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Mohammad Abu Bin Nyeem
Department of Unani Medicine, Hamdard University Bangladesh

AKM Mamun Ur Rashid
Department of Public Health, American International University-Bangladesh

Meher Nowrose
Department of Public Health, ASA University Bangladesh

Md. Abu Hossain
Department of Public Health, North South University Bangladesh

Correspondence
Mohammad Abu Bin Nyeem
Department of Unani Medicine, Hamdard University Bangladesh

Solanum nigrum (Maku): A review of pharmacological activities and clinical effects

Mohammad Abu Bin Nyeem, AKM Mamun Ur Rashid, Meher Nowrose and Md. Abu Hossain

Abstract
Solanum nigrum is an important plant in traditional medicines belongs to the family of solanaceae. It is used in hepatitis, fever, dysentery, and stomach complaint. The juice of the plant used on ulcers and other skin diseases. The fruits are used as a laxative, appetite stimulant, and for treating asthma and "excessive thirst". Traditionally the plant was used to treat tuberculosis. It is known as *peddakasha pandla koora* in the Telangana region. This plant's leaves are used to treat mouth ulcers that happen during winter periods. It is known as *manathakkali keerai* in Tamil Nadu and *kage soppu* in Karnataka, and apart from its use as a home remedy for mouth ulcers, is used in cooking like spinach. The boiled extracts of leaves and berries are also used to alleviate liver-related ailments, including jaundice. The juice from its roots is used against asthma and whooping cough. *S. nigrum* is a widely used plant in oriental medicine where it is considered to be antitumorigenic, antioxidant, anti-inflammatory, hepatoprotective, diuretic, and antipyretic activity. Chinese experiments confirm that the plant inhibits growth of cervical carcinoma.

Keywords: *Solanum nigrum, Kakamachi,* Solanaceae, Maku

Introduction
Medicinal plants have been used by humans for centuries in folklore medicine [1]. In the plant family Solanaceae[2] the genus Solanum is a very large group of about 1400 species found throughout in the temperate and tropical regions of the world like Solanum aviculare (Europe, New Zealand), S. dulcamara (Europe), S. incanum (Africa), S. khasianum (Indian subcontinent), S. laciniatum (New Zealand, Australia), S. nigrum (cosmopolite), S. pseudocapsicum (an ornamental, cultivated in greenhouses), S. tuberosum (potatoe) and S. melongena (eggplant, aubergine).
Solanum nigrum commonly known as Maku or black nightshade usually grows as a weed in moist habitats in different kinds of soils. S. nigrum has been extensively used traditionally to treat various ailments such as hepatitis, pain, inflammation and fever [3-4]. The plant is also used in the Oriental systems of medicine for various purposes – as an antitumorigenic, antioxidant[4], anti-inflammatory [3], hepatoprotective [5], diuretic [3], and antipyretic agent [3]. Various compounds have been identified which are responsible for diverse activities. *S. nigrum* is widely used in many traditional systems of medicine worldwide for disparate ailments but has not garnered attention for modern therapeutic use.

Traditional Uses
The berries and leaves are mainly used for medicinal purposes, besides the other parts of the whole plant. The leaves are used as poultice for rheumatic and gouty joints, skin diseases, used in the treatment of anti-tuberculosis and are said to produce Diaphoresis. Leaves are also used in dropsy, nausea and nervous disorders. The decoction of the berries and flowers are useful in cough. These are remedy for pulmonary tuberculosis and bronchitis, diuretic. The juice of the berries used as an antidiarrhoