-hydroxy xanthone and (c) 4-hydroxy xanthone

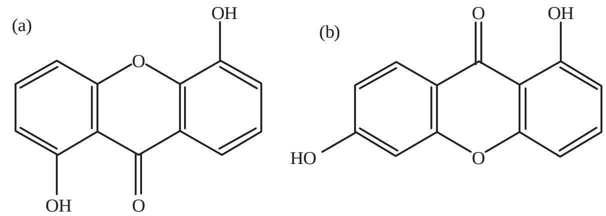

Fig. 3(a-b): Structure of dioxygenated xanthone, (a) 1,5 di-hydroxy xanthone and (b) 1,6 di-hydroxy xanthone

Table 1: Isolated xanthone from *Swertia* species

| Plant's | Xanthones | References |
|---|---|---|
| *S. mussotii* | 3,7,8-trimethoxyxanthone 1-O-(β-D-glucopyranoside) | Mao *et al.*[17] |
| | 1,8-dihydroxy- 3-methoxyxanthone 7-O-[α-L-rhamnopyranosyl (1→2)-β-D-xylopyranoside] | |
| | 1,8-dihydroxy-3,4-dimethoxyxanthone 7-O-[β-D-glucopyranoside] | |
| | 1,8-dihydroxy-3-methoxyxanthone 7-O-[β-D-glucopyranoside] | |
| | 1-hydroxy-3,4-dimethoxyxanthone 7-O-[β-D-glucopyranoside] | |
| *S. macrosperma* | 1-hydroxy-3,7,8-trimethoxy-xanthone | Wang *et al.*[18] |
| | 1,3,7,8-tetrahydroxyxanthone-8-O-beta-D-glucopyranoside | |
| | Norswertianolin | |
| | Swertianolin | |
| *S. ciliata* | Mangiferin (2,-C-β-D-glucopyranosyl-1,3,6,7-tetrahydroxyxanthone) | Chauhan and Dutt[19] |
| *S. cordata* | 1-hydroxy-2,3,7-trimethoxyxanthone | Karan *et al.*[20] |
| | 1-hydroxy-2,3,4,7-tetramethoxyxanthone | |
| *S. paniculata* | 1,5-dihydroxy-3-methoxyxanthone-8-O-b-D-glucopyranoside (swertianolin) | Pant *et al.*[21] |
| *S. corymbosa* | 1,5, 8-trihydroxy-3-methoxyxanthone | Saraswathy and Ariyanathan[22] |
| *S. punicea* | 1,5-dihydroxy-8-O-β-D-glucopyranosyl-3-methoxyxanthone | Zhang *et al.*[23] |
| | 2-C-β-D-glucopyranosyl-1,3,6,7-tetrahydroxyxanthone (mangiferin) | |
| *S. davidi* | 1,3,5,8-tetrahydroxy xanthones | Zhang *et al.*[24] |
| *S. chirayita* | 2-C-β-D-glucopyranosyl-1,3,6,7-tetrahydroxyxanthone | Suryawanshi *et al.*[25] |
| *S. japonica* | 6'-O-α-L-arabinopyranosylswertiamarin | Kikuchi and Kikuchi[26] |
| | 3'-O-β-D-glucopyranosylswertiamarin | |
| | 4'-O-β-D-glucopyranosylswertiamarin | |
| | 3'-O-β-D-galactopyranosylswertiamarin | |
| | 6'-O-α-D-galactopyranosylswertiamarin | |
| | 6'-O-α-D-manopyranosylswertiamarin | |
| | 6'-O-β-D-fructofuranosylpyranosylswertiamarin | |
| | 5'-O-β-D-glucopyranosylamaroswerin | |
| *S. alata* | 1,8-dihydroxy-3,7-dimethoxyxanthone | Karan *et al.*[27] |
| | 1,7,8-trihydroxy-3-methoxyxanthone | |
| | 1-hydroxy-3,7,8-trimethoxyxanthone | |
| *S. bifolia* | 1-hydroxy-3,5-dimethoxyxanthone | Ji[28] |
| | 1,7-dihydroxy-3,8-dimethoxyxanthone | |
| | 1,8-dihydroxy-3,7-dimethoxyxanthone | |
| | 1-hydroxy-3,7,8-trimethoxyxanthone | |
| *S. nervosa* | 1,7-dihydroxy-3,8-dimethoxyxanthone | Bhatia *et al.*[29] |
| | 1,8-dihydroxy-3,7-dimethoxyxanthone | |
| | 1-hydroxy-3,7,8-trimethoxyxanthone | |
| *S. speciosa* | 6-hydroxy-3,5-dimethoxy-1-[(primverosyl)oxy] xanthonea) | Negi *et al.*[30] |
| *S. ciliata* | 1,8-dihydroxy-3-methoxyxanthone-7-0-glucopyranoside | Inayat-Ur-Rahman *et al.*[31] |

