APPENDIX-II

Publications

1. A brief Review on Phytoconstituents and Ethnopharmacology of *Scoparia dulcis* Linn. (Scrophulariaceae)


   International Journal of Phytomedicine 3 (2011) 422-438. (Published)

2. Microscopical characterization of *Scoparia dulcis* Linn. (Scrophulariaceae)


   Ancient Science of Life
A Brief Review on Phytoconstituents and Ethnopharmacology of *Scoparia Dulcis* Linn. (Scrophulariaceae)

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**ABSTRACT**

*Scoparia dulcis* Linn.(S. dulcis) or sweet broom weed commonly known as Mithipatti and Bana Dhania in Western Orissa, it is also known as ‘GhodaTulsi’in Hindi. The present review attempts to narrate the chemical constituents of *S.dulcis* and their uses. *S.dulcis* is rich in flavones, terpenes and steroids. Main chemical constituents such as scoparic acid A-C, scopadulcic acid A and B, scopadulciol, scopadulin and ammelin have been shown to contribute to the observed medicinal effect of the plant. In this review we have composed the structure and functions of those active ingredients with their melting point and other physical properties individually. Some aspects of the several speculated pharmacological properties of *S. dulcis* have been validated by scientific research, which includes the presence of hypoglycaemic and antitumour promoting compound. It also has antimicrobial and antifungal effects as well as antihyperlipidemic action.

**Keywords:** *Scoparia dulcis*, scoparic acid, ammelin, medicinal effect.

**Introduction**

*Scoparia dulcis* Linn.is an erect annual herb with互ated leaves, producing white flowers and -asuring up to a half meter in height when fully互m, it is an herb widely distributed in tropical and -ropical regions. Its ethno-medicinal uses amongst互ious indigenous tribes in the rain-forest zone are互-documented [1]. In fresh or dried form *S. dulcis*互nts have been traditionally used as remedies for -etes mellitus in India and hypertension in Taiwan

It is used in curing ailments such as fever, -rhoea, ulcer, cancer, wounds, skin rash, cough and -erculosis. The fresh or dried plant has been used -reating stomach aches, inflammation, bronchitis, -norhoids and hepatitis. In the western part of -ssa its root is traditionally used as an effective -edy for Jaundice and diarrhoea. It is also used as -algescic and antipyretic, in stomach troubles,[2] -inchilis, as well as inhibition of herpes simplex virus replication, gastric H⁺,K⁺-ATPase activation and antitumor activity. It is deemed to be a panacea for all ills. In Gambia, a lotion prepared from the plant is used in curing fever. A hot water infusion or decoction of the leaves or whole plant is used medicinally by indigenous tribes of Nicaragua to treat malaria, stomach disorders, menstrual disorders, insect bites, fevers, heart problems, liver disorders and venereal diseases. It has been used for blood cleansing, in childbirth and as a general tonic. [3] Phytochemical screening has revealed that the plant contains diterpenoids, flavonoids, tannins, alkaloids, triterpenes, hexacosonol, ß-sitosterol, ketone-dulcitone and ammelin, an antidiabetic compound [2-4]. The diterpenoid, scoparic acid A, isolated from the plant has been reported to be a potent ß-glucuronidase inhibitor [5]. The constituents, scopadulciol, scopadulcic acid-B and diacetylscopadiol, have been shown to be responsible for the inhibitory activity of the plant on gastric H⁺-K⁺ ATPase enzyme [6]. The

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The available information on S. dulcis has been divided into four sections, i.e., Plant profile ethnopharmacology, phytoconstituents, pharmacological reports. The reports in which S. dulcis species have been used as a domestic remedy by common men without any prescription for the treatment of various ailments have been discussed under ethnopharmacology.

**Plant Profile of Scoparia dulcis Linn.**


- **Terpenoid, scopadulcic acid-B and flavone, imenoxin, have been shown to exhibit cytotoxic and antitumor activity [7].**

In objective for studying medicinal plants is the discovery of new bioactive components, in the search for promising drugs. This review emphasizes the traditional uses and clinical potential of S. dulcis. Through this review, authors hope to attract the attention of natural product researchers throughout the world to focus on the unexplored potential of weed-like S. dulcis (mithipatti).

