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Research article

Carpesterol - A novel phytosterol obtained from the plants of the family solanaceae with evaluation of antineoplastic activity

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ABSTRACT

Solanaceae family commonly known as 'Black nightshade' are extensively used in traditional medicine in India and other parts of the world to cure liver disorders, chronic skin ailments (psoriasis and ringworm), inflammatory conditions, painful periods, fevers, diarrhea, eye diseases, hydrophobia, etc. It has been found that Solanum nigrum contains alkaloid, steroid glycoalkaloids, steroidal saponins and glycoprotein, exhibiting anti-tumor activity.

In Indian traditional medicine, the plant is used as a hepatoprotective agent. In this review, we have explored the phyto-pharmacological properties of the Solanaceae family plant and compiled its vast pharmacological applications to comprehend and synthesize the subject of its potential image of multipurpose medicinal agent. The review covers the simple sterols, the steroidal sapogenins and the steroidal alkaloids found in these plants, and their metabolism as well as biosynthesis is considered. Solanocarpidine and a phyto-sterol known as Carpesterol are also present. Potassium nitrate, a fatty acid, a resinous and phenolic substance, diosgenin and sitosterol are present. Seed oil contains Carpesterol. The presence of Solanine has been reported in roots, leaves and fruits. Air dried leaves contain 0.32 % of total alkaloids. Diosgenin, lanosterol, sitosterol. Solasonnine, solamargine and solasidine have been isolated from the plant. A glycoalkaloids, solasonine on hydrolysis afforded solasodine, sugars, glucose, galactose and rhamnose.Innovative research efforts to define the advantage of traditional system of medicine with respect to their safety and efficacy could result in a better utilization of these complementary systems of medicine. The roots and fruits are used for medicinal purpose. The herb is useful both internally as well as externally. The apoptotic effects and the amount of DNA fragmentation increased in a dose dependant manner after the treatment with the protein. Authors believe this glycoprotein as a natural anticancer agent due to its potential to induce apoptosis in the HTC-29 cell. Its antitumor property can be attributed to its immunomodulatory ability, which alters the host's immune response.

Keywords: Carpesterol, Solanum nigrum, Solanum indicum, Solanaceae, antitumor activity.

INTRODUCTION

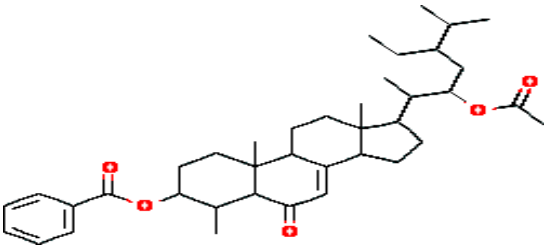
The plant Solanum nigrum Linn (Solanaceae) commonly called as black night shade in English, Makoi in Hindi, Kachchipandu in Telugu, Munatakali in Tamil, Piludi in Gujarati & Kamuni in Marathi. It is an erect, divaricately branched, unarmed, suffrutescent annual herb. Leaves ovate or oblong, sinuate-toothed or lobed, glabrous; flowers 3-8 in extra-axcillary drooping subumbellate cymes; fruits purplish black or reddish berries; seeds many, discoid, yellow, minutely. Herbal medicines are being used by about 80% of the world population primarily in the developing countries for primary health care. They have stood the test of time for their safety, efficacy, cultural acceptability and lesser side effects. The chemical constituents present in them are a part of the physiological functions of living flora and hence they are believed to have better compatibility with the human body .

The current status of health care system in adequacies of

synthetic drugs is likely to be more glaring in the coming years. It has been reported that there has been an alarming increase in number of diseases and disorders caused by synthetic drugs prompting a switch over to traditional herbal medicines. India has over 1, 08,276 species of bacteria, fungi, animals and plants already identified and described. Out of these about 84% species constitutes fungi (21.2%), flowering plants (13.9%) and insects (49.3%). Natural products, including plants, animals and minerals have been the basis of treatment of human diseases. The current accepted modern medicine or allopathy has gradually developed over the years by scientific and observational efforts of scientists. However, the basis of its development remains rooted in traditional medicine and therapies. Selection of scientific and systematic approach for the biological evaluation of plant products based on their use in the traditional systems of medicine forms the basis for an ideal approach in the development of new drugs from plants. Ancient literature also mentions herbal medicines for age-related diseases namely memory loss, osteoporosis, diabetic wounds, immune and liver disorders, etc. for which no modern medicine or only palliative therapy is available [1].

