Review Article **www.ijcps.com**

International Journal of Chemical and Pharmaceutical Sciences
2017, Mar., Vol. 8 (1)

ISSN: 0976-9390
IJCPS

A review on pharmacological activities of *Smilax China* and *Smilax zeylanica*

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Received: 22th Mar 2017, Revised and Accepted: 27th Mar 2017

ABSTRACT

In recent years, the search of biomarkers from plants has been of great interest to scientists. The present review was carried to seek the different activities of various parts of the *Smilax china* and *Smilax zeylanica* L. The review is aimed to bring out scientific evidence for the therapeutic usage of *Smilax china* and *Smilax zeylanica* then focused on pharmacological activities of both plants. it is one of the safe and efficacious medicines used traditionally for the treatment of various ailments. This review describes various facets like active constituents, morphological characters and pharmacological properties of its individual ingredients. In various pharmacological studies undergone earlier the both plants of *Smilax china* and *Smilax zeylanica* showed antimicrobial, anthelmintic, anti oxidant, anticancer, hepatoprotective property. This review is carried out to scientifically indicate the traditional use of both plants of *Smilax china* and *Smilax zeylanica*.

Keywords: *Smilax china, Smilax zeylanica,* Antidiabetic activity and Anthelmintic activity.

1. INTRODUCTION

1.1. Botanical description

Smilax China

Scientific Name: *Smilax China*

Family: Liliaceae

Common name: China root

Tamil name: Parangisakkai

Part used: Rhizomes

Uses: The rhizomes are bitter, acrid, thermogenic, anodyne, anti-inflammatory, digestive, laxative, depurative, diuretic, febrifuge and tonic. It is used in dyspepsia, flatulence, colic, constipation and helminthiasis. It is useful in skin diseases, leprosy and psoriasis. It is used in fever, epilepsy, insanity and neuralgia. It is used syphilis, strangury, seminal weakness and general debility. Detoxifies organs, cleanses blood, aids absorption and kills bacteria. It also stimulates digestion, increases urination, protects liver and promotes perspiration[1].

Smilax zeylanica

Scientific Name: Smilax zeylanica

Family: Liliaceae

Habitat: Common in eastern Himalayas

Tamil name: Tirunamapalai, Kattukodi, Parangipattai

Uses: As per Ayurveda the plant is useful against skin disease, pitta, insanity, diarrhea, colic, vata, syphallis, gonorrhea, fever, arthritis, leucorrhoea, impotency and general weakness etc. Till nowvarious pharmacological activities had been done on different parts of the plant like antidiabetic,antihelmentic, antioxidant, antiepileptic, pesticidal, antigonorreal[2].

Plants are vital component of the world's biodiversity and essential natural resources for Human wellbeing. Besides sustenance, the plants1-have been used as therapeutic aid for alleviating from very ancient times, Such plants commonly referred to as Medicinal plants, have been one of the valuable tools in the traditional system of medicine and are also known to provide ingredients for formulation of new medicines in pharmaceutical industry. In fact, WHO has listed over 21,000 plant species to be of medicinal use around the world. More than 60% of the world's human population relies on plant medicine for primary health care needs. Plants are critical to other life on this planet because they form the basis of all food webs. Most plants are autotrophic, creating their own food using water, carbon dioxide and light through a process called photosynthesis. Some of the earliest fossils found

have been aged at 3.8 billion years. This fossils deposits show evidence of photosynthesis, so plants or the plant like ancestors of plants, have lived on this planet longer that most other groups of organisms [3]