**Terpenoids:** There are many different classes of naturally occurring compounds. Terpenoids also form a group of naturally occurring compounds majority of which occur in plants, a few of them have also been obtained from other sources. Terpenoids are volatile substances which give plants and flowers their fragrance. They occur widely in the leaves and fruits of higher plants, conifers, Citrus and Eucalyptus[32]. By the modern definition: "Terpenoids are the hydrocarbons of plant origin of the general formula $(C_5H_8)n$ as well as their oxygenated, hydrogenated and dehydrogenated derivatives". Terpenoids are classified according to containing number of carbon atoms[33] are listed in Table 2.

Individual compounds are more frequently used than the oil as such in medicinal preparations. Some widely used terpenoids in herbal preparation are:

- Terpenoids : Uses
- Camphor : Counter irritant
- Bornyl isovalerate : Sedative
- Menthol : In cough drops
- Terpinyl hydrate : Expectorant
- Chamazulene : Anti-inflammatory agent[34]
- β-caryophyllene : Non-steriodal anti-inflammatory agents

Terpenoids with basic steroidal frameworks have been isolated from different *Swertia* species and are collected and listed in Table 3.

**Irridoid and seco-irridoid glycosides:** Iridoids are considered a typical monoterpenoid compounds, based on a methylcyclopentan-[C]-pyran skeleton, often fused to a

Table 2: Classification of terpenes

| No. of carbon atom | No. of value | Class |
|---|---|---|
| 10 | 2 | Monoterpenoids ($C_{10}H_{16}$) (Fig. 4) |
| 15 | 3 | Sesquiterpenoids ($C_{15}H_{24}$) (Fig. 5) |
| 20 | 4 | Diterpenoids ($C_{20}H_{32}$) (Fig. 6) |
| 25 | 5 | Sesterpenoids ($C_{25}H_{40}$) |
| 30 | 6 | Troterpenoids ($C_{30}H_{48}$) |
| 40 | 8 | Tetraterpenoids ($C_{40}H_{64}$) |
| >40 | >8 | Polyterpenoids $(C_5H_8)_n$ |

Table 3: Isolated terpenoids from *Swertia* species

| Plant's name | Isolated terpenoids | References |
|---|---|---|
| *S. macrosperma* | Oleanolic acid, β-sitosterol and daucosterol | Wang *et al.*[18] |
| *S. purpurascens* | Queretoric acid, oleanolic acid and β-sitosterol-D-glycoside | Sajwan *et al.*[35] |
| *S. corymbosa* | Lupeol and friedelin epi-friedelinol | Cao *et al.*[36] and Ramesh *et al.*[37] |
| *S. speciosa* | Taraxer-14-en-3-one | Rana and Rawat[38] |
| *S. chirayita* | Chiratane | Ji[28] |
| *S. bifolia* | β-daucosterol | Ji[28] |
| *S. japonica* | Hederagenin, maslinic acid, erythrodiol-3-O-palmitate and 3β-hydroxy-11-oxoolean-12-ene-28-oic acid | Kikuchi and Kikuchi[39] |
| *S. mileensis* | Glycoside mileenside | Di *et al.*[40] |
| *S. yunnanensis* | Thysanolactone | Zi *et al.*[41] |
| *S. ciliata* | β-sitosterol | Inayat-Ur-Rahman *et al.*[31] |
| *S. punicea* | Glycoside and 2,6-dimethyl-2E,6E-octadienoic acid-1,6'-lactone-8-β-D-glucopyranoside | Ming *et al.*[42] |

