Journal of Scientific & Industrial Research
Vol. 69, October 2010, pp. 732-740

Phytochemistry of *Solanum xanthocarpum*: an amazing traditional healer

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Received 16 February 2010; revised 29 July 2010; accepted 02 August 2010

Solanum xanthocarpum contains alkaloids, phenolics, flavanoids, sterol, saponins and their glycosides, and has a wide range of medicinal values. This review presents chemical constituents of *S. xanthocarpum* and its biological activities.

Keywords: Anti-fertility activity, Larvicidal activity, *Solanum xanthocarpum*, Steroids, Solasodine

Introduction

Solanam xanthocarpum Schradt. & Wendl. (*Solanaceae*), a herb (Fig. 1), grows as wild plant in many parts of India, particularly in hills and valley of Manipur (Leipung-Khanga in Manipuri). Fruits are edible and local people of Manipur use fruits for treatment of various ailments as traditional folk medicine. India is one of the raw material-producing nations of South Asia[1], with rich plant diversity of Himalaya (> 8000 angiosperms, 44 gymnosperms, 600 pteridophytes, 1737 bryophytes, 1159 lichens, etc.) and a source of medicine for millions of people in India and abroad[2]. Indian Himalayan Region (IHR) supports over 1748 (32.2% of India) plant species of known medicinal value[3]. Manipur has been known for its richness in medicinal plants[4]. More than 300 plants having medicinal values and also commonly used by local people have been identified by ethnobotanical survey works[5]. This review focuses on biology, chemistry, and medicinal value of *S. xanthocarpum*.

S. xanthocarpum

Description and Distribution

S. xanthocarpum is an annual herbaceous plant comprising 90 genera and 2000-3000 species[6]. In Hindi, it is called Kantkari. Its other names are Choti Katheri, Kateli, Bhatkatiya and Bhachkatiya. In India, it is mainly grown in Utter Pradesh, Bihar, Uttaranchal, Punjab, West Bengal, Assam and other North-Eastern States. In Manipur, it is grown as a wild plant and distributed throughout the hills and valley. It is generally grown in March-April and bears fruits in May-June. It grows on all kinds of soil but does well on dry and hot temperate regions. It is a very prickly diffuse, bright green perennial herb, 2-3 m high; stems zigzag; prickles compressed, straight, yellow and shining; leaves 5-10 by 2.5-5.7 cm ovate or elliptic, sinuate or sub pinnatified, hairy on both sides, petiole prickly. Flowers are small, in extra-axilliary few flowered cymes. Corolla is purple, lobes deltoid, hairy outside. Fruits are of 1.3 cm diameter berry, yellow or white with green veins, surrounded by enlarged calyx.

S. xanthocarpum fruits yield solanocarpidine and a sterol, carpesterol. Root is one of the constituents of *Dasamulasava*[7]. Seeds are used as diuretic[2]. Juice of berries is reported to be useful in sore throat. A decoction of plant is used in gonorrhoea and it also said to promote conception in females. Kantakari is reported useful in Kasa Roga (cough)[8] and also in Tamakwasa (bronchial asthma)[9]. In Chhattisgarh, it is considered as a most valuable herb for traditional healers in treatment of over 100 common diseases alone or in combination with other local and exotic herbs. According to Ayurveda, it is bitter, appetiser, laxative, anthelmintic, stomachic, and useful in bronchitis, asthma, fever, lumbago, pains, piles (specially bleeding piles), thirst, urinary and heart diseases.

Chemical Constituents

Plant contains alkaloids, sterols, saponins, flavonoids and their glycosides and also carbohydrates, fatty acids, amino acids etc.[10-31]