Accordingly, the WHO consultative group on medicinal plants has formulated a definition of medicinal plants in the following way. "A medicinal plant is any plant which, in one or more of its organs, contains substances that can be used for therapeutic purposes or which is a precursor of synthesis of useful drugs". Unfortunately, this definition of the WHO group includes only the medicinal plants whose therapeutic properties and chemical constituents have been established scientifically. But it does not take into consideration the vast majority of the medicinal plants, which have not yet been subjected to through scientific studies. These medicinal plants have been used in traditional medicine for hundreds of years with reputation as efficacious remedies although there may not be sufficient scientific data to substantiate their efficacy. Selection of the medicinal plants by early man, without any prior knowledge about them, was largely based on intuition, guesswork or trial and error. Curiosity and search for food had contributed considerably to his knowledge about the plants and their virtues. Superficial resemblance between a specific plant part and the affected organ or some Symptoms of the ailment had also guided ancient man in his selection of medicinal plants. The world health organization (WHO) has defined traditional medicine as the sum total of all knowledge and practice, whether applicable or not, used in the diagnosis, prevention and elimination of physical, mental or social imbalance, relying exclusively on practical experience and observations handed down from generation, verbally in writing. However, the forms and practice of traditional medicine vary from the highly organized and long established Chinese and Ayurvedic systems to the largely herbalist and spiritualist type common in rural areas of Asia and Africa. As evident from historical records, traditional medicine has been practiced in its various forms all over the world since time immemorial and even today about 80 percent of the rural population of most developing countries on traditional medicine for maintaining health and well-being**.**

Approximately 80,000 of the World's population exclusively use plants for various healing purposes. In the industrially developed countries almost 35% of drugs contain active principles of natural origin and the consumption of medicinal plants is increasing. The practice of traditional medicine in China Is finely established. Approximately more than 5000 kinds of Chinese medicinal herbs are used medicinal plant.

About 500 species are being used here in the purpose of traditional medication. From a survey from illness approximately 14% of them go to qualified allopathic doctors, 29% approach quack and 19% contact homeopaths. The survey represents an extensive use of medicinal plants most of which are served in a crude and substandard form by the different types of traditional practitioners. But the use of the medicinal plants in crude or substandard form in sometimes hazardous for the health. For which, we should standardize our traditional use of the medicinal plants. Thus to maintain a safer traditional practice, we should make more research with our medicinal plants to determine their chemical entities and biological activities properly [4].

1.2. Pharmacological studies

1.2.1. Smilax China

Anti-inflammatory activity

The presence of Sieboldogenin in *Smilax china* shows the significant lipoxygenase inhibition (IC50: 38μM). It also exhibited significant inhibition ($p<0.05$) of carrageenan-induced hind paw edema at the doses of 10 and 50mg/kg. Computational molecular docking shows that the molecular interaction with essential amino acid residues in the catalytic site of lipoxygenase, revealing its potential binding form at molecular level [5].

Anticancer activity

The anticancer activity of eight crude extracts of *Smilax china* rhizome (SCR) against HeLa cells was assessed by MTT assay and clonogenic assay, the fraction rich in flavonoids had showngood activity against HeLa cells. A bioassay-guided separation on this extract lead to the detection of kaempferol-7-O-β-D-glucoside (KG), which belongs to flavonoid glycoside, displayed marked anticancer activity [6]**.**

Antioxidant activity

The ethyl acetate fraction of *Smilax china* showed the highest antioxidant property, correlating with the high phenolic levels, particularly catechin and epicatechin [7].

In this study, a possible presence of antioxidant activity of Smilax china root extract was investigated. Methanol extract (Me) revealed the presence of high 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging activity (IC50 7.4 μg/ml) and protective property of cell's viability. Further fractionation with various solvent extraction and assay showed high

levels of DPPH free radical scavenging activity in the ethyl acetate, butanol and water extracted fractions. In addition, V79-4 cells treated with Me of Smilax china root induced an increase of superoxide dismutase, catalase and glutathione peroxidase activities in a dose-dependent manner between 4-100 µg/ml. These results suggest that the medicinal component of the root of Smilax china extracts also contains antioxidant activity [8].

Smilax China protecting induction of lipid peroxidation

The alcoholic extract of *Smilax china* protects the induction of lipid peroxidation, induced by $FeSO_4$. This may be due to chelation of iron, conversion of $Fe^{2+}$to Fe^{3+}, by increased level of reduced glutathione, or by scavenging hydroxyl, superoxide radicals, and other oxygen molecules responsible for lipid peroxidation [9].

Testicular free radical scavenging activity

The ethanolic extract of *Smilax china* rhizomes at 100 and 200mg/kg b.w doses showed significant testicular free radical scavenging activity and restoration to normal spermatological parameters [10].

Antidiabetic activity

The methanolic extract of *Smilax china* has significant Antidiabetic activity in Alloxan induced diabetes in rats. The maximum reduction in glucose level was seen at the dose of 400mg/kg b.w.The antidiabetic activity may be due to promotion of insulin secretion by closure of potassium-ATP channels, membrane depolarization and stimulation of Calcium influx, an initial key step in insulin secretion [11].

Smilax china L., a native plant found in Asian countries, has several medicinal properties including antioxidant, anti-inflammatory, and anti-cancer effects. Although the root of the plant is commonly used as traditional herbal medicine in Korea and China, the medicinal properties of the leaves have not gained the same attention. In this study, we analyzed the antioxidant activity, α-glucosidase inhibitory effect and lipid accumulation inhibition effect of Smilax china L. leaf water extract (SCLE) and its solvent fractions. SCLE was fractionated by using a series of organic solvents, including ethylacetate (EA) and n-butanol (BuOH). The EA fraction had the highest total polyphenol content (440.20 ± 12.67 mg GAE/g) and total flavonoid content (215.14 ± 24.83 mg QE/g). The radical scavenging activity IC50 values of the EA fraction for 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2-azino-bis-(3-ethylbenzthiazoline)-6-sulfonic acid (ABTS) were 0.022 mg/mL and 0.13 mg/mL, respectively. Further, SOD-like activity and reducing power values of the EA fraction were higher than those of the other fractions. However, both the α-glucosidase and lipid accumulation inhibition assays showed that the BuOH fraction (83.35 ± 4.18% at 1 mg/mL) and water extract (11.27 ± 2.67%) were more effective than the EA fraction (64.13 ± 6.35%, and 45.66 ± 7.20%). These results provide new insights into the potential anti-diabetic and anti-obesity effects of Smilax china L. leaf [12].

Anti-obesity activity

In this study, the anti-obesity activity of Smilax china methanol extract (SCME) was evaluated using a pancreatic lipase enzyme inhibition assay, and a cell culture model system. Results indicated that, SCME effectively inhibited pancreatic lipase enzyme activity in a dose-dependent manner. Furthermore, SCME significantly suppressed insulin, dexamethasone, 3-isobutyl-1-methyl xanthine-induced adipocyte differentiation, lipid accumulation, and triglyceride contents on 3T3-L1 preadipocytes, in a dose-dependent manner. The anti-adipogenic effect was modulated by cytidine-cytidine-adenosine-adenosine-thymidine (CCAAT)/ enhancer binding proteins (C/EBP) a, C/EBPp, and the peroxisome proliferator-activated receptor y gene and protein expressions. Moreover, SCME triggered lipolysis effects dose-dependently on adipocyte. Taken together, these results provide an important new insight into SCME, indicating that it possesses anti-obesity activity through pancreatic lipase inhibition, anti-adi-pogenic and lipolysis effects. SCME may therefore be utilized as a promising source in the field of nutraceuticals. The identification of active compounds that confer the anti-obesity activities of SCME may be a logical next step [13].

Endothelial Dysfunction study

This study investigated the effects of compounds isolated from 70% ethanol (EtOH) extraction of Smilax china L. (SCE), a plant belonging to the family Smilacaceae on nicotine-induced endothelial dysfunction (ED) in human umbilical vein endothelial cells. We isolated 10 compounds from ethyl acetate (EtOAc) fraction of 70% EtOH extract of SCE and investigated their inhibitory effect on nicotine-induced ED in endothelial cells. Kaempferol, kaempferol 7-O-α-L-rhamnopyranoside, puerarin and ferulic acid showed strong inhibition of nicotine-induced vascular cell adhesion molecule (VCAM-1) expression while kaempferol, kaempferin, and caffeic acid attenuated intercellular adhesion molecule (ICAM-1) expression. Lepidoside, caffeic acid and methylsuccinic acid caused the highest up-regulated expression of endothelial nitric oxide

synthase at the protein level with caffeic acid and ferulic acid showing strong inhibitory effects on inducible nitric oxide synthase (iNOS) expression. In addition, ferulic acid and kaempferol showed inhibition against interleukin-8 (IL-8) and interleukin-1β (IL-1β) expression while ferulic acid and caffeic acid showed comparatively higher inhibition of ED associated tumor necrosis factor-α (TNF-α) expression. These results show the potential of the aforementioned compounds to reverse the toxic effects of nicotine on the endothelium [14].

