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Research Paper

Ethno medicinal, phytochemical and pharmacological aspects of solanum incanum (lin.)

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Abstract

Solanum incanum is used in Africa and other parts of world as a folklore remedy for various ailments that include; sore throat, angina, stomach ache, ear inflammation, snake bites, wounds, liver disorders, skin ailments (ringworm), warts, inflammatory conditions, painful periods and fever.
Phytochemical studies of this herb indicate that it contains substances such as steroidal alkaloids, glyco-alkaloids, antioxidants (flavonoids and chlorogenics), saponins and even carcinogenic substances. The herbal extract posses' antinociceptive, antipyretic, anti-spasmolytic, orexic, anorexic, hypoglycemic, antimicrobial, anti-schistosomal, anti-fungal, and anti-cancer activity.
The herb is therefore likely to be a major source of novel, affordable and effective therapeutic substances against myriad ailments afflicting people in the world.
This review explores the phyto-pharmacological effects of the S. incanum and compiles vital information that may assist researchers on what is known about this herb and gaps for further investigation.

Keywords: *Anticancer, Antimicrobial, Antinociceptive, Antipyretic, Solanum Incanum.*

1. Introduction

Solanum incanum or Sodom/bitter apple (English), entulele (Maasai), mtula (Swahili) is a perennial, wild shrub like herb that belongs to Solanaceae family which grows in many regions of Africa, Middle East and Far East Asia. It is an erect or spreading perennial shrub with leaves and stem occasionally having small prickles. The fruits are small berries of 2-3 cm in diameter and yellowish orange or brown in color when ripe (Matu 2008). Controversy surrounds the name of this plant because it was given different descriptions by different authors that vary widely (Anaso & Ouzo 1990). In Africa the herb is used as a folklore remedy for sore throat, angina, stomach-ache, colic, headache (Kokwaro 1993, Dold & Cocks 2000) and in wounds (Bussmann et al. 2006). Other uses include; relieve of painful menstruation, liver problems and pain caused by onchocerciasis, pleurisy, pneumonia and rheumatism. The plant parts are also widely used to alleviate skin problems, such as infections, whitlow, ringworm, burns, sores, rashes, wounds, warts, carbuncles, ulcers, inflammations and benign tumors. In West Africa, leaves are eaten or added to soup to improve flavor, while fruits are used as vegetables. Alternatively, the roots are chewed or its infusions applied externally on scarifications. Similarly, decoctions derived from leaves, roots and fruits are either gargled or drunk. Leaf parts are also used for washing painful areas, while in some cases they are burnt and the ash mixed with fat for use as an ointment. Conditions in which the various plant parts are used by different African communities include, pain relieve in toothache and as a cure for snake bites and sexually transmitted disease. It is also used as an ingredient of arrow poison, as spice to improve flavor and as well as in curdling milk or in cheese making. In Ethiopia it is used in leather tanning and soap making (Matu 2008).

2. Photochemistry

Table1: Shows some phytochemicals isolated from S. incanum

S/No.	Chemical Name	Chemical formula
1.	Incanumine (Lin *et al*. 1990)	$C_{49}H_{79}NO_{19}$
2.	Solasodine (Lin *et al*. 1990)	$C_{27}H_{43}NO_2$
3.	Carpesterol (Lin *et al*. 1990)	$C_{37}H_{54}O_4$
4.	β-Sitosterol (Lin *et al*. 1990)	$C_{29}H_{50}O$
5.	Stigmasterol(Lin *et al*.1990)	$C_{35}H_{58}O_6$
6.	Khasianine (Lin *et al*. 1990)	$C_{39}H_{63}NO_{11}$
7.	Adenosine (Yun-lian *et al*. 2000)	$C_{10}H_{13}N_5O_4$
8.	Kaempferol 3-O-b-D glucopyranosyl (1®2)-b-D-glucopyranoside (Yun-lian *et al*. 2000)	$C_{27}H_{30}O_{16}$
9.	Quercetin3-O-b-D-glucopyranosyl (1®2)-b-D-glucopyranoside (Yun-lian *et al*. 2000)	
10.	Kaempferol (Yun-lian *et al*. 2000)	$C_{15}H_{10}O_6$
11.	Chlorogenic acid (Yun-lian *et al*. 2000)	$C_{16}H_{18}O_9$
12.	Benzyl O-b-D-xylopyranosyl (1®2)-b-D-glucopyranoside (Yun-lian *et al*. 2000)	$C_{58}H_{94}O_{26}$
13.	Quercetin (Yun-lian *et al*. 2000)	$C_{15}H_{10}O_7$
14.	Astragalin (Yun-lian *et al*. 2000)	$C_{21}H_{20}O_{11}$
15.	Isoquercitrin (Yun-lian *et al*. 2000)	$C_{21}H_{20}O_{12}$
16.	Protocatechuic acid (Yun-lian *et al*. 2000)	$C_7H_6O_4$