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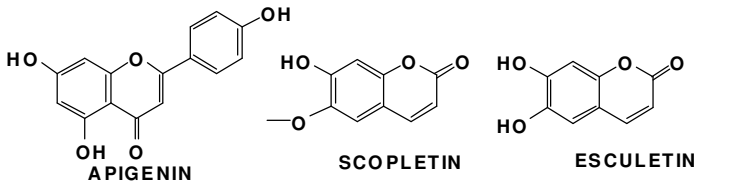
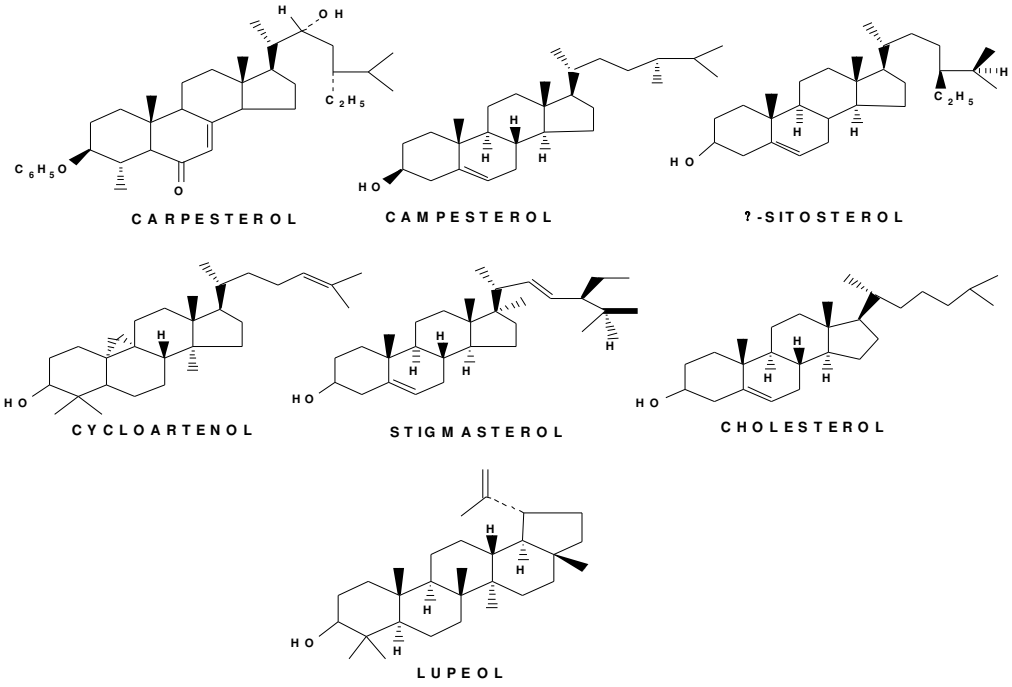
Fig. 1—*Solanum xanthocarpum*