Anti-metastatic activity on Human breast cancer cells

This study was to investigate the effect of a SCL ethanol extract (SCLE) on the proliferation and migration of MDA-MB-231 human breast cancer cells, as well as the expression of urokinase plasminogen activator (uPA), uPA receptor (uPAR) and tissue inhibitors of metalloproteinases (TIMPs). Cell proliferation was assessed using the Cell Counting Kit-8 and cell migration was determined by wound healing assay. Quantitative polymerase chain reaction was performed to quantify the mRNA levels of uPA, uPAR and TIMPs. SCLE markedly inhibited the proliferation and migration of MDA-MB-231 cells, and reduced the mRNA levels of the extracellular matrix (ECM) degradation-associated molecules uPA, uPAR. By contrast, SCLE significantly increased the mRNA levels of TIMP1 and TIMP2. These findings show that SCLE exerts an anti-metastatic effect on human breast cancer cells, which may involve the modulation of ECM degradation [15].

Testicular antioxidant activity and spermatological parameters

The aim of the present study was to investigate the potential benefits of ethanolic extract of *Smilax china* Linn. on testicular antioxidant activity and spermatological parameters in rats subjected to forced swimming stress. Animals of the experimental groups except vehicle control were subjected to forced swimming stress (FSS) 15 min/day for 52 days. Animals were pretreated with two doses of ethanolic extract of *Smilax china* rhizomes (100 and 200 mg/kg b.w., p.o.) for 15 days prior to the starting of FSS and were continued further for 52 days along with induction of stress. Testicular SOD, catalase and lipid peroxidation were determined. The cauda epididymis was isolated and sperms were released into saline and sperm count, viability, morphology and motility were analysed. Rats with forced swimming stress showed a significant increase in lipid peroxidation and decrease in testicular SOD, catalase, sperm count, viability and motility. Many abnormal forms of sperms were seen. Rats pretreated with ethanolic extract of *Smilax china* rhizomes at both doses significantly prevented the stress induced changes. Hence, ethanolic extract of *Smilax china* rhizomes at both doses showed good protection against testicular antioxidant activity and spermatological parameters in rats subjected to forced swimming stress [16].

Isolation of Smilax China

Bioassay-guided fractionation of an ethanol extract of *Smilax china* led to the isolation of nine phenylpropanoids including six new compounds, smilasides A–F (**1**-**6**), and three known phenylpropanoids, smiglaside E, heloniosides B, and 2‘,6‘-diacetyl-3,6-diferuloylsucrose. Structural elucidation of isolates **1**–**6** was based on spectroscopic data analysis. These new phenylpropanoids were evaluated against several human tumor cell lines [17].

Hepatoprotective activity

Smilax chinensis extract affords hepato protection against carbon tetrachloride through cell membrane stabilization and hepatic cell regeneration [18].

Anti-inflammatory and Analgesic activity

The ethyl acetate and methanolic extract of *Smilax china* showed dose dependent anti-inflammatory activity and produced reduction in the duration of licking in the late phase in analgesic activity, which was found to be statistically significant at higher concentration in acute carrageenan induced rat paw edema model and eddy’s hotplate method respectively [19].

Anti-hyperuricemic activity

Ethylacetate fraction (250 mg/kg) of *Smilax chinensis* exhibited stronger anti-hyperuricemic activity in hyperuricemic mice. Caffeic acid, resveratrol, rutin and oxyresveratrol isolated from ethylacetate fraction showed different inhibitory activities on xanthine oxidase in vitro,with the IC(50) values of 42.60, 37.53, 42.20 and 40.69μM, respectively, and exhibited competitive or mixed inhibitory actions. Moreover, it (125, 250 and 500 mg/kg) markedly reversed the serum uric acid level ($p<0.05$, $p<0.01$ and $p<0.001$, respectively), fractional excretion of urate ($p<0.05$, $p<0.01$ and $p<0.01$, respectively) and blood urea nitrogen ($p<0.05$, $p<0.01$ and $p<0.01$, respectively) to their normalstates, and prevented the renal damage against tubulointerstitial pathologies in hyperuricemic rats [20].

1.3. Smilax zeylanica

Antidiabetic activity

The continuous treatment of*Smilax zeylanica* leaf extract for a period of 15 days produced a significant decrease in blood glucose level instreptozotocin induced diabetic rats which is comparable to that of standard drug Glibenclamide which is used in treatment of type II diabetes mellitus. The standard drug Glibenclamide stimulates insulin secretion from beta cells of islets of langerhans. From the study, it is suggested that the possible mechanism by which the plant extract decreases the blood glucose level may be by potentiation of insulin effect either by increase in pancreatic secretion of insulin from beta cells of islets of langerhans or by increase in peripheral glucose uptake [21].

Anthelmintic activity

The anthelmintic activity of petroleum ether, benzene, chloroform and methanolic extracts of *Smilax zeylanica* on Indian adult earthworm (Pheretimaposthuma) has been evaluated and reported .Petroleum ether and chloroform extract showed potent anthelmentic activity than the standard drug, albendazole. The benzene extract is inactive at low concentration but have dose dependent action on paralysis and death at high dose. The methanolic extract showed dose dependent anthelmenticavtivity. Paralytic condition was achieved faster by petroleum ether extract even at 20mg/ml whereas death of test organism was early with methanolic extract. The result signifies that steroidal components would be active for achievement of paralytic condition, whereas flavanoids and polyphenolic compounds would somehow responsible for the death of Pheretima posthuma [22].

Antioxidant activity of leaves of Smilax zeylanica

The in-vitro and in-vivo antioxidant activity of methanolic and aqueous extractof *Smilax zeylanica* leaves has been evaluated and reported. In-vitro models used for evaluation were DPPH, hydrogen peroxide, ABTS, nitric oxide and superoxides free radical whereas that for in-vivo models were catalase activity, peroxidase activity, glutathione reductase activity and SOD activity on CCL4 induced hepatotoxic system. The extracts from leaves of *Smilax zeylanica* exhibited strong antioxidant and free radical scavenging effects in different in vitro and in vivo systems. In vitro antioxidant scavenging activities were expressed in terms of IC50, which is the concentration of sample required to cause 50% inhibition of free radicals. Both extracts of *Smilax zeylanica* showed scavenging effects to different extents in the different models studied. The scavenging effect may be due to the hydrogen donating ability of *Smilax zeylanica*. *Smilax zeylanica* leaf extracts are relatively non toxic which renders them suitable as potential therapeutic agents [23].

In-vivo Antioxidant effect of roots and rhizomes of Smilax zeylanica

This study is to revealed that the antioxidant property of *Smilax zeylanica.* Hepatotoxicity was induced in Wistar albino rats by administration of CCl_4 (0.5 ml/kg/day p.o. for 7 days). Methanol extract of *S. zeylanica* roots and rhizomes (SZRM) was administered to the experimental animals at doses 200, 400 and 600 mg/kg/day, p.o. for 7 days. Antioxidant effect was assessed by the estimation of hepatic levels of SOD, catalase, peroxidase, reduced glutathione, total proteins and malondialdehyde. In methanol extract-treated animals, the toxic effect of CCl_4 was controlled by restoration of the levels of hepatic antioxidant enzymes as compared to the positive control and standard drug silymarin-treated groups. The methanol extract at different doses exhibited significant increase in SOD, peroxidase, glutathione and proteins. The level of malondialdehyde was also significantly reduced. The study revealed that the *Smilax zeylanica* possesses strong antioxidant property [24].