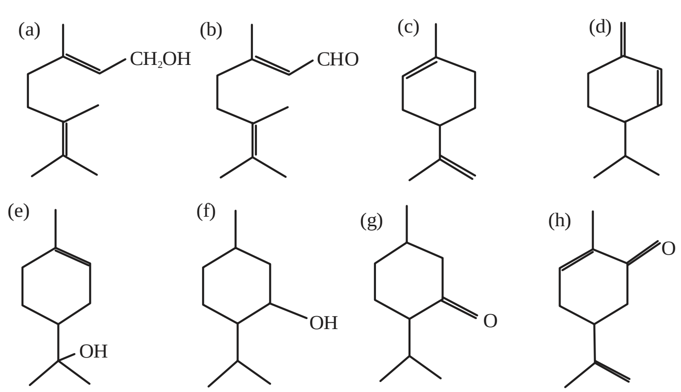


Fig. 4(a-h): Structure of monoterpenoids, (a) Geraniol, (b) Citral, (c) Limonene, (d) β-phellandrene, (e) α-terpineol, (f) Menthol, (g) Menthone and (h) Carvone six-membered oxygen ring consisting of ten, nine or in rare cases, eight carbon atoms[43,44]. More than 2500 iridoid compounds have been described in nature, with structura differences related mainly to the degree and type of substitution in the cyclopentane ring skeleton[45]. The bitter principles of the genus Swertia can be classified into three groups:

- Iridoid glycosides
- Secoiridoid glycosides
- Biphenyl glycosides

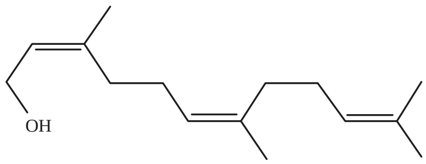


Fig. 5: Structure of sesquiterpenoids (Farnesol)

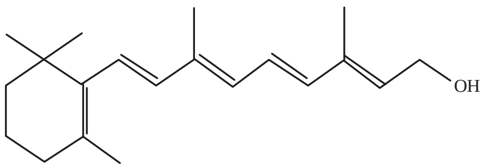


Fig. 6: Structure of diterpenoids (Vitamin A)

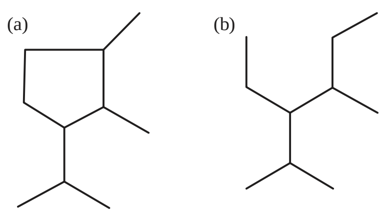


Fig. 7(a-b): Structure of iridane and secoiridane nucleus, (a) Iridane nucleus and (b) Secoiridane nucleus

Irridoid and secoiridoids are a class of compounds having iridane and secoiridane nucleus (Fig. 7). The irridoid and seco-irridoid glycosides isolated and characterized from various *Swertia* species so far are listed in Table 4.

**Flavonoids and flavonoid glycosides:** Flavonoids are a large and complex group of compounds containing a three ring structure with two aromatic centers (rings A and B) and a central oxygenated heterocyclic ring (C)[51,52]. The six major classes of flavonoids are flavones, flavonols, flavonones, catechins (flavanols) anthocyanidins and isoflavones[51,53-56]. Flavonoids have several proven medicinal properties, such as antiinflammatory, anti-oxidant, anti cancer, antibacterial and antiviral properties[52,57-59]. Flavonoids have been isolated from different *Swertia* species and are collected and listed in Table 5.

**Lignans and alkaloids:** The lignans comprise a class of natural plant products which are derived from cinnamic

Table 4: Isolated irridoid and seco-irridoid glycosides from *Swertia* species

| Plant's name | Irridoid and seco-irridoid glycosides | References |
|---|---|---|
| *S. ciliata* | Amarogentin and amaroswerin | Chauhan and Dutt[19] |
| *S. longifolia* | Gentiopicroside and loganic acid | Hajimehdipoor *et al.*[5] |
| *S. punicea* | Amarogentin | Wang *et al.*[46] |
| *S. delavayi* | Swertiamarin | Xia *et al.*[47] |
| *S. binchuanensis* | Gentiopicroside | Xia *et al.*[47] |
| *S. nervosa* | Swertiamarin | Guo *et al.*[48] |
| *S. chirata* | Sweroside | Suryawanshi *et al.*[25] |
| *S. pseudochinensis* | Amaroswerin | Li *et al.*[49] |
| *S. japonica* | 6'-O-α-Dmannopyranoslyswertiamarin and 6'-O-β-D-fructofuranosylswertiamarin | Kikuchi and Kikuchi[39] |
| *S. cordata* | Swertiamarin | Bhandari *et al.*[50] |