Flavones, Phenolics & Coumarins



Steroids and triterpenoids



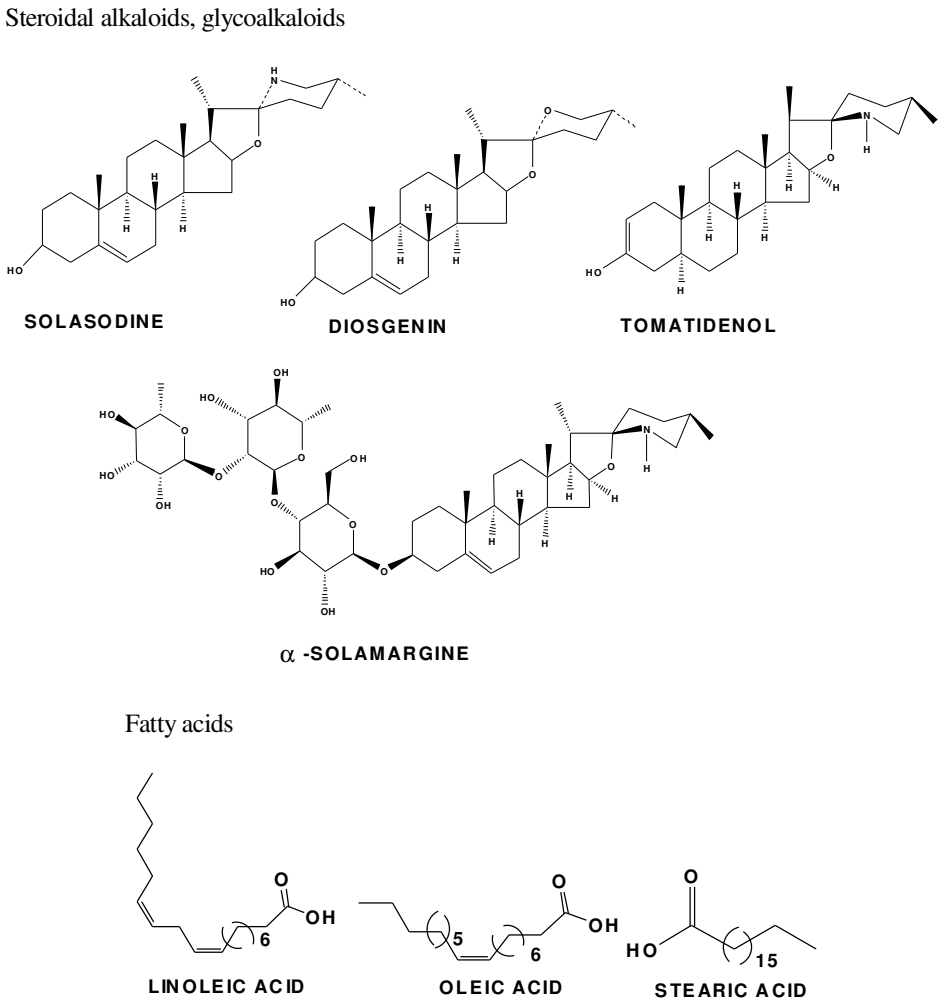


Fig. 2—Structures of some phytoactive compounds isolated from *S. xanthocarpum*

(Fig. 2, Table 1). Verbist & Monnet[31] found that fruits from French plant (4.6%) were richer in solasodine glycoside than those of Nepalese origin (1.6%), besides plants of both natives contained traces of tomatidenol. In India, glycoalkaloid content of fruits collected from Jammu & Kashmir is reported to be 3.5% (total alkaloid, 1.1%). Plant samples collected from Calcutta contained solasodine (0.0287%). Plant contains diosgenin[19]. Seeds yield greenish yellow, semi-drying oil (19.3%) with a characteristic odour. Unsaponifiable matter of fruits contains two sterols, one of which is carpesterol[11].

Biological Activity

Antifertility Activity

Solasodine, an alkaloid of *S. xanthocarpum* possesses antispermatogenic activity[32,33]. Chronic administration of solasodine (20 mg/kg alternate day for 30 days) caused testicular lesions resulting in a severe impairment of spermatogenic elements. Epididymides were devoid of spermatozoa. Total protein, sialic acid and glycogen contents of testis and epididymis were reduced significantly whereas testicular cholesterol was elevated. Acid phosphatase enzyme activity of testes was low after solasodine treatment. Serum enzymes (SGPT, alkaline phosphatase), serum protein, triglycerides, non-esterified fatty acid levels were in normal range when compared with their controls. Cholesterol and phospholipid levels were elevated after solasodine treatment to intact dogs. Reduced androgen production was reflected in low levels of sialic acid in testes and epididymides and reduced Leydig cell nuclei. Castration alone brought about reduction in size of epididymis. Castration followed by solasodine treatment caused epididymal degeneration. Solasodine administration in dogs definitely rendered male infertile