**Plant Profile of Scoparia dulcis Linn.**

**Fig. 1: Plant S. dulcis.**

**Fig. 2: Plant S. dulcis Herbarium.**

**Macular Name**

**Name:** Asmaghni

**Local:** Mithi Patti, Ghoda Tulsi, Ban Dhania

**English:** Sweet broom, Broom weed, Vassourinha

**System:**

- **Domain:** Plante
- **Kingdom:** Trachcobionta
- **Phylum:** Magnoliophyta
- **Class:** Magnoliopsida
- **Order:** Asteridae
- **Family:** Scrophulariaceae
- **Genus:** Scoparia
- **Species:** dulcis

**Scientific name:** Scoparia dulcis Linn.

**Botany**

**Scoparia dulcis** is a small, much branched, glabrous, leafy annual herb or under shrub with erect or ascending branches; leaves opposite and 3-notely whorled, rhomboid, elliptic or elliptic lanceolate, obtuse at apex, base tapering, margins serrate; Flowers many, in terminal panicles, pedicellate, pedicels slender, rigid, Calyx lobes 4, oblong, Corolla white, tube very short, Capsule globose; seeds minute, many. [8-9]

**Additional Uses of Scoparia dulcis Linn. [8-11]**

<table>
<thead>
<tr>
<th>Plant Part</th>
<th>Aerial Part</th>
<th>Root</th>
<th>Whole Plant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coughs, diarrhoea, eye problems, fever, headaches, hemorrhoids, infections, insect bites, intestinal worms, kidney disease, liver disorders, malaria, menstrual disorders, migraines, snake bites, stomach disorders, tonic, ulcers, urinary tract disorders, vomiting, wounds, anemia, burns, and cough</td>
<td>Bronchitis, diarrhoea, fever, jaundice, liver disorders, malaria, menstrual disorders, skin infections, stomach pains</td>
<td>Anemia, bronchitis, burns, coughs, diabetes, diarrhoea, dysentry, expectorant, fever, gastric disorders, headache, hemorrhoids, hepatitis, hypertension, infections, insect bites, intestinal worms, jaundice, liver disease, malaria, menstrual disorders, pain, rash, snake bites, swelling and toothache</td>
<td></td>
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**Phytoconstituents**

Available literature on phytochemical reports of the *S. dulcis* reveals that it comprises mainly terpenes and alkaloids. Fig. 3 to 38 summarizes phytoconstituents reported from various plant parts of *S. dulcis*.

**Plant resources:** Whole plants of *Scoparia dulcis* Linn. (Scrophulariaceae)  Fig-3.4

[12] **Compound: Scopadulcic Acid A** (Diterpene)
Molecular Formula (M.F.) - C_{27}H_{34}O_{6}
Melting point (m.p.) 172-174°C
Colorless prisms (from MeOH)
[^D] {27} -5.7° (MeOH)
Biological activity: Falciparum malaria,

[13] **Compound: Scopadulcic Acid B** (Diterpene)
M.F. - C_{27}H_{34}O_{5}
m.p. 228-232°C,
Colorless prisms (from MeOH)
[^D] {27} -49.6° (c = 1.02, MeOH)
Biological activity: Antiviral, antitumor activity in various human cell lines.
**Compound: Scoparic Acid A (Diterpene)**
- M.F. - C_{27}H_{36}O_{5}
- m.p. colorless amorphous powder
- [\delta]_{D26}^{23} = 38.3° (c = 1.00, CHCl₃)
- Biological activity: β-glucuronidase inhibition

**Compound: Scoparic Acid B (Diterpene)**
- M.F. - C_{25}H_{32}O_{5}
- m.p. colorless amorphous powder
- [\delta]_{D23}^{23} = 9.8° (c = 0.63, CHCl₃)
- Biological activity: Antiviral

**Compound: Scoparic Acid C (Diterpene)**
- M.F. - C_{26}H_{30}O_{5}
- m.p. colorless amorphous powder
- [\delta]_{D22}^{22} = 13.9° (c = 0.69, CHCl₃)
- Biological activity: β-glucuronidase inhibition

**Compound: Apigenin (Flavone)**
- M.F. - C_{15}H_{10}O_{5}
- m.p. 315°C
- yellow crystalline powder
- Biological activity: Antioxidant, radical scavenger, anti-inflammatory, carbohydrate metabolism promoter, immunity system modulator.
Compound: Acacetin (Flavone)
M.F.-C_{16}H_{12}O_{5}
m.p. 268-272°C Pale-yellow needles
[α]D22–13.9° (c = 0.69, CHCl3)
Biological activity: Inhibits Human Atrial Repolarization Potassium Currents, Antioxidant, radical scavenger, anti-inflammatory, carbohydrate metabolism promoter, immunomodulator.