Hepatoprotective activity

This study evaluated the hepatoprotective effect of *Smilax zeylanica* against paracetamol induced hepatotoxicity in Wistar rats. The protective effects of the methanol extract (200 and 400 mg/kg) of root and rhizome of *Smilax zeylanica* were studied on paracetamol induced (1 g/kg) hepatic damage in Wistar rats by estimating the serum levels of AST, ALT, alkaline phosphatase (ALP), total proteins, total bilirubin and albumin. Sections of liver were observed for histopathological changes in liver architecture. Rats were protected from the hepatotoxic action of paracetamol as evidenced by the significant reduction in the elevated serum levels of ALT ($P<0.001$), AST ($P< 0.01$, $P< 0.001$), ALP ($P<0.05$, $P< 0.001$), total bilirubin ($P< 0.05$) and an increased level of total protein ($P< 0.05$) and albumin ($P< 0.05$, $P<0.01$) with a significant reduction in liver weight ($P<0.001$), when compared with the paracetamol control. Silymarin (100 mg/kg) was used as the standard. The biochemical observations were supplemented by the histopathological studies on the liver sections of different groups. The methanol extract of *Smilax zeylanica* was found to alter the damage caused to hepatocytes by paracetamol and prevent the leakage of vital serum markers, which confirmed the hepatoprotective effect of this plant [25].

In-vitro antioxidant activity of roots and rhizomes of Smilax zeylanica

The present study was conducted to investigate the antioxidant property of roots and rhizomes of Smilax zeylanica L. by in vitro methods. Methanol and aqueous extracts of the drug were evaluated for invitro antioxidant activity. Methanol extract showed potential scavenging effect against DPPH, hydrogen peroxide and ABTS free radicals. HPTLC studies were also performed on both extracts. The study revealed that the extracts of S.zeylanica exhibited strong antioxidant effect in different invitro systems [26].

1.4. PHYTOCHEMICAL STUDIES

Smilax china

The phytochemical activity of the methanol extract extract of root tuber of Smilax china was studied to fix the parameters of pharmacogostical standards. These created an interest to test the possible phytochemical activity of the plant. In the screening process of Smilax china indicate the presence of fat, Saponins, glucosides, gum, starch, flavonoids, tannins and alkaloids [3].

Phytochemical screening of Smilax china extracts revealed the presence of different phytochemical constituents like steroids, terpenoids,flavanoids,alkaloids, glycosides, tannins, carbohydrates, oils and amino acids [27].

Table -1: Qualitative chemical analysis of phytoconstituents of the root tuber powder and various extracts of Smilax china[25].

Group Test	Name of the test	Observation of Extract					
		Acetone	Ethanolic	Methanolic	Aqueous	Chloroform	N - Hexane
Carbohydrate & Gums	Molish Test	+	+	+	+	-	+
Reducing Sugar	Fehling's solution test	+	+	+	+	-	-
	Benedicts's Test	+	+	+	+	-	-
Alkaloids	Mayer's Test	+	+	+	-	+	+
	Dragendroff's Test	+	-	-	+	+	+
	Wagner's Test	+	+	+	-	+	+
	Hagner's Test	+	-	+	+	+	+
Steroides	Salkowski Reaction	+	+	+	+	+	+
	Libermann-Burchared Reaction	+	+	+	+	+	+
Glycosides	Salkowski Reaction	-	-	+	-	-	+
	Libermann-Burchared Reaction	-	-	+	-	-	+
Tanins	Ferric chloride Test	-	-	+	-	+	-
	Potassium Chloride Test	-	-	+	-	+	-
	Keller-Kiliani Test	-	-	+	-	+	-
Flavonoids	Hydrochloric Acid Test	+	-	+	-	-	-
Saponins	Foam Test	-	+	+	-	-	-

+ = present , - = Absent

Smilax zeylanica

The preliminary phytochemical analysis of the rhizome and root of *S. zeylanica* revealed presence of glycosides, saponins, phytosterols and tannins. HPTLC fingerprinting detected the presence of diosgenin, a biomarker compound [28].

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