Table1—Compounds isolated from *solanum xanthocarpum*

Sl No.	Compound	Class	Plant part	Country
1	Apigenin[10]	flavonoid	DL, RT, FT	India
2	Arachidic acid[11]	fatty acid	SO	India
3	α-Solamargine[12]	alkaloid	PD, SD	China
4	β-Solamargine[13]	steroid	FT	Japan
5	β-Sitosterol[14,15]	steroid	TC, FT	India
6	Campesterol[13]	steroid	FT	Japan
7	Coumarin[16]	phenolic	DL, RT, FT	India
8	Cholesterol[13]	steroid	FT	Japan
9	Cycloartanol[13]	steroid	FT	Japan
10	Carpesterol[17]	glycoalkaloid	DF	Japan
11	Caffeic acid[18]	phenolic	BR	India
12	Diosgenin[14,19,20]	sapogenin	TC, PNS, TC	India
13	Esculetin[16]	coumarin	DL, RT, FT	India
14	Esculin[16]	coumarin	DL, RT, FT	India
15	Galactoside of β-sitosterol[18]	glycoside	BR	India
16	Glucose[21-23]	carbohydrate	DF, SD, DF	India
17	Galactose[21,23]	carbohydrate	DF, DF	India
18	Oleic acid[11]	fatty acid	SO	India
19	Lupeol[15,24]	triterpenoid	TC, FT	India
20	Linoleic acid[11]	fatty acid	SD	India
21	Lysine[25]	amino acid	SD	India
22	Leucine[25]	amino acid	SD	India
23	Methyl caffeate[18]	phenolic	BR	India
24	Norcarpesterol[26]	steroid	PNS	Japan
25	Palmitic acid[11]	fatty acid	SO	India
26	Rhamnose[21-23]	carbohydrate	DF, SD, DF	India
27	Solasodine[20,21,23,27,28]	steroidal alkaloid	DF, FL	Japan, India
28	Scopoletin[16]	coumarin	DL,RT,FT	India
29	Sitosterol[10]	steroid	FT	Japan
31	Solasonine[18,23,28,29]	steroidal alkaloid	BR, DF, DF, TC	India
32	Solasurine[18]	steroidal alkaloid	BR	India
33	Solanine[21]	steroidal alkaloid	DF	India
34	Solanidine[21]	steroidal alkaloid	DF	India
35	Solanacarpine[22]	glycoalkaloid steroidal lactone	SD	India
37	Solanacarpigenin[22]	steroidal aglycone	SD	India
38	Stearic acid[11]	fatty acid	SD	India
39	Stigmasterol[13]	steroid	FT	Japan
40	Sitosteryl glucoside[13]	steroid	FT	Japan
41	Stigmasteryl glucoside[13]	steroid	FT	Japan
42	4α-Methyl-24ξ-ethyl-5α-cholest-7-en-3β,22ξ-diol[30]	steroid	FT	Japan
43	3β,22ξ-Dihydroxy-4α-methyl-24ξ-ethyl-5α-cholest-7-en-6-one[13]	steroid	FT	Japan
44	3β-Benzoxy-14β,22ξ-dihydroxy-4α-methyl-24ξ-ethyl-5α-cholest-7-en-6-one[13]	steroid	FT	Japan
45	3β-Benzoxy-14β,22ξ-dihydroxy-4α-methyl-24ξ-ethyl-5α-cholest-7-en-6-one[13]	steroid	FT	Japan
46	3β-(*p*-Hydroxy)-benzoxy-22ξ-hydroxy-4α-methyl-24ξ-ethyl-5α-cholest-7-en-6-one[13]	steroid	FT	Japan
47	4α-Methyl-(24*R*)-ethylcholest-7-en-3β-ol[13]	steroid	FT	Japan
48	4α-Methyl-24ξ-methylcholest-7-ene-3β,22ξ-diol[26]	steroid	PNS	Japan
49	Quercetin 3-*O*-β-D -glucosyl-*O*-β-D -mannoside[10]	flavonol	FL	India
50	Tomatidenol[31]	alkaloid	FT	France

ST, Stem; RT, Root; SD, Seed; SO, Seed oil; BR, Berries; FT, Fruit; FL, Flower; LF, Leaf; DF, Dry fruit; TC, Tissue culture; PNS, Part not specified.

as evidenced by absence of sperms in cauda epididymis and ductus deferens.

Pyretic Body Temperature Effect

Action of solasodine was studied on normal and pyretic body temperature of rats and mice[34]. In rats, a single dosage (3 mg/kg) depressed by an average of -1.5+/-0.3°C normal temperature for 24 h. With larger dosages or longer treatment, effect could not be intensified and tolerance was also not observed. In mice, temperature decrease was even more explicit; -2.0+/-0.2°C lasting 48 h. Effect was reproducible by repeated treatment. In mice, fever provoked by a suspension of killed bacteria, Pyrago or by 2, 4-dinitrophenol (DNP) could be counteracted with solasodine (1 mmol/kg). Body temperature depressed with solasodine was not raised by Pyrago but became higher after administration of DNP, in part of animals even comparable to normal initial averages. Following solasodine treatment, body temperature of normothermic rats and mice decreased to subnormal values. Pyrexia produced either with centrally acting Pyrago or with peripherally acting DNP was depressed with small solasodine dosages. Previous administration of alkaloid counteracted Pyrago effect but could not inhibit development of DNP action. These data are pertaining to possible central effect of solasodine.

Anticancer Effect

Lupeol[35], apigenin[36] and solamargine[37] exhibited anticancer property. Appearance in solamargine-treated cells of chromatin condensation, DNA fragmentation, and a sub-G_1 peak in a DNA histogram suggested that solamargine induced cell death by apoptosis. Maximum number of dead Hep3B cells was detected within 2 h of incubation with constant concentrations of solamargine, and no further cell death was observed after an extended incubation with solamargine, indicating that action of solamargine was irreversible. To determine susceptibility of cell phases to solamargine-mediated apoptosis, Hep3B cells were synchronized at defined cell cycles by cyclosporin A, colchicine, and genistein, followed by values of solamargine for control, G_0/G_1-, M-, and G_2/M-synchronized Hep3B cells were 5.0, 10, 3.7, and 3.1 ìg/ml, implying that cells in G_2/M phases are relatively susceptible to solamargine-mediated apoptosis. Hep3B cells were 5.0, 10, 3.7, and 3.1 µg/ml, implying that cells in G2/M phases are relatively susceptible to solamargine-mediated apoptosis. addition, a parallel up-regulation of tumour necrosis factor receptor (TNFR)-I and -II on Hep3B cells was detected after solamargine treatment, and solamargine-mediated cytotoxicity could be neutralized with either TNFR-I or -II specific antibody. Therefore, actions of TNFR-I and -II on Hep3B cells may be independent, and both are involved in mechanism of solamargine-mediated apoptosis.

Inhibition of Fungal Growth

Fewell *et al*[38] studied inhibition of mycelium development in *Phoma medicaginis* and *Rhizoctonia solani* by solamargine and solasonine, which generally increased with increasing pH. *P. medicaginis* was more susceptible and solamargine more potent compound. Solasonine was inactive against *R. solani* over tested pH range (5-8). Dose-response curves confirmed these differential effects. Solamargine caused 50% growth inhibition in *P. medicaginis* at 60 µM (pH 7), whereas no other treatment achieved this effect at 100 µM. Combinations of 50 µM of each glycoalkaloid produced synergistic effects against both fungi, especially *Rhizooctonia solani,* which was essentially unaffected by either compound, but significantly inhibited by a 1:1 mixture of the two. Magnitude of synergism was not affected by a pH change (6-7). Spore germination in *Alternaria brassicicola* was markedly inhibited by 100 µM solamargine but unaffected by 100 µM solasonine or either compound at 50 µM. In *P. medicaginis*, neither glycoalkaloid was inhibitory up to 150 µM. In combination, two compounds caused synergistic effects in both species, but to a greater extent in *A. brassicicola*.

Snail-killing Activity

α-Solamargine from fruit of *S. xanthocarpum*[12] shows an excellent effect in killing (100% at 28 °C) Oncomelania snails in solution of alpha-solamarrgine (0.2 mg/l).

Anti-allergy Activity

Apigenin has shown anti-allergic effect of apigenin in ovalbumin (OVA)-induced asthma model mice[39]. OVA-induced mice showed allergic airway reactions and included an increase in number of eosinophils in bronchoalveolar lavage (BAL) fluid, an increase in inflammatory cell infiltration into lung around blood vessels and airways, airway luminal narrowing, and development of airway hyper-responsiveness (AHR). Administration of apigenin before last airway OVA challenge resulted in a significant inhibition of all asthmatic reactions.

