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THERAPEUTIC POTENTIAL OF *SOLANUM NIGRUM* (*MAKO*) IN TRADITIONAL AND MODERN MEDICINE

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Abstract

Solanum nigrum Linn, commonly known as Black Nightshade in English, *Mako* in Urdu, *Manittakkali* in Tamil, and *Kalukammeriya* in Sinhala, is a medicinal plant belonging to the family Solanaceae. It is widely distributed across tropical and temperate regions of the world and has long been utilized in various traditional medicinal systems. This review aims to summarize the phytochemical constituents, traditional uses, and pharmacological properties of *Mako*, highlighting its potential as a valuable medicinal plant. A comprehensive literature search was conducted using electronic databases such as PubMed and Google Scholar. Articles published in English up to January 2024 were reviewed, focusing on pharmacological studies related to *Solanum nigrum*. Search terms such as '*Mako*', '*Solanum nigrum*' combined with 'Anti-inflammatory', 'Hepatoprotective' and 'Nephroprotective' were used for articles published up to 2024. A total of 36 articles were filtered and scrutinized. The plant is known for its rich phytochemical composition, including flavonoids, alkaloids, saponins, tannins, glycosides, terpenoids, proteins, carbohydrates, acetic compounds, and resins. Interestingly, it lacks certain phytoconstituents such as sterols, steroids, and anthraquinones, which differentiates its pharmacological profile from other medicinal herbs. Preclinical studies have revealed a broad spectrum of biological activities associated with *Solanum nigrum*, suggesting its potential therapeutic applications. Documented pharmacological effects include hepatoprotective, nephroprotective, anti-diabetic, anti-inflammatory, anticancer (or antitumor), antioxidant, antimicrobial, and antihyperlipidemic activities. These effects are attributed to the presence of various bioactive constituents that modulate oxidative stress, inflammatory pathways, and metabolic processes. Despite the promising findings from in vitro and in vivo models, clinical evidence on the safety and efficacy of *Solanum nigrum* in humans remains limited. Therefore, further well-designed clinical trials are necessary to validate its traditional uses and establish safe dosage parameters for therapeutic applications.

Key words: Anti-inflammatory, Hepatoprotective, *Mako,* Nephroprotective, *Solanum nigrum*

Introduction

Solanum nigrum Linn., commonly known as Black Nightshade in English, *Mako* in Urdu, *Manittakkali* in Tamil, and *Kalukammeriya* in Sinhala, belongs to the family Solanaceae. It is widely distributed across tropical and temperate regions around the world and has been traditionally used for its medicinal and nutritional properties. In addition to its wild growth, the plant is also cultivated, primarily for its edible berries, which are used in various culinary and therapeutic applications. Botanically, *Solanum nigrum* is characterized as an erect, diffusely branched, shrubby herb. It exhibits extensive branching and a relatively compact growth habit. The leaves are ovate in shape, measuring approximately 4–8 cm in length and 2.5–4 cm in width. They are typically dark green in color and can be sinuate (wavy) or lobed along the margins. The plant produces small, white, star-shaped flowers that are borne in drooping, sub-umbellate, extra-axillary cymes—an arrangement where the flower clusters emerge just above the leaf axils. The berries are spherical, measuring about 0.8 to 1.0 cm in diameter. When mature, they appear either red or black, with a smooth, polished surface. Inside the berries are numerous small seeds, which are reniform (kidney-shaped), smooth, and yellow in color. Due to its adaptability and wide availability, *Solanum nigrum* is considered a valuable plant both nutritionally and medicinally. Its morphological characteristics make it easily identifiable in both cultivated and wild settings.[1]

Aims and Objectives

This review aims to summarize the phytochemical constituents, traditional uses, and pharmacological properties of *Mako*, highlighting its potential as a valuable medicinal plant.

Materials and Methods

A comprehensive literature search was conducted using electronic databases such as PubMed and Google Scholar. Articles published in English up to January 2024 were reviewed, focusing on pharmacological studies related to *Solanum nigrum*. Search terms such as '*Mako'*, '*Solanum nigrum'* combined with 'Anti-inflammatory', 'Hepatoprotective' and 'Nephroprotective' were used for articles published up to 2024. A total of 36 articles were filtered and scrutinized.

Inclusion criteria:

Studies conducted using *Solanum nigrum* as single drug only.

Human, animal and laboratory studies of the *Solanum nigrum*.

Exclusion criteria:

Studies conducted using compound preparation of *Solanum nigrum.*

Duplicated experimental data.

Data did not directly relate with the review.

Results and Discussion

Taxonomical Classification [2]

Division : Embryophyta

Sub-division : Angiospermae

Class : Dicotyledoneae

Order : Tubeflorae

Sub-order : Solanales

Family : Solanaceae

Genus : *Solanum*

Species : *Solanum nigrum* L.

Parts Used

Leaves, stems, flowers, seeds, roots and fruits. The berries and leaves are mainly used for medicinal purposes, besides the other parts of the whole plant.[1]

Morphology

Macroscopic:

The crude drug consists of the unripe berries of *Solanum nigrum* Linn. The berries occur either singly or in small clusters of 2 to 3, with persistent peduncles. The surface of the berries is wrinkled when dried (smooth when fresh) and they vary in size from 0.4 cm to 0.9 cm in diameter. Their color ranges from brownish black to light yellow. The seeds are small, numerous, yellow, and slightly reniform (kidney-shaped) to nearly smooth, measuring approximately 0.5 mm to 1.0 mm in diameter. The peduncles are slender, measuring 1.5 cm to 2.0 cm in length and 0.5 mm to 0.6 mm in thickness. The taste of the unripe berries is slightly pungent, becoming bitter over time. They are odorless, soft, and brittle when dry. The average weight of 100 fruits is approximately 2.65 grams.[1]

Microscopic:

The fruit of *Solanum nigrum* is anatomically differentiated into an outer single-layered epidermis and an inner fleshy mesocarp in which the seeds are embedded. The epidermis is cutinized, and its cells are rectangular to polygonal in shape. Beneath the epidermis lies a sub-epidermal collenchymatous layer, providing mechanical support. The ground tissue of the mesocarp is composed of parenchymatous cells, which are filled with starch grains. These starch grains may be simple or compound; the compound grains typically consist of 2 to 4 simple grains. The testa (seed coat) is light brown to yellowish, smooth in texture, and measures approximately 15 to 20 microns in thickness. It comprises a single layer of stone cells, which provide mechanical protection. The hilum is located at the acute edge near the narrower end of the seed. The internal portion of the seed contains an oily endosperm, within which a cylindrical embryo is embedded. The embryo measures 0.25 to 0.5 mm in thickness and consists of a hypocotyl and a radicle. The radicle is directed towards the hilum and is coiled parallel to the flat surfaces of the seed, positioning the cotyledon tips adjacent to the radicle. The endosperm cells contain aleurone grains, which serve as the primary food reserve.[1]

***Mizaj* (Temperament)** **:** Cold 2^0 Dry 2^0

***Badal* (Substitute)** **:** *Kaknaj* (*Physalis alkekengi* Linn.).

Side effect : Related to bladder

Corrective : Honey

Substitute : *Achillea millefolium*

Dose : 5-10g

Chemical Constituents

Phytochemical analysis of the aqueous extract of *Solanum nigrum* Linn. berries revealed the presence of various bioactive compounds, including flavonoids, alkaloids, saponins, tannins, glycosides, terpenoids, proteins, carbohydrates, acetic compounds, and resins. Notably, sterols, steroids, and anthraquinones were absent.[3] The organic constituents identified include alkaloids, reducing sugars, glucosides, saponins, and steroids. The inorganic elements present in the extract include potassium, calcium, iron, sulfur, and phosphorus.

Scientific Evidence of Mako

1. Hepatoprotective activity

Liu F.P, et al in 2016 conducted a study on "Hepatoprotective effects of *Solanum nigrum* against ethanol-induced injury in primary hepatocytes and mice with analysis of glutathione S-transferase". This study shows, Mice that received S. *nigrum* aqueous extracts (150 mg/kg) with ethanol showed marked attenuation of ethanol-induced hepatotoxicity, as evidenced by significant reductions of serum transaminases ($p < 0.01$), and variation of hepatic oxidative indices ($p < 0.05$) and GSTA1 ($p < 0.05$), compared with the model group and mice that received S. *nigrum* aqueous extracts (200 mg/kg). All the detection indexes were significantly different ($p < 0.01$) from those of the model group, and the protective effects were almost the same as those of the positive drug group. These results suggested that S. *nigrum* has hepatoprotective effects against ethanol-induced injury both in vitro and in vivo and can protect the integrity of hepatocytes and thus reduce the release of liver GSTA1, which contributes to improved liver detoxification.[4]

Abdel-Rahim E.A, et al in 2014 conducted a study on "Hepatoprotective effects of *Solanum nigrum* Linn fruits against cadmium chloride toxicity in albino rats". This study was aimed to investigate the toxicity of 1/20 LD50 of cadmium chloride (CdCl2) on male albino rats by oral ingestion and to determine the hepatoprotective effect of *Solanum nigrum* Linn (SN) dried fruits and their ethanolic extract against CdCl2 toxicity using biochemical parameters. The treatment with dried fruits and their ethanolic extracts in CdCl2-intoxicated rats (groups 5 and 6) ameliorated and improved these harmful effects in all above parameters either for blood or liver. The results of this study suggest the protective effect of S. *nigrum* against liver injury happened by CdCl2 which may be attributed to its hepatoprotective activity and thereby.[5]

Lin H.M, et al in 2008 conducted a study on "Hepatoprotective effects of *Solanum nigrum* Linn extract against CCl (4)-induced oxidative damage in rats". This study reveals that the protective effects of water extract of SN (SNE) against liver damage were evaluated in carbon tetrachloride (CCl4)-induced chronic hepatotoxicity in rats. Sprague-Dawley (SD) rats were orally fed with SNE (0.2, 0.5, and 1.0 g kg (-1) bw) along with administration of CCl4 (20% CCl4/corn oil; 0.5 mL kg (-1) bw) for 6 weeks. The results showed that the treatment of SNE significantly lowered the CCl4-induced serum levels of hepatic enzyme markers (GOT, GPT, ALP, and total bilirubin), superoxide and hydroxyl radical. This study suggests that SNE could

protect liver against the CCl4-induced oxidative damage in rats, and this hepatoprotective effect might be contributed to its modulation on detoxification enzymes and its antioxidant and free radical scavenger effects.[6]

Hsieh C.C, et al in 2008 conducted a study on "Inhibitory effect of *Solanum nigrum* on thioacetamide - induced liver fibrosis in mice". In this study, Hepatic fibrosis was produced by TAA (0.2 g/kg, i.p.) three times a week for 12 weeks. Mice in the three TAA groups were treated daily with distilled water and SNE (0.2 or 1.0 g/kg) via gastrogavage throughout the experimental period. Results of this study show that SNE reduced the hepatic hydroxyproline and alpha-smooth muscle actin protein levels of TAA-treated mice. SNE inhibited TAA-induced collagen (alpha1) (I) and transforming growth factor-beta1 (TGF-beta1) mRNA levels in the liver. Histological examination also confirmed that SNE reduced the degree of fibrosis caused by TAA treatment.[7]

Raju K, et al in 2003 conducted a study on "Effect of dried fruits of *Solanum nigrum* LINN against CCl4-induced hepatic damage in rats". In this study, the activity was evaluated using biochemical parameters such as serum aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP) and total bilirubin. The histopathological changes of liver samples in treated animals were compared with respect to control. The ethanol extract showed remarkable hepatoprotective activity.[8]

2. Nephroprotective activity

Fariba A, et al in 2017 conducted a study "Effect of the Administration of *Solanum nigrum* Fruit on Prevention of Diabetic Nephropathy in Streptozotocin-induced Diabetic Rats" In this study the aqueous extract of *Solanum nigrum* Linn fruit (SNE) (1 g/L via drinking water) was studied on streptozotocin-induced diabetic rats to prevent diabetic nephropathy (DN). SNE could decrease blood glucose level in diabetic rats. In addition, SNE was more effective than insulin in controlling blood glucose. Plasma and kidney levels of NO and MDA also decreased. The results of this study suggest that SNE in addition to the management of diabetes could have a beneficial effect on the prevention of DN. [9]

Prashanth K.V, et al in 2001 conducted a study on "Cytoprotective role of *Solanum nigrum* against gentamicin-induced kidney cell (Vero cells) damage in vitro". In this study, the 50% ethanol extract of the whole plant of *Solanum nigrum* was tested in vitro for its cytoprotecting against gentamicin-induced toxicity on Vero cells. Cytotoxicity was significantly inhibited as

assessed by the Trypan blue exclusion assay and mitochondrial dehydrogenase activity (MTT) assay. The test extract also exhibited significant hydroxyl radical scavenging potential, thus suggesting its probable mechanism of cytoprotectant.[10]

3. Anti-diabetic activity:

Aqueous extract of *Solanum nigrum* Linn berries in the dose of 200 mg/kg/day produced significant blood glucose reduction ($p<0.01$) from day 7 and 400 mg/kg/day produced highly significant reduction in blood glucose from day 7 ($p<0.001$). The standard drug glimepiride reduced the blood glucose as equal to normal on day 21 ($p<0.001$). Histopathological examination showed the regeneration of pancreatic beta cells in AESNB group.[3]

4. Anti-inflammatory activity

Wang Y, et al in 2017 conducted a study on "Potential Anti-inflammatory Steroidal Saponins from the Berries of *Solanum nigrum* L. (European Black Nightshade)". In this study, nine new steroidal saponins, solanigrosides Y1-Y9 (1-6, 10-12), together with seven known congeners, were isolated from the berries of S. *nigrum*. Their potential inhibitory effects on nitric oxide (NO) and IL-6 and IL-1β production induced by lipopolysaccharide (LPS) in macrophages cell line RAW 264.7 were evaluated. Compound 1 exhibited significant inhibition on NO production with an IC_{50} value of 9.7 μM, and some compounds exhibited significant inhibition effects on the LPS-induced IL-6 and IL-1β production. These results suggest that the steroidal saponins from berries of S. *nigrum* demonstrated pronounced anti-inflammatory activity and might be explored as a healthy benefit agent.[11]

Xiang L, et al in 2018 conducted a study on "Anti-inflammatory steroidal glycosides from the berries of *Solanum nigrum* L. (European black nightshade)'". In this study, seven previously undescribed steroidal glycosides, along with three known congeners were isolated from the unripe berries of *Solanum nigrum* L. (Solanaceae). The potential inhibitory effects on nitric oxide (NO) production induced by lipopolysaccharide in RAW 264.7 cell line and the anti-proliferative activities against five cancer cell lines (HL-60, U-937, Jurkat, K562 and HepG2) were evaluated. Seven compounds exhibited inhibition activities on NO production with IC_{50} values ranging from 11.33 to 49.35 μM. Structure-activity relationships of the isolated compounds were also discussed.[12]

Solanine A is a novel steroidal alkaloid isolated from *Solanum nigrum* Linn., a medicinal and edible plant which is widely used for treating various inflammatory diseases.Zhao L, et al in

2018 conducted a study on "Steroidal alkaloid solanine A from *Solanum nigrum* Linn. exhibits anti-inflammatory activity in lipopolysaccharide/interferon γ-activated murine macrophages and animal models of inflammation". In this study, we found that solanine A markedly suppressed the production of nitric oxide (NO) and prostaglandin E_2 (PGE_2) in lipopolysaccharide/interferon-γ (LPS/IFNγ)-stimulated RAW264.7 cells, and attenuated xylene, carrageenan and agar-induced inflammation in mice.[13]

Kang H, et al in 2011 conducted a study on "The chloroform fraction of *Solanum nigrum* suppresses nitric oxide and tumor necrosis factor-α in LPS-stimulated mouse peritoneal macrophages through inhibition of p38, JNK and ERK1/2". This study was aimed at determining the anti-inflammatory active fraction of S. *nigrum* by serial extractions. S. *nigrum* was first extracted with methanol, then fractionated with chloroform and water. The effects of S. *nigrum* fractions, diosgenin and α-solanine on LPS/interferon-gamma-induced nitric oxide (NO) and inducible NO synthase (iNOS), or LPS-induced tumor necrosis factor-α (TNF-α) and interleukin (IL)-6, in mouse peritoneal macrophages were determined. These results indicate that the anti-inflammatory compounds of S. *nigrum* exist preferentially in the nonpolar fraction, ruling out the possibility that diosgenin and α-solanine are the likely candidates.[14]

Gu X.Y, et al in 2018 conducted a study on "Bioactive steroidal alkaloids from the fruits of *Solanum nigrum*". In this study, Solanine A showed the most potent inhibitory activity against the LPS-induced NO production in murine RAW264.7 macrophages with an IC_{50} value of 3.85 ± 0.71 μM and significant cytotoxicity against MGC803, HepG2 and SW480 cancer cell lines with IC_{50} values of 6.00 ± 0.52 μM, 9.25 ± 0.49 μM and 6.23 ± 0.26.[15]

Shi F, et al in 2019 conducted a study on "Preparative isolation and purification of steroidal glycoalkaloid from the ripe berries of *Solanum nigrum* L. by preparative HPLC-MS and UHPLC-TOF-MS/MS and its anti-non-small cell lung tumors effects in vitro and in vivo". The study was carried out to evaluate the antinociceptive, anti-inflammatory and antipyretic effects of the aqueous extract of *Solanum nigrum* leaves using various animal models. The extract, at concentrations of 10, 50 and 100%, was prepared by soaking (1:20; w/v) air-dried powdered leaves (20 g) in distilled water (dH2O) for 72 h. The extract solutions were administered subcutaneously in mice/rats 30 min prior to the tests. The extract exhibited significant ($P < 0.05$) antinociceptive activity when assessed using the abdominal constriction, hot plate and formalin tests. The extract also produced significant ($P < 0.05$)

anti-inflammatory and antipyretic activities when assessed using the carrageenan-induced paw edema and brewer's yeast-induced pyrexia tests, respectively. This study demonstrated that S. *nigrum* leaves possessed antinociceptive, anti-inflammatory and antipyretic effects and thus supported traditional claims of its medicinal uses.[16]

5. Anti-cancer or Anti tumour activity

Lai Y.J, et al in 2016 conducted a study on "Anti-Cancer Activity of *Solanum nigrum* (AESN) through Suppression of Mitochondrial Function and Epithelial-Mesenchymal Transition (EMT) in Breast Cancer Cells". In this study, A novel active compound in S. *nigrum*, solaoiacid, was successfully separated and purified from S. *nigrum* by preparative high-performance liquid chromatography with mass spectrometry and ultra-high performance liquid chromatography with time-of-flight tandem mass spectrometry. The IC_{50} of solaoiacid on lung cancer cells was 2.3 μmol/L, which was significantly lower than that of the known steroidal glycoalkaloid. Label-free proteomics and STRING Network analysis were used to identify significantly deregulated proteins in lung cancer cells that were treated with the fresh ripe fruit extracts of S. *nigrum*. S. *nigrum* regulates multiple signal pathways, including the epidermal growth factor receptor pathway. S. *nigrum* downregulated 24 main proteins with direct roles in fatty acid biosynthesis. Both S. *nigrum* and solaoiacid showed strong downregulation of the fatty acid synthase-epidermal growth factor receptor and anti-non-small cell lung cancer effects and thus will become a novel drug for the treatment of non-small cell lung cancer.[17]

Ni X, et al in 2018 conducted a study on "Anti-Cancer Effect of α-Solanine by Down-Regulating S100P Expression in Colorectal Cancer Cells". This study aimed to evaluate the suppression of EMT in MCF-7 breast cancer cells treated with aqueous extract of *Solanum nigrum* (AESN). Mitochondrial morphology was investigated using Mitotracker Deep-Red FM stain. Our results indicated that AESN markedly inhibited cell viability of MCF-7 breast cancer cells through apoptosis induction and cell cycle arrest mediated by activation of caspase-3 and production of reactive oxygen species. These results suggested that AESN could inhibit EMT of MCF-7 breast cancer cells mediated by attenuation of mitochondrial function.[18]

Uen W.C, et al in 2017 conducted a study on "Inhibition of aqueous extracts of *Solanum nigrum* (AESN) on oral cancer through regulation of mitochondrial fission". In this study, researchers investigated the anti-cancer effects of α-solanine which is the most important and active component of *Solanum nigrum* against CRC cells in vitro and in vivo. They

demonstrated that α-solanine inhibited CRC cells (SW480, SW620 and HT-29) growth as well as migration and invasion, induced cell cycle arrest and apoptosis in vitro, and suppressed tumor growth in vivo. Their findings suggest that α-solanine is a potential agent for the treatment of CRC, and the anti-tumor effect of α-solanine in the CRC cells may be mediated at least partly by the downregulation of S100P. [19]

Zhang X, et al in 2018 conducted a study on "Solamargine derived from *Solanum nigrum* induces apoptosis of human cholangiocarcinoma QBC939 cells". This study was aimed to evaluate the effect of aqueous extracts of *S. nigrum* (AESN) on cancer cell proliferation, cell cycle, mitochondrial function and apoptosis. The human oral squamous cancer cells (SCC)-4 SCC-4 cells were treated by AESN to evaluate the inhibition of cell proliferation and mitochondrial function *in vitro*. The results of the study suggested that AESN has potential to be used as a functional food in adjuvant chemotherapy for treating human oral cancer by suppression of mitochondrial function.[20]

Liu J.H, et al in 2020 conducted a study on "Molecular mechanism of *Solanum nigrum* in treatment of hepatocarcinoma based on network pharmacology and molecular docking". In this study, the molecular mechanism underlying the anti-cancer effect of solamargine was assessed in human cholangiocarcinoma QBC939 cells. Therefore, the results of this study revealed that solamargine may induce apoptosis via the mitochondrial pathway and alter the level of apoptosis-associated proteins in human cholangiocarcinoma QBC939 cells. This *in vitro* study demonstrated that solamargine may be an effective chemotherapeutic agent against cholangiocarcinoma in clinical practice.[21]

Chen H, et in 2013 conducted a study on "The effect of polysaccharides from *Solanum nigrum* Linne on cellular immune function in tumour-bearing mice". This study aimed to explore the main active ingredients and potential targets of *Solanum nigrum* (SN), to reveal the potential molecular mechanism of SN in the treatment of hepatocellular carcinoma (HCC) based on network pharmacology and molecular docking. This study revealed the potential active ingredients and the possible molecular mechanism of SN for treatment of HCC, providing scientific basis for follow-up exploration of the molecular mechanism of SN against HCC.[22]

Shokrzadeh M, et al in 2010 conducted a study on "Cytotoxicity of hydro-alcoholic extracts of Cucurbitapepo and *Solanum nigrum* on HepG2 and CT26 cancer cell lines". This study was aimed to investigate the anti-tumour effect of polysaccharides from *Solanum nigrum* Linne, and its relationship with the immune function of tumour-bearing organisms. MTT assay was

used to observe the effect of different doses of polysaccharides from *Solanum nigrum* Linne on proliferation of lymphocytes in tumour-bearing mice. ELISA assay was also used to detect the levels of IL-2 in mice, and a laser scanning confocal microscope was used to detect the effect of polysaccharides from *Solanum nigrum* Linne on intralymphocytic free calcium ion concentration in tumour-bearing mice. Different doses of polysaccharides from *Solanum nigrum* Linne significantly inhibited the growth of mouse H22 solid tumours, improved the survival time of tumour-bearing mice, increased the proliferation of lymphocytes, elevated the levels of IL-2, and increased the concentration of calcium ions in the lymphocytes. Polysaccharides from *Solanum nigrum* Linne have certain anti-tumour effect, which is related with the cellular immune function that regulates the body.[23]

Zakaria Z.A, et in in 2009 conducted a study on "Antinociceptive, anti-inflammatory and antipyretic effects of *Solanum nigrum* aqueous extract in animal models". In this study, cytotoxicity of specific concentrations of hydro-alcoholic extracts of C. pepo and S. *nigrum* was studied on normal [Chinese hamster ovarian cells (CHO) and rat fibroblast] and cancer (HepG2 and CT26) cell lines. The cytotoxic effects and IC (50) of the extracts on the selected cell lines were studied followed by colonogenic assay method. The results showed that IC (50) of S. *nigrum* extract was significantly lower than that of the C. pepo extract on all four cell lines ($P < 0.05$). On the other hand, IC(50) of S. *nigrum* extract was significantly higher than the extract of Taxus baccata and Cisplatin, herbal and chemical control positive anticancer compounds, respectively, on all four cell lines ($P < 0.05$). As a result, it is concluded that the extract of S. *nigrum* has almost similar cytotoxicity to the extract of T. baccata on cancer cells.[24]

Li J, et al in 2010 conducted a study on "Protective effects of fraction 1a of polysaccharides isolated from *Solanum nigrum* Linne on thymus in tumor-bearing mice". This study was aimed to further find out the anti-tumor active compound of polysaccharides isolated from *Solanum nigrum* Linne (SNL-P), SNL-P was separated and purified by column chromatography, and its anti-cervical cancer activity was evaluated by mice models injected of ascites U14 cells. Furthermore, the protective effect of fraction 1a of SNL-P (SNL-P1a) on the thymus tissue of tumor-bearing mice was evaluated by histological study and TUNEL staining. Finally, the protein expression of Bcl-2 and Bax gene were assayed by immunohistochemistry. SNL-P1a had significant growth inhibition effect on U14 cervical cancer and protective effect on thymus tissue of tumor-bearing mice.[25]

Lim K.T. in 2005 conducted a study on "Glycoprotein isolated from *Solanum nigrum* L. kills HT-29 cells through apoptosis". This study investigated the apoptotic signal pathway triggered by glycoprotein isolated from SNL in HT-29 cells. Treatment of HT-29 cells with SNL glycoprotein (60 microg/mL) for 4 hours resulted in a cytotoxic effect of more than 60%, compared with the control. To explain the apoptotic effects of SNL glycoprotein, we investigated its effects on 12-O-tetradecanoylphorbol 13-acetate (TPA)-stimulated protein kinase C (PKC) alpha activity and DNA-binding activity of nuclear factor (NF) kappaB in HT-29 cells, using western blot analysis and electrophoretic mobility shift assays. Results from these experiments showed that SNL glycoprotein has remarkable inhibitory effects on the activities of TPA (100 nM)-stimulated PKCalpha and NF-kappaB in HT-29 cells. This study suggests that SNL glycoprotein is a natural anti-cancer agent due to its potential to induce apoptosis in HT-29 cells.[26]

Lin H.M, et al in 2007 conducted a study on "Induction of autophagy and apoptosis by the extract of *Solanum nigrum* Linn in HepG2 cells". In this study, reserachers demonstrated that the extract of SN (SNE) induced a strong cytotoxic effect toward HepG2 cells but much less to Chang liver and WRL-68 cells. The mechanisms of the cytotoxic effect were concentration dependent. High doses of SNE (2 and 5 mg/mL) induced apoptotic cell death in HepG2 cells, as evidenced by increases in the expressions of p-JNK and Bax, mitochondrial release of cytochrome c, and caspase activation. On the other hand, cells treated with low concentrations of SNE (50-1000 microg/mL) revealed morphological and ultrastructural changes of auto phagocytic death under electron microscopic observation. The findings indicate that SNE induced cell death in hepatoma cells via two distinct antineoplastic activities of SNE, the ability to induce apoptosis and auto phagocytosis, therefore suggesting that it may provide leverage to treat liver cancer.[27]

Ji Y.B, in 2008 conducted a study on "Induction of apoptosis in HepG2 cells by solanine and Bcl-2 protein". This study was aimed at observing the effect of anti-tumor and mechanism of solanine. The MTT assay was used to evaluate the IC (50) on the three digestive system tumor cell lines. The effect on morphology was observed with a laser confocal microscopy; the rate of apoptosis and the cell cycle were measured using flow cytometry (FCM); the expression of Bcl-2 protein was measured by Western blot. The results show that the IC (50) for HepG(2), SGC-7901, and LS-174 were 14.47, >50, and >50 microg/ml, respectively; the morphology of cells in the negative control was normal; for the treated groups, typical signs for apoptosis

were found. Therefore, the target of solanine inducing apoptosis in HepG(2) cells seems to be mediated by the inhibition in the expression of Bcl-2 protein.[28]

Lee S.J, in 2004 conducted a study on "A 150-kDa glycoprotein isolated from *Solanum nigrum* L. has cytotoxic and apoptotic effects by inhibiting the effects of protein kinase C alpha, nuclear factor-kappa B and inducible nitric oxide in HCT-116 cells". This study was carried out to investigate the anticancer effects of a 150-kDa glycoprotein isolated from *Solanum nigrum* L. (SNL glycoprotein) on spontaneously and experimentally induced tumor promotion in HCT-116 cells. For spontaneously induced tumor promotion, researchers evaluated the cytotoxic and apoptotic effects in HCT-116 cells using 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrazolium bromide (MTT), DNA fragmentation, and H33342 and ethidium bromide staining assays. SNL glycoprotein had remarkable, dose-dependent cytotoxic and apoptosis-inducing effects at low concentrations. The results of the study suggest that SNL glycoprotein can induce apoptosis through the modulation of signal mediators. Therefore, researchers speculate that it could be used as a chemotherapy agent even at low concentrations in HCT-116 cells.[29]

6. Antioxidant activity

Son Y.O, in 2003 conducted a study on "Ripe fruit of *Solanum nigrum* L. inhibits cell growth and induces apoptosis in MCF-7 cells". In this study, researchers prepared an ethanol extract from ripe fruits of SNL and investigated the mechanism involved in its growth-inhibitory effect on MCF-7 human breast cancer cells. Results from proliferation assay using tritium uptake showed that the proliferative capacity of MCF-7 cells was strongly suppressed in the presence of SNL ethanol extract. This was further confirmed through MTT assay and trypan blue exclusion experiments, which showed a very close correlation between the SNL extract concentration and the surviving cell numbers. The SNL extract-mediated suppression of cell growth was verified to be apoptotic, based on the appearance of DNA laddering, increase in DNA fragmentation, and low fluorescence intensity in nuclei after propidium iodide staining of the cells. Furthermore, the SNL extract was revealed to be a potential scavenger of hydroxyl radicals and DPPH radicals rather than superoxide anions. Collectively, their findings suggest that SNL fruit extract could be used as an antioxidant and cancer chemo-preventive material.[30]

Heo K.S, & Lim K.T. in 2004 conducted a study on "Antioxidative effects of glycoprotein isolated from *Solanum nigrum* L". In this study, the antioxidative effects of SNL glycoprotein

on superoxide anion and hydroxyl radical under optimal conditions revealed that SNL glycoprotein has remarkable scavenging effects on both radicals but exhibited slightly higher scavenging effects on superoxide anion generated by the enzymatic hypoxanthine/xanthine oxidase system than on hydroxyl radicals generated by the Fenton reaction. However, SNL glycoprotein was more effective against hydroxyl radials in cell cultures (NIH/3T3). Consequently, 20 microg/mL SNL glycoprotein has a scavenging ability against superoxide anion corresponding to that of ascorbic acid. On the other hand, its hydroxyl radical scavenging activity corresponds to 0.1 microg/mL catalase. From these results, researchers suggest that SNL glycoprotein has potent antioxidative potential.[31]

Jeong J.B, et al in 2010 conducted a study on "Lunasin peptide purified from *Solanum nigrum* L. protects DNA from oxidative damage by suppressing the generation of hydroxyl radical via blocking fenton reaction". In this study, researchers report here the protective effect of lunasin purified from *Solanum nigrum* L. against oxidative DNA. Lunasin protected DNA from the oxidative damage induced by Fe (2+) ion and hydroxyl radical. To better understand the mechanism for the protective effect of lunasin against DNA damage, the abilities to chelate Fe (2+), scavenge the generated hydroxyl radical and block the generation of hydroxyl radical were evaluated. Although it did not scavenge generate hydroxyl radical, lunasin blocked the generation of hydroxyl radical by chelating Fe (2+) ion. Researchers conclude that lunasin protects DNA from oxidation by blocking fenton reaction between Fe (2+) and H(2)O(2) by chelating Fe (2+) and that consumption of lunasin may play an important role in the chemoprevention for the oxidative carcinogenesis.[32]

Campisi A, in 2019 conducted a study on "Antioxidant Activities of *Solanum Nigrum* L. Leaf Extracts Determined in *in vitro* Cellular Models". This study was carried out to assess the antioxidant effect of two leave extracts of *Solanum nigrum* L. (SN). Then methanolic/water (80:20) (SN1) and water (SN2) leaves extracts were prepared. The total polyphenolic content and the concentration of phenolic acids and flavones compounds were determined. To verify whether examined extracts were able to restore the oxidative status, modified by glutamate in primary cultures of astrocytes, the study evaluated the glutathione levels, the intracellular oxidative stress, and the cytotoxicity of SN1 and SN2 extracts. Both extracts were able to quench the radical in an *in vitro* free cellular system and restore the oxidative status in *in vitro* primary cultures of rat astroglial cells exposed to glutamate. These extracts prevented

the increase in glutamate uptake and inhibited glutamate excitotoxicity, which leads to cell damage and shows a notable antioxidant property.[33]

Khan H.J, et al in 2016 conducted a study on "Identification of Anticancer and Antioxidant phytoconstituents from chloroform fraction of *Solanum nigrum* L. berries using GC-MS/MS analysis". In this study, phytochemical investigation of CFSn was well supported by its total phenolic content and antioxidant activity which we evaluated subsequently. Further, researchers investigated the anticancer activity against breast cancer cell lines (MDA-MB-231 and MCF-7) as well. Our in vitro results indicated that CFSn exhibited significant antiproliferative activity against both these cell lines and due induction of cancer cell death through apoptosis. This study emphasizes the need for isolation and characterization of specific bioactive compounds of CFSn and determination of their mechanism of action responsible for its anticancer activity in breast cancer cells.[34]

Zaidi S.K, et al in 2014 conducted a study on "Protective Effect of *Solanum nigrum* Leaves Extract on Immobilization Stress Induced Changes in Rat's Brain". In this study, the prophylactic or curative antioxidant efficacy of crude extract and the active constituent of S. *nigrum* leaves were evaluated in modulating inherent antioxidant system altered due to immobilization stress in rat brain tissues, in terms of measurement of glutathione (GSH), lipid peroxidation (thiobarbituric acid reactive substances, TBARS), and free radical scavenging enzymes activities. Rats were treated with single dose of crude extract of S. *nigrum* prior to and after 6 h of immobilization stress exposure. Treatment of S. *nigrum* extract and its active constituents to both pre- and post-stressed rats resulted in significant modulation in the above mentioned parameters towards their control values with a relative dominance by the latter. Brain is vulnerable to stress induced prooxidant insult due to high levels of fat content. Thus, as a safe herbal medication the S. *nigrum* leaves extract or its isolated constituents can be used as nutritional supplement for scavenging free radicals generated in the brain due to physical or psychological stress or any neuronal diseases per se. [35]

7. Antimicrobial activity

Sunitha J, et al in 2017 conducted a study on "Antimicrobial Effect of Leaves of *Phyllanthus niruri* and *Solanum nigrum* on Caries Causing Bacteria: An In vitro Study". This study was aimed to assess and compare the antibacterial efficacy of the crude alcoholic extract of the

leaves of *Solanum nigrum* and *Phyllanthus niruri* against five cariogenic organisms. The antibacterial zones of inhibition obtained for the herb *Solanum nigrum* was in the range of 12.3-14.6 mm and ranged from 9.7-11.6 mm for the herb *Phyllanthus niruri*. When the zones of inhibition were compared for the herbs, *Solanum nigrum* showed significantly greater zones of inhibition compared to *Phyllanthus niruri* for the organisms *Streptococcus sanguis*, *Streptococcus salivarius*, *Streptococcus oralis* and *Streptococcus mutans* (p-value<0.05). The alcoholic extract of leaves of *Solanum nigrum* and *Phyllanthus niruri* showed significant antibacterial activity against cariogenic organisms, with *Solanum nigrum* being more anti-cariogenic than *Phyllanthus niruri*.[36]

8. Anti-hyperlipidemic activity

Chang J.J, in 2017 conducted a study on "*Solanum nigrum* Polyphenol Extracts Inhibit Hepatic Inflammation, Oxidative Stress, and Lipogenesis in High-Fat-Diet-Treated Mice". This study investigated the in vivo and in vitro effects of an SNE on nonalcoholic fatty liver (NAFL)-induced hepatitis. In vivo data demonstrated that the SNE reduced blood triglyceride, sugar, and cholesterol levels, as well as fat accumulation, oxidative stress, and lipid peroxidation in high-fat-diet-treated mice. The results indicated that the SNE downregulated the expression of fatty acid synthase, 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase), and sterol regulatory element-binding proteins (SREBPs) through the AMP-activated protein kinase (AMPK) pathway and upregulated the expression of carnitine palmitoyl transferase 1 (CPT1) and peroxisome proliferator-activated receptor alpha. [37]

Arulmozhi V, et al in 2010 conducted a study on "Antioxidant and antihyperlipidemic effect of *Solanum nigrum* fruit extract on the experimental model against chronic ethanol toxicity". In this study possible protective effect of *Solanum nigrum* fruit extract (SNFEt) was investigated for its antioxidant and antihyperlipidemic activity against ethanol-induced toxicity in rats. The experimental animals were intoxicated with 20% ethanol (7.9 g/kg/day) for 30 days via gastric intubation. SNFEt was administered at the dose of 250 mg/kg body weight along with the daily dose of ethanol for 30 days. In the lipid profiles, the levels of total cholesterol (TC), triglycerides (TG), low density lipoproteins (LDL), very low density lipoproteins (VLDL), free fatty acids (FFA), and phospholipids were significantly elevated in the ethanol-induced group, whereas, the high density lipoproteins (HDL) were found to be reduced in the plasma, and the phospholipid levels were significantly decreased in the

tissues. Thus, the findings of this study indicated a significant antioxidant and antihyperlipidemic activity of *Solanum nigrum* fruits, which offered protection against ethanol-induced toxicity.[38]

Discussion

The present study highlights the significant therapeutic potential of *Solanum nigrum* Linn. (commonly known as Mako), particularly its wide spectrum of pharmacological activities. Phytochemical investigations have confirmed the presence of various bioactive constituents such as flavonoids, alkaloids, saponins, tannins, glycosides, and terpenoids, which are believed to contribute to its medicinal properties.

Preclinical studies have demonstrated that *Solanum nigrum* possesses multiple biological activities, including hepatoprotective, nephroprotective, anti-diabetic, anti-inflammatory, anticancer (or antitumor), antioxidant, antimicrobial, and antihyperlipidemic effects. These findings suggest that the plant holds considerable promise as a natural therapeutic agent for the management and prevention of various chronic and degenerative diseases.

However, despite these encouraging results, the current body of evidence is largely based on in vitro and in vivo animal models. There remains a significant gap in clinical data regarding its safety, efficacy, and mechanisms of action in human populations.

Conclusion

In conclusion, *Solanum nigrum* represents a valuable medicinal resource with diverse pharmacological applications. With continued scientific investigation, this plant could play a substantial role in the development of novel herbal formulations and integrative therapies in modern medicine. Further research is essential, particularly well-designed clinical trials and toxicological evaluations to validate its traditional uses and to determine safe dosage ranges for human consumption.

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