Compound: Amyrin, alpha (Triterpine)
M.F.-C_{30}H_{50}O
m.p- 188°C
White crystalline powder
Biological activity: Anti-elastase activity, and modulates the membrane fluidity PGE2 release inhibition, strong anti-inflammatory activity, PKA inhibitor as well as a selective protease inhibitor.

Compound: Benzoxazin-3-one, 1-4: 2(h): 2-hydroxy (Nitrogen heterocy)
M.F.-C_{8}H_{7}N_{2}O_{2}
m.p.- 172-176 °C
Biological activity: Antimicrobial, anticancer and anti-inflammatory.

Compound: Benzoxazolinone (Nitrogen heterocy)
M.F.-C_{7}H_{5}NO_{2}
m.p.- 82-86°C
Light brown-pink Crystalline powder
Biological activity: Adrenergic and antihypertensive properties.
Compound: Betulinic Acid (Triterpene)

- M.F.: $\text{C}_{30}\text{H}_{48}\text{O}_3$
- m.p.: 295 - 298 °C (decomposes)
- White crystalline powder
- Optical Rotation: $+7^\circ$ - $+9^\circ$ (c=0.9 in pyridine)

Compound: Benzoxazolin-2-one, 6-methoxy (Nitrogen heterocy):

- M.F.: $\text{CaH}_7\text{NO}_3$
- m.p.: 151-156 °C (lit.)
- Light tancolour
- Biological activity: Antimicrobial and anti-inflammatory.

Compound: Cirsimin (Flavone)

- M.F.: $\text{C}_{22}\text{H}_{24}\text{O}_{11}$
- m.p.: 244-246 °C

Compound: Benzoxazolene, 2(3H) 6-methoxy (Nitrogen heterocy):

- M.F.: $\text{C}_9\text{H}_7\text{NO}_3$
- m.p.: 152-156 °C
- Biological activity: Antimicrobial, analgesic and anti-inflammatory.
Compound: Cirsitakaoside (Flavone)
M.F. \( \text{C}_{23}\text{H}_{24}\text{O}_{1n} \)
m.p. - 246-247°C
Biological activity: Respiratory disease, gastric, hepatic disturbances, anti-inflammatory, anti-diabetic and hypotension.

Compound: Cynaroside (Flavone)
M.F. \( \text{C}_{21}\text{H}_{20}\text{O}_{11} \)
m.p. - 266-268 °C
Yellow amorphous powder
Biological activity: Antioxidant, anti-diabetic.

Compound: Coumaric Acid, para (Phenylpropanoid)
M.F. \( \text{C}_{9}\text{H}_{8}\text{O}_{3} \)
m.p.-210-213 °C
Biological activity: Inhibits the development of stomach cancer.

Compound: Dulcitol (Diterpene)
M.F. \( \text{C}_{9}\text{H}_{4}\text{O}_{6} \)
m.p.-188-189 °C
Biological activity: Antiviral and cytotoxic activity.
[33] Compound: Daucosterol (Steroid)
M.F.: C36H60O6
m.p.: 295 °C
Biological activity: Immunomodulator

[26] Compound: Dulcioic Acid (Triterpene)
M.F.: C30H48O3
m.p.: 300 °C
Biological activity: Significant inhibitory effect on cytokine production, antispasmodic.

[35] Compound: Friedelin (Triterpene)
M.F.: C30H50O
m.p.: 262-265 °C
Biological activity: Estrogenic, Anti-inflammatory, analgesic and antipyretic.

[34] Compound: Gentisic acid (Benzenoid)
M.F.: C7H6O4
m.p.: 200 - 205 °C
white to yellow powder
Biological activity: Antispasmodic, local anesthetic, antioxidant and anticonvulsant.
### Fig-25, 26

**Compound: Glutinol (Triterpene)**
- M.F.: C₃₀H₅₆O₆
- M.p.: 206-208°C
- Biological activity: Anti-inflammatory, analgesic.

**Compound: Hymenoxin (Flavone)**
- M.F.: C₁₉H₁₈O₈
- M.p.: 215-216°C
- Biological activity: Estrogenic, antispasmodic.

### Fig-27, 28

**Compound: Ifflaionic Acid (Triterpene)**
- M.F.: C₃₀H₄₆O₃
- M.p.: 303°C
- Biological activity: Hypotensive

**Compound: Linarin (Flavone)**
- M.F.: C₂₆H₃₂O₁₄
- M.p.: 258-260°C
- Biological activity: Sedative and sleep-enhancing properties.