Carpesterol

Chemistry, Pharmacology and biogenesis



Molecular Formula: $C_{39}H_{56}O_5$ English: Carpesterol acetate

IUPAC:[17-(3-acetyloxy-5-ethyl-6-methylheptan-2- yl)-4,10,13-trimethyl-6-oxo- 1,2,3,4,5,9,11,12,14,15,16,17-

Dodecahydrocyclopenta [a] phenanthren-3- yl] benzoate

Molecular Weight: 604.859 g/mol Exact Mass: 604.413 g/mol Monoisotopic Mass: 604.413 g/mol Rf value: 0.462.

IR Data: The sharp peak at 1060, 1239 cm-1 indicated presence of C-O-C (ether).

UV: The isolated compound solasodine in Methanol showed absorbance peak at 210 nm [2].

Uses of Carpesterol

The juice of the herb or an ointment prepared from it is externally applied to cure certain skin problems and tumors. A decoction of the stalk, leaves, and roots of black nightshade is beneficial for wounds and cancerous sores. Freshly prepared extract of the plant is effective in treating cirrhosis of the liver and also works as an antidote to poisoning by opium.

Therapeutic Properties

Anti-seizure, Anti-poison, Anti-inflammatory, Anti- pyretic, Antiproliferative, Phytoremediation, Wound healer, Hepatoprotective and Antioxidant [3].

Carpesterol bearing Solanaceae Plants

Figure 1: Solanum nigrum

Figure 2: Solanum indicum

Figure 3: Solanum melongena

Common name

Black nightshade, Black-berry night shade, Nightshade, Poison berry

Malayalam: Mulaku-thakkali Telugu: Kasaka

Marathi: Laghukavali Urdu: Makoya

Family: *Solanaceae*

Black nightshade is a plant, an annual weed that grows up to 60cm tall, is branched and usually erect, growing wild in wastelands and crop fields. Alternate leaves are ovate deep green with an indented margin and acuminate at the tip. Flowers are white with yellow colored centre. The berries are green at early stage and turn to orange or black when ripened [4].

Medicinal Uses

Black nightshade is used for skin diseases, rheumatism, and gout. Juice of the herb is given in chronic enlargement of the liver. It can cure ear, and eye diseases. It is sometimes prescribed to "remove the

effect of old age." By eating the berries of *S. nigrum* the following symptoms are observed: a feeling of sickness, vomiting, and stomachache, and intense thirst, pupils dilated with impaired vision, headache, giddiness, delirium, purging, convulsions and sleep ending in cotna. Solanine in doses of 200-400 mg can cause similar picture. The alkaloid is teratogenic [4].

Phytochemistry

This led to the isolation of glycoalkaloids, solasonine Solanacarpine, Solanocarpidine, Carpesterol. From the non alkaloidal portion, a glycoside of β- sitosterol with galactose as a sugar moiety has been obtained along with two phenolic substances, which could be identified as methyl caffeate and caffeic acid. The fruits are reported to contain several steroidal alkaloids like solanacarpine and Solamargine. Other constituents like caffeic acid coumarins like aesculetin and aesculin, steroids Carpesterol, diosgenin, campesterol, Daucosterol and triterpenes like cycloartenol and cycloartenol were reported from the fruits. Steroidal glycoalkaloids are naturally occurring, secondary plant metabolites that are formed in a number of foods including potatoes, tomatoes, and eggplants. Although they are reported to be potentially toxic, glycoalkaloids and hydrolysis products without the carbohydrate side chain (aglycons) also have beneficial effects. Carpesterol acetate is obtained from the plant of *Solanaceae* family.

Evaluation of New Biological Activity of Carpesterol

The study was aimed to evaluation of the anticancer activity of the fruits of Solanum Nigrum on the *HeLa* cell line. The fruits of *Solanum Nigrum* methanolic extract were tested for its inhibitory effect on *HeLa* Cell Line. The percentage viability of the cell line was carried out by using Trypan blue dye exclusion method. The cytotoxicity of Solanum Nigrum on *HeLa* cell was evaluated by the SRB assay and MTT assay. *Solanum Nigrum* methanolic extract has significant cytotoxicity effect on *HeLa* Cell Line in concentration range between 10 mg/ml to 0.0196 mg/ml by using SRB assay and study also showed that inhibitory action on *HeLa* cell line in concentration range between 10 mg/ml to 0.0196 mg/ml by using MTT assay. IC50 value and R2 value of *Solanum Nigrum* on *HeLa* cell and *Vero* cell were 847.8 and 0.8724, 908.8 and 0.1017 respectively by SRB assay. IC50 value and R2 value of Solanum [5].

Nigrum on *HeLa* cell was 265.0 and 0.9496 respectively by MTT assay. IC50 value of Solanum Nigrum on *Vero* cell was 6.862 by MTT assay. R2 value of Solanum Nigrum was not found by MTT assay. From the performed assay, methanolic extract of these drug shows greater activity on *HeLa* cell line and little activity on *Vero* cell line and that mean Solanum Nigrum can be used as anticancer activity 11).

Plants have served as an important source of potent anticancer drugs for decades. The search for anti-cancer drugs from plant sources started in the 1950s, with the discovery of the vinca alkaloids (vinblastine and vincristine) and podophyllotoxin. This search spanned over four decades till 1990s, when taxanes and camptothecins were launched as anti-cancer drugs. The success of plant based molecules still inspires researchers for searching newer anticancer agents from plants. Steroidal compounds are important class of secondary metabolites, which have been reported to exhibit wide range of pharmacological properties that include hypocholesterolemic, antioxidant and antidiabetic etc. However of particular interest is the apoptosis inducing activity of steroidal compounds. Amongst the steroidal class of compounds, diosgenin has been previously reported to induce apoptosis in different human cancer cell lines. Thus, in order to identify an effective apoptosis inducing agents, we have tested several steroidal compounds, structurally related to diosgenin (including diosgenin) which were isolated from two Indian medicinal plants namely *Solanum nigrum.*

Effects of Herbal Drugs on Human Health

Herbal Medicines are readily available in the market from health food stores without prescriptions and are widely used in India, China, and USA and all over the world. According to recent survey the majority of people who use herbal medicines do not inform their physicians about their consumptions that can cause abnormal test results and confusion in proper diagnosis [6].

Drug herb interactions can results in unexpected concentration of therapeutic drug. Several herbal products interfere with immunoassays used for monitoring the concentrations of therapeutic drugs. Herbal medicines can also cause undesired effects. Therefore, the common belief that anything natural is safe is not correct. This review summarizes abnormal test results associated with use of herbal medicine, as well as interactions between modern western medicines and herbal Products.

The US food and drug administration mandates that only medicine have to be proven to be safe before being released into market. Herbal products do not fall under the category of drugs as long as they are not marketed for the preventions of any diseases, its use is much more because of their easy accessibility, no expert consultation required, are considered safe to use and also because primary health care services fall short of peoples' need both in qualitative and quantitative terms. We should make all these easily marketed ayurvedic, and other herbal medicines FDA approved and increase public awareness about pros and cons of their uses. The common belief that anything natural is safe is not correct. In United Kingdom any product that is not granted a license as a medical product by Medicine Control Agency, is treated as food, and no health claim or medical advice can be given on the label. Labeling of herbal products may not actually reflect the content and adverse events or interactions attributed to specific herb may be related to misidentification of plant. Many commonly used herbal medicine in their irregular, high doses or with other medications in long term are toxic. Toxic effects of herbal medicines range from allergic reactions to cardiovascular, hepatic, renal, neurological and dermatologic toxic effects.

The manufacturers of these products are not required to submit proof of safety and efficacy to the U.S. Food and Drug Administration

before marketing. For this reason, the adverse effects and drug interactions associated with herbal remedies are largely unknown. Ginkgo biloba extract, advertised as improving cognitive functioning, has been reported to cause spontaneous bleeding, and it may interact with anticoagulants and antiplatelet agents. The herb is useful both internally as well as externally. Natural sources such as Indian medicinal plants and herbal drugs derived from them require special attention. Antioxidants neutralize the toxic and 'volatile' free radicals. The humans get exposed to adverse physiochemical, environmental or pathological agents this delicately maintained balance is shifted in favors of pro-oxidants resulting in oxidative stress [7, 8].

CONCLUSION

Carpesterol, a novel Phytosterol obtained from different plants of the family Solanaceae possesses several pharmacological activities not previously found within the group have been discovered. The most notable of these new properties are anti- inflammatory, anti-hyperlipidemic activity, and digitalis like activity, coronary dilatory activity and central nervous system activity. At the same time some new biological activities are also being mentioned i.e. with androgenic, estrogenic, progestesional and anti-tumor activity. In recent advantage related to anticancer drug research, it is an established fact that cox-1/cox-2 have significant role in apoptosis. Cox-2 inhibition of leucotriens on human erythroleukemia (HEL) and human acute monocytic leukemia (Mono Mac 6) cell lines clearly indicated that the compound having cox-2 inhibition can be co-related in anti-cancer activity. Carpesterol by virtue of its structure (basic steroidal nucleus) possesses all the activities as mentioned under steroids. More over attachment group further contribute in anti-fertility; cancer of human reproductive system, HIV mediated cancers like other Phytosterol for e.g. β-sitosterol is also Phytosterol.

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