Table 5: Isolated flavonoids and flavonoid glycosides from *Swertia* species

| Plant's name | Isolated flavonoids | References |
|---|---|---|
| *S. mussotii* | Isoorientin | Li *et al.*[60] |
| *S. franchetiana* | Swertisin and isoswertisin | Tian *et al.*[61] |
| *S. decora* | Quercetin | Xiao *et al.*[62] |
| *S. przewalskii* | Luteolin | Pan *et al.*[63] |
| *S. punicea* | Isovitexin | Ming *et al.*[42] |
| *S. longifolia* | Gentisein | Handa[64] |
| *S. hookerii* | 3,4,5,7-tetra-O-methyl-3-O-stearylquercetin | Ghosal *et al.*[65] |
| *S. japonica* | Swertiajaponin | Kubota *et al.*[66] |
| *S. perennis* | Isovitexin | Hostettmann and Jacot-Guillarmod[67] |

Table 6: Isolated lignans and alkaloids from *Swertia* species

| Plant's name | Isolated lignans and alkaloids | References |
|---|---|---|
| *S. japonica* | glycoside 7R,7'R,8S,8'S-(+)-neo-olivil-4-O-β-D-glucopyranoside | Kikuchi and Kikuchi[26] |
| *S. yunnanensis* | Gentianine | Zi *et al.*[68] |
| *S. purpurascens* | Gentiocrucine | Sharma[69] |
| *S. chirata* | Enicoflavine | Sharma[70] |
| *S. elegans* | Sweetinine | Balandrin and Kinghorn[71] |
| *S. japonica* | Gentianine | Yamahara *et al.*[72] |
| *S. marginata* | Gentianamine | Rakhamatullaev *et al.*[73] |

Table 7: Isolated miscellaneous compound from *Swertia* species

| Plant's name | Isolated compounds | References |
|---|---|---|
| *S. macrosperma* | Sinapaldehyde, balanophonin, decentapicrin and coniferl aldehyde | Wang *et al.*[18] |
| *S. longifolia* | Gentiolactone and uridine | Hajimehdipoor *et al.*[5] |
| *S. mussotii* | Polysaccharides | Li[74] |
| *S. chirata* | m-hydroxybenzoic acid, deacetylcentapicrin and vanillic acid | Cai *et al.*[75] |
| *S. japonica* | 3-butenyl 6'-O-α-L-arabinopyranosyl-β-dglucopyranoside | Kikuchi and Kikuchi[26] |
| *S. franchetiana* | 1-oxoisochroman-5-carboxaldehyde | Wang *et al.*[76] |
| *S. chirata* | Nonacosanyl-hentriacontanoate | Pant *et al.*[21] |
| *S. japonica* | (-)-semburin and (-)-isosemburin | Kadota *et al.*[77] |
| *S. punicea* | Epieustomoside | Ming *et al.*[42] |

acid derivatives and which are related biochemically to phenylalanine metabolism. They fall into five major subgroups and the nomenclature in use is either consistent between the groups or even within a subgroup. Many lignans show physiological activity, such as the tumor-inhibiting podophyllotoxins. This specific activity leads to interference with cell division by two different mechanisms in animals including humans.

Alkaloids often contain one or more rings of carbon atoms, usually with a nitrogen atom in the ring. Many have declared pharmacological activity[58]. Most alkaloids have a strong bittertaste and are very toxic, for these reasons they are used by plant to protect themselves against herbivory and attacks by microbial pathogens and invertebratepests[58].

Several alkaloid containing medicinal herbs are reported to have been used by the early man as pain relievers as recreational stimulantsor in religious ceremonies to enter a psychological state to achieve communication with ancestors or God. Lignans, alkaloids have been isolated from different *Swertia* species and are collected and listed in Table 6.

## MISCELLANEOUS

Some miscellaneous compound isolated from different *Swertia* species and is collected and listed in Table 7.

## CONCLUSION

This systematic review contains specific time bound data completion of isolated xanthones and other class of natural compounds form genus Swertia and fairly useful for research aspirates working on this genus. From the above discussion, it is clear that the family Gentianaceae is an important plant family with respect to its ethnomedicinal importance. It is widely used in traditional health care system. So, this importance builds a pressure on the plant regarding its use. So, practical steps are needed for its conservation which include *ex situ* and *in situ* conservation. Much more work should be done on studies phytochemistry and essential oils. The structures and composition of different chemical components present in it should be determined for recognizing its further activities. This type of information is required for drug production from this plant for treating various diseases.

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