**Fig-29, 30**

**Compound: Luteolin (Flavone)**
M.F.- $C_{15}H_{10}O_{6}$
m.p.- $>330^\circ$ C
yellow crystalline compound
Biological activity: Anti-oxidant, anti-cancer, immunomodulator, anti-inflammatory.

**Compound: Mannitol, d (Carbohydrate)**
M.F.- $C_{6}H_{12}O_{6}$
m.p.- 164 – 169 $^\circ$ C
white, crystalline
Biological activity: Diuretic, of Alzheimer's disease, chemotherapy for brain tumors.

**Fig-31, 32**

**Compound: Scutellarein (Flavone)**
M.F.- $C_{21}H_{18}O_{12}$
m.p.- 218-220$^\circ$ C
Biological activity: Induce apoptosis of ovarian and breast tumor cells in vitro.

**Compound: Scoparinol (Diterpene)**
M.F.- $C_{27}H_{38}O_{4}$
m.p.-
Biological activity: Anti-inflammatory, analgesic
### Compound: Sitosterol, beta (Steroid)

- M.F.: C_{29}H_{50}O
- m.p.: 136-140 °C
- Biological activity: Antioxidant, anti-cancer, anti-tumor, reduce blood cholesterol levels.

### Compound: Stigmasterol (Steroid)

- M.F.: C_{29}H_{48}O
- m.p.: 161-170 °C
- Biological activity: Anti-cancer, lower serum cholesterol, antioxidant, hypoglycemic.

### Compound: Taraxerol (Steroid)

- M.F.: C_{30}H_{50}O
- m.p.: 282-285 °C
- Biological activity: Anti-cancer, anti-tumor

### Compound: Vicenin 2 (Flavone)

- M.F.: C_{27}H_{30}O_{15}
- m.p.: 271-272 °C
- Biological activity: Anti-cancer, anti-inflammatory
**Pharmacological Activity**

The use of the whole herb of *S. dulcis* in painful conditions, both centrally and peripherally, is well documented. It was found that the observed analgesia was demonstrated by the active constituents, Glutoni, a triterpene [60-61] and parinol, a diterpene [62] isolated from the plant. These act through a peripherally acting mechanism similar to non-steroidal anti-inflammatory agents, such as indomethacin and diclofenac sodium.

The possible antioxidant property of the aqueous extract of *S. dulcis* was tested in rats exposed to cadmium. The results showed that relative to controls, cadmium significantly reduced superoxide dismutase activity, significantly increasing catalase activity and lipid peroxidation levels in the liver and kidney.

The study summarizes the effect of *S. dulcis* on the population of immune cells during a 28 day experimental *T. brucei* infection in rabbits. The results obtained showed that infection resulted in an initial rise in both total white blood cells (WBC) and the absolute number of circulating lymphocytes followed by a progressive decrease in total WBC and all WBC subtypes, namely: lymphocytes, monocytes and granulocytes, although the % lymphocytes (lymphocytes expressed as % of total WBC) remained consistently higher than normal throughout the study period. Treatment with *S. dulcis* at a daily oral dose of 25 mg/Kg body weight significantly reduced the severity of the observed lesions (*p < 0.05*) when compared with untreated infected animals. Thus the herb demonstrates significant potency in protecting against the parasite induced decrease in the population of immunologically active cells.

The antioxidant efficacy of *S. dulcis* in STZ diabetic rats was compared with Glibencamide. A significant increase in the activities of plasma insulin, superoxide dismutase, catalase, glutathione peroxidase, glutathione-S-transferase and reduced glutathione was observed in brain on treatment with 200 mg/kg body weight of *S. dulcis* plant aqueous extract and glibenclamide for 6 weeks. Both the treated groups showed a significant increase in the antioxidant enzymes compared to untreated diabetic rats.

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**Fig-37, 38**

[Chemical structures of flavones and isoflavones were shown, along with their properties.]