Table 2 — Biological activities for extracts of *Solanum xanthocarpum*

Sl No.	Extract	Plant part	Country	LC_{50}/MIC /Conc.used	Species
Larvicidal activity					
1	Petroleum ether	RT	India	+-1.41±0.42	*A. stephensi*[46]
2	Carbon tetrachloride	RT	India	+-22.5±4.16	*A. stephensi*[46]
3	Methanol	RT	India	+-161.55±39.62	*A. stephensi*[46]
4	Aqueous	FT	India	+-0.112	*An. culicifacies*[47]
5	Aqueous	FT	India	+-0.058	*An. stephensi*[47]
6	Aqueous	FT	India	+-0.052	*Ae. aegypti*[47]
7	Aqueous	RT	India	+-1.160	*An. culicifacies*[47]
8	Aqueous	RT	India	+-1.080	*An. stephensi*[47]
9	Aqueous	RT	India	+-1.150	*Ae. aegypti*[47]
10	Methanol	FT	India	-	*An. stephensi*[48]
11	Petroleum ether	FT	India	-	*An. stephensi*[48]
12	Carbon tetrachloride	FT	India	+-5.11ppm	*An. stephensi*[48]
13	Methanol	FT	India	+-5.11ppm	*Cx. quinquefasciatus*[48]
14	Petroleum ether	FT	India	+-62.62 ppm	*Cx. quinquefasciatus*[48]
15	Carbon tetrachloride	FT	India	+-62.62 ppm	*Cx. quinquefasciatus*[48]
16	Methanol	FTWS	India	+-79.6 ml/l	*An. culicifaceis*[49]
17	Methanol	FTWS	India	+-131.4 ml/l	*An. stephensi*[49]
18	Methanol	FTWS	India	+-273.4 ml/l	*Ae. aegypti*[49]
19	Methanol	FTWS	India	+-384.9 ml/l	*Cx. quinque fasciatus*[49]
20	Methanol	WF	India	+-91.7 ml/l	*An. culicifaceis*[49]
21	Methanol	WF	India	+-186.9 ml/l	*An. stephensi*[49]
22	Methanol	WF	India	+-290.9 ml/l	*Ae. aegypti*[49]
23	Methanol	WF	India	+-450.6 ml/l	*Cx. quinque-fasciatus*[49]
24	Methanol	SD	India	+-131.7 ml/l	*An. culicifaceis*[49]
25	Methanol	SD	India	+-195.6 ml/l	*An. stephensi*[49]
26	Methanol	SD	India	+-377.6 ml/l	*Ae. aegypti*[49]
27	Methanol	SD	India	+-520.0 ml/l	*Cx. quinque-fasciatus*[49]
Antibacterial activity					
1	Aqueous	LF	India	+2 mm	*S. aureus*[50]
2	Aqueous	LF	India	+17.7 mm	*E. coli*[50]
3	Aqueous	LF	India	+1 mm	*P. aeruginose*[50]
4	Aqueous	LF	India	+1 mm	*K. pneumoniae*[50]
5	Ethanol	LF	India	-	*S. aureus*[50]
6	Ethanol	LF	India	+13 mm	*E. coli*50
7	Ethanol	LF	India	+14 mm	*P. aeruginose*[50]
8	Ethanol	LF	India	+5 mm	*K. pneumoniae*[50]
9	Saponin fraction	LF	India	+1 mm	*S. aureus*[50]
10	Saponin fraction	LF	India	+19.2 mm	*E. coli*[50]
11	Saponin fraction	LF	India	0	*P. aeruginose*[50]
12	Saponin fraction	LF	India	+10 mm	*Kl. pneumoniae*[50]
Anti-oxidant activity					
1	Methanol	PNS	Hong Kong	++2.72 µmol/g	*FRAP assay*[51]
Anti-histamine activity					
1	Ethanol	AP	India	++100 mg/kg	*Mice*[52]
Anti-fungal activity					
1	Methanol	PNS	India	--1.25-2.50 mg/ml	*A. fumigatus*[53]
2	Methanol	PNS	India	--1.25-2.50 mg/ml	*A. flvus*[53]
3	Methanol	PNS	India	--1.25-2.50 mg/ml	*A. niger*[53]
4	Ethanol	LF	India	+22 mm	*A. niger*[50]
5	Ethanol	LF	India	+26 mm	*A. fumigatus*[50]
6	Methanol	LF	India	+32 mm	*A. niger*[50]
7	Methanol	LF	India	+34 mm	*A. fumigatus*[50]
8	Saponin fraction	LF	India	+83 mm	*A. flvus*[50]
9	Saponin fraction	LF	India	0	*A. niger*[50]
10	Compd 1(carpesterol)	FT	India	+100 mm	*T. viride*[54]
11	Compd 2(carpesterol derivative)	FT	India	+86.65 mm	*T. viride*[54]

Cont.Table-2

Sl No.	Extract		Plant part	Country	LC_{50}/MIC /Conc.used	Species
Antifungal activity						
12	Compd. related)	3(carpesterol	FT	India	+100 mm	*T. viride*[54]
13	Compd derivative)	4(carpesterol	FT	India	+100 mm	*T. viride*[54]
14	Compd derivative)	5(carpesterol	FT	India	+64.29 mm	*T. viride*[54]
Hypoglycaemic activity						
1	Aqueous		FT	India	-	*Rat & mice*[55]
Toxicity						
1	-		PNS	-	++4.321mg/ml	*Snails & fish*[56]
2	Methanol		FT	India	+62.5 μg/ml	*A. brassicae*[57]
Antinociceptive activity						
1	Methanol		AP	Bangladesh	++125 mg/kg	*Mice*[58]

+, Zone of inhibition; +-, LC_{50}; --, Minimum inhibition concn; ++, Conc. used; -, Not assigned; AP, Aerial part; RT, Root; SD, Seed; FT, Fruit; LF, Leaf; PNS, Part not specified; FTWS, Fruit without seeds; WF, Whole fruits

Condensation Effect

Su Y *et al*[40] studied effects of incorporation of cholesterol, sitosterol and stigmasterol into dipalmitoylphosphatidylcholine (DPPC) monolayers and observed that sitosterol and stigmasterol interacted less effectively than cholesterol with phospholipid. These sterol molecules could all cause condensation effect on DPPC monolayers. Attractive interactions between DPPC and sterol molecules, or hydrophobic effect, was found to play an important role, testified by negative excess molecular areas at particularly low surface pressures and negative partial molecular area of three sterols at low surface pressures. Minimum extreme points for excess area were all located at around 0.3 mol fractions for three sterols at 30 mN/m, suggesting DPPC/ sterol (2:1) in ordered structures.

Suppressing Effect

Diosgenin from *S. xanthocarpum* was found to be effective in suppressing FAS expression in HER2-overexpressing breast cancer cells[41]. It preferentially inhibited proliferation and induced apoptosis in HER2-overexpressing cancer cells. It inhibited phosphorylation of Akt and mTOR, and enhanced phosphorylation of JNK. Use of pharmacological inhibitors revealed that modulation of Akt, mTOR and JNK phosphorylation was required for diosgenin-induced FAS suppression. Diosgenin could enhance paclitaxel-induced cytotoxicity in HER2-overexpressing cancer cells. Thus diosgenin has potential to advance as chemopreventive agent for cancers that overexpress HER2.

Anti-inflammation Effect

Stigmasterol[42], carpesterol[43] and diosgenin[44] showed anti-inflammatory effect. Lupeol in *S. xanthocarpum* also acted as multi-target agent with immense anti-inflammatory potential, targeting key molecular pathways, which involved nuclear factor kappa B (NFκB), cFLIP, Fas, Kras, phosphatidylinositol-3-kinase (P13)/Akt and Wnt/β-catenin in a variety of cells. Lupeol at its effective therapeutic doses exhibited no toxicity to normal cells and tissues. Hence, it may serve as a therapeutic and chemopreventive agent for treatment of inflammation[45].

Thus, biological activities of *S. xanthocarpum* include anti-fertility, rheumatism, anti-cancer, hypoglycaemic-activity etc[32-45] (Table 2).

Conclusions

S. xanthocarpum is non-toxic and safe for human use and is regarded as a valuable plant in both Ayurvedic and modern drug development areas for its versatile medicinal uses. Solasodine from this plant has been widely used as an antifertility agent; use of this plant as a potential fungicide can be explored. Further

studies of other phytoactive compounds will possibly lead to exploration of new method for therapeutic and industrial application.

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