17.	trans-p-coumaric acid (Yun-lian *et al*. 2000)	$C_9H_8O_3$
18.	Luteolin 7-O-b-D-glucopyranoside (Yun-lian *et al*. 2000)	$C_{21}H_{20}O_{11}$
19.	Isorhamnetin 3-O-b-D-glucopyranoside (Yun-lian *et al*. 2000)	$C_{22}H_{22}O_{12}$
20.	Caffeic acid (Yun-lian *et al*. 2000)	$C_9H_8O_4$
21.	Baicalin (Yun-lian *et al*. 2000)	$C_{21}H_{18}O_{11}$
22.	Kaempferol 3-O-(6²¢-O-2,5-dihydroxycinnamoyl)-b-D-glucopyranosyl (1®2) b- D glucopyranoside (Yun-lian *et al*. 2000)	$C_{36}H_{36}O_{19}$
23.	Solasonine (Eltayeb *et al*. 1997)	$C_{45}H_{73}NO_{16}$
24.	Solamargine (Eltayeb *et al*. 1997)	$C_{45}H_{73}NO_{15}$
25.	Diosgenin(Matu 2008)	$C_{27}H_{42}O_3$
26.	Yamogenin (Matu 2008)	$C_{27}H_{42}O_3$
27.	Dimethylnitrosamine (Matu 2008)	$C_2H_6N_2O$
28.	Vitamin B_2 (Auta &Ali 2011)	$C_{17}H_{20}N_4O_6$
29.	Vitamin C (Auta & Ali 2011)	$C_6H_8O_6$

Table 2: Shows a list of some minerals found in S. incanum and their respective concentrations in ashes.

S/No.	Name of the ions	Concentration parts per million (pmm)
1.	Sodium (Auta & Ali 2011)	3.81
2.	Potassium (Auta & Ali 2011)	1.58
3.	Zinc (Auta & Ali 2011)	3.91
4.	Copper (Auta &Ali 2011)	2.10
5.	Cadmium (Auta & Ali 2011)	1.19
6.	Chromium (Auta & Ali 2011)	1.60

3. Pharmacological activity

3.1. General Uses

Solasodine is used commercially as precursors for the production of steroidal compounds for medicinal use particularly as contraceptives (Matu 2008).

3.2. Anti-microbial and antifungal effects

Previous reports indicate that the water soluble crystals derived from unripe fruits of S. incanum exhibited marked broad spectrum antibacterial effect on several gram positive and gram negative bacteria such as Streptococcus pyogenes, Staphylococcus aureus, Clostridium perfringens, Bacillus anthracis, Brucella arbutus and Salmonella species. It also inhibited a number of fungi like Microsporum species, Trichophyton tonsurans, Cryptococcus neoformans, Candida albicans etc. Exposure of these fungi to Solanum extract distorted the hyphae and inhibited sporulation which may suggest that either S. incanum extract inhibited a vital cellular pathway or act as an anti-metabolite (Mbaya & Muhammed 1976). Ethanol extract of S. incanum fruit exhibited potent antibacterial effect (Alamri & Moustafa 2012), while leaf extracts showed antimicrobial activity against the Escherichia coli (Britto & Senthinkumar 2001), Streptococcus pyogenes, Staphylococcus aureus, and Pseudomonas aeuruginosa (Taye et al. 2011). In a study to investigate the herbs anti-schistosomal effects using methanol and aqueous extracts, the former took the shortest time to kill cercariae compared to aqueous group (Muchika et al. 2011).

3.3. Antipyretic effects

In a study conducted to evaluate the antipyretic effect of the herb, an intraperitonial injection of 50 and 100 mg/kg doses of diclomethane/methanol root extract of the S. incanum exhibited significant antipyretic effect on endotoxic induced fever in rats. The anti-pyressis was comparable to that of 100 mg/kg of aspirin (Mwonjoria et al. 2011). On this basis, it is highly probable that the plant contains compound(s) with antipyretic effect.

3.4. Antinociceptive effects

Solanum incanum root extract was also found to possess analgesic effect. In this study, CBA mice were injected with 100, and 200 mg/kg of the diclomethane/methanol extract of the S. incanum root. In the tail flick test, the 100 and 200 mg/kg doses of the extract exhibited significant antinociceptive effect that was comparable to that of aspirin. Similar results were obtained in the hot plate test (Mwonjoria et al. 2011). Both tail flick and hotplate test responses are integrated in the centrally nervous system. The tail flick response is integrated at the spinal cord level while integrated response of the hot plate occurs in a supra-spinal region (Le Bars et al. 2001). Therefore, the S. incanum extract may have exerted the antinociceptive effect via both spinal and supra-spinal integrated mechanisms.

3.5. Hypoglycemic and an-orexic effects

In an experiment to investigate the effects of S. incanum root and fruit extracts on blood sugar, the fruit extract lowered the blood glucose levels and appetite in rats. The sugar lowering effects were comparable to those of metformin or glibenclaride. However, the root extract increased the food intake in addition to decreasing the blood glucose levels. The rats also developed diarrhea. In the two cases, the insulin level remained unaffected implying that the observed hypoglycemia may have been due to either anorexia or reduction in glucose absorption (Musabayane et al. 2006). The juice obtained by chewing or squeezing S. incanum leaves significantly reduced the postprandial glucose surge in normoglycemic humans (Uchenna et al. 2009)

3.6. Insect repellant properties

Chlorogenic acid has antioxidant and insect repellent properties and retards growth and development when ingested by insects (Matu 2008).

3.7. Spasmolytic effects

The spasmolytic activity of aqueous root extract of S. incanum was assessed on contractions of isolated guinea pig ileum, induced by acetylcholine, and compared with the effect of atropine a non-specific anti -cholinergic drug. The aqueous root extract of S. incanum inhibited the response to acetylcholine in a concentration-dependent manner similar to atropine. The extract inhibited charcoal travel in mice intestine by 36.28, 51.45, 52.93 and 38.53 percent in doses of 50, 100, 200 and 400 mg/kg body weight respectively (Assefa et al. 2006).

3.8. Anticancer effects

Solanum species have been used in many parts of the world for treatment of tumors for a long time. One of the earliest reports on anti-tumor effect of the species was by Kupchan and others who demonstrated that the crude extract of S. dulcamara inhibited sarcoma in mice (Kupchan et al. 1965). Solamargine, an alkaloid from S. incanum has been shown to disrupt phosphatidylcholine or cholesterol liposomes (Roddick et al. 1990) and was also reported to possess a potent cytotoxicity to human hepatocytes (Hep3B) and normal skin fibroblast by apoptosis through the up-regulation of tumor necrosis factor receptor-1 (TNFR-1) expression (Hsu et al. 1996). Similarly, solamargine triggered apoptosis in human hepatoma cells besides elevating the level of TNFR-1 and 2 on the hepatoma cells. These effects were neutralized with TNFR-1and 2 specific antibodies (Kuo et al. 2000) Solamargine was found to induce the HA549 lung adenocarcinoma cell apoptosis. In this study, the compound caused morphological changes in chromatin condensation, DNA fragmentation and sub-G (1) peak in a DNA histogram of A549n cells. It

also elevated the TNFR-1 and 2 expression thereby overcoming the resistance to TNF α and β besides, sensitizing the tumor cells through TNFRs and mitochondrial mediated pathways which may indicate that it has a potential against TNFs and Cisplatin resistance lung cancer cells (Chia-Hua et al. 2004). In addition the alkaloid induced several apoptotic processes such as release of cytochrome C from the mitochondria, down regulation of anti-apoptotic Bcl2 and Bcc-xL, it also increased the levels of caspace-3 activity and DNA fragmentation (Zhou et al. 2008). Another study involving the use of cell lines indicated that solamargine modulated TNFR and Tumor necrotic factor receptor-1 associated death domain protein / Fas-associated protein with death domain (TRADD/FADD) signaling pathway and enhanced binding of TNF α and β to lung cancers cells. Additionally, it triggered the intrinsic resistant cancer cells to become susceptible to TNF α & β. Other effects included enhanced release of cytochrome c, down regulation of anti-apoptotic Bcl-2 and Bcl-xL, elevation of caspasce-3 activity and DNA fragmentation (Li-Feng et al. 2004). The drug resistance and poor prognosis encountered in breast cancer correlates with over expression of Human epidermal growth factor (HER2/neu) receptor expression (Ross & Fletcher, 1998 and Weiya et al. 2004). However, solamargine modulated the HER2/neu gene of HER2/neu high expressing human cell line ZR-72-1. It also decreased the number of HER2/neu receptors in highly HER2/neu expressing breast cancer cells. A combination of solamargine with methotrexate, 5-flurouracil or cisplatin increased the susceptibility of breast cancer cells expressing high levels of HER2/neu (Shiu et al. 2008). In breast cancer, solamargine was found to induce apoptosis by up regulating the expression of external death receptors such as TNFR-1, Fas, TNFR-1- associated death domain (FADD) and activated mitochondrial mediated death pathway by enhancing the intrinsic ratio of Bax to Bcl-2. The latter effect involved up regulation of Bax and down regulation of Bcl-2 and Bcl-xL expression resulting in release of mitochondrial cytochrome-C and activation of caspace-9 and -3 in the cell. Cisplastin anticancer cells apoptotic activity is associated with caspace -8/-3 and Bax /cytochrome c pathways. However, resistance to Cisplastin correlates with Bcl-2 and Bcl-xL over expression (Michaud et al. 2009), which is suppressed by solamargine (Shiu et al. 2007).

Solamargine rapidly induce acute cell injury and bursting tumor cells by damaging the cell membrane in Human K562 leukemia and squamous cell carcinoma KB cells. This cytotoxic effect did not correlate with the expression of multidrug resistance and was triggered rapidly by the 50μg dose of the alkaloid. It also caused a rapid absorption of propidium iodide, release of lactate dehydrogenase and leakage of cytoplasmic contents which indicates that the cytotoxicity might have involved plasma membrane disruption. The alkaloid also rapidly induced membrane blebbing which could not be prevented by chelating either the intracellular or extracellular calcium ions though it was inhibited by some polyethylene glycols. It also disrupted the cytoplasmic actin and microtubules (Sun et al. 2011).The alkaloid also killed the MDR sub-lines namely the human myelogenous leukemia K562 cell line and its multidrug - resistant counterpart K562/A02, squamous cell carcinoma KB parental cell lines the VCR-selected MDR KB/VCR sub-line, the human NSCLC H460 cells and its multidrug- resistant counterpart H460/paclitaxel (Taxol) (Xia et al. 2011). Solamargine is also shown to induce pro-apoptotic effects in MDR K562/A02 cells lines by down regulating MDR1 mRNA and decreasing the mRNA expression of P-glycoprotein and actin in the cells (Xia et al. 2011, Ding et al. 2012). In another study, Solamargine obtained from S. nigrum induced apoptosis in Human squamous cell carcinoma cell lines by up-regulating the TNFRs, Fas and some of the adaptors associated with the signaling cascade. In addition, it also activated the mitochondrial apoptotic pathway and cleared the papillomas in hairless mice within 10 weeks (Chia-Hua et al. 2004). Flavonoids are a potent antioxidants and free radical scavengers which prevent oxidative cell damage (Salah et al. 1995). The herb also contains vitamin B_2, C (a major water-soluble anti-oxidant in extracellular fluid) and vitamin E a major lipid soluble anti-oxidant that prevents peroxidation (Auta & Ali 2011).

3.9. Toxicity

The highest concentration of the alkaloid is found in the smallest leaves of S. incanum while the roots and stem were initially shown to have similar concentration of the alkaloid (Eltayeb et al. 1997). The fruits contain dimethylnitrosamine, a potent carcinogen that may be associated with high incidence of esophageal cancer in areas of Africa where the fruit sap is used to curdle milk. Similarly, extracts of the fruits has been found to cause skin cancer in animals. The unripe fruits of S. incanum were found to exhibited toxic effects in goats (Thaiya et al. 2010).However, oral administration of up to 15,000 mg/kg doses of the extract to mice did not show signs of conventional toxicity (Assefa et al. 2006)

4. Conclusion

S. incanum has been used as folklore remedy for various ailments afflicting people in various parts of the world for a long time. However, research interest to evaluate its therapeutic potential has developed recently perhaps on realization that this herb may contain novel chemicals that exhibit a wide range of pharmacological effects. The anticancer effect of this herb is currently under intensive research with much interest focusing on Solamargine. With rising cases of cancer mortality globally, more research is required to establish the mechanism through which this phytochemicals induces apoptosis and its potential in developing a safe and effective drug for various types of cancer. Nevertheless, with the exception of anticancer effects, little or no attempt has been made to elucidate the modes of action of a wide range of pharmacological effects associated with this herb. Therefore, more studies are required on the alkaloids and other phytochemicals of this herb.

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