**Compound: Vitexin (Flavone)**

M.F.-C_{21}H_{20}O_{10}
m.p.- 256-257°C

Biological activity: Antioxidant, hypotensive

**Compound: Vitexin, iso (Flavone)**

M.F.- C_{21}H_{20}O_{10}
m.p.- 203-204°C

Biological activity: Antioxidant, hypotensive
•wed significant decrease in thiobarbituric acid-
active substances (TBARS) and hydroperoxides
ation in brain, suggesting its role in protection
l lipid peroxidation induced membrane damage.
ay be concluded that in diabetes, brain tissue:
more vulnerable to oxidative stress and showed
ased lipid peroxidation. The above observation
t that the aqueous extract of S. dulcis plant
ses antioxidant activity, which could exert a
ficial action against pathological alterations
sed by the presence of free radicals in STZ
etes.

A group of experiments were performed on normal and
perimental male Wistar rats treated with S. dulcis
tract. The effect of extract was tested on
streptozotocin (STZ) treated Rat insulinoma cell lines
(RINm5F cells) and isolated islets in vitro.

The extract markedly reduced the STZ-induced lipid
peroxidation in RINm5F cells. Further, extract
ected cytochrome P450-mediated cytotoxicity and nitric oxide
(NO) production in RINm5F cells. Treatment of
INm5F cells with 5mMSTZ and 10g of extract
pletely abrogated apoptosis induced by STZ,
suggesting the involvement of oxidative stress. Flow
cytometric assessment on the level of intracellular
peroxides using fluorescent probe 2′-
dichlorofluorescein diacetate (DCF-DA) confirmed that
TZ (46%) induced an intracellular oxidative stress in
INm5F cells, which was suppressed by extract
(21%). In addition, extract also reduced (33%) the
TZ-induced apoptosis (72%) in RINm5F cells
icating the mode of protection of extract on RIN
m5F cells, islets, and pan-creatic cell mass
( histopathological observations). Present study thus
irms antihyperglycemic effect of extract and also
demonstrated the consistently strong antioxidant
eties of S. dulcis used in the traditional medicine
[63-65].

Much of the recent research on S. dulcis has centered
around one powerful phytochemical called scopadulcic
acid B (SDB). In a 1993 clinical study, SDB inhibited
the growth of tumors in a test tube and in mice. The
otency of SDB proved to be stronger than that of
other natural antitumor-promoting terpenoids, such as
glycyrrhetic acid. [66]. One of the chemical
constituent is an aphidicolin-like tetracyclic diterpene
amed scopadulciol (SDC), which was isolated from S.
S. dulcis showed stimulatory effect on antiviral activity of acyclovir (ACV) or ganciclovir (GCV).

The effect of S. dulcis on T. brucei induced anaemia was investigated on rabbits. Changes in Packed cell volume (PCV), Haemoglobin (Hb) concentration, Red blood cell count (RBC), Mean cell haemoglobin (MCH), Mean cell haemoglobin concentration (MCHC) and Mean cell volume (MCV) were monitored. The results obtained indicate that infection with T. brucei results in a significant decrease in PCV, Hb concentration and RBC. No significant changes were observed in MCH, MCHC and MCV. However the severity of observed anaemia was significantly less pronounced in the treated rabbits that were treated with S. dulcis when compared with their infected but untreated counterparts. It was concluded that S. dulcis therapy may prove useful in the management of T. brucei anaemia, and possibly other forms of anaemia. The plant may possess a measure of trypanocidal activity or mono-stimulating properties that help to put the site in check and thus also control the deleterious act of uncontrolled parasite proliferation. The plant has also been used in the management of sickle cell anaemia from decades (Hilda Ogbe, personal communication).

Juice, Seed Extract and leaf extract of S. dulcis used for the mineralization of calcium oxalate, ammonium carbonate and calcium phosphate. Four experimental models namely 'simultaneous flow model' (S.S.M.), 'simultaneous flow dynamic model' (S.D.M.), 'reservoir static model' (R.S.M.) and 'reservoir dynamic model' (R.D.M.) were used for the study. The study suggests that the increased rate of fruits juice and seed extract of Scoparia dulcis could be helpful in urinary stone prophylaxis.

Conclusion

In this review we can conclude that studies with active principles obtained from the whole plant of Scoparia dulcis can result in novel and effective form of treatment. Chemical substances derived from this plant have been used to treat human illnesses since the dawn of medicine. This plant may provide leads to find therapeutically useful compounds. Thus more efforts should be made towards isolation and characterization of the active principles and their structure activity relationship. The combination of traditional and modern knowledge can produce better drugs for the treatment of various ailments with fewer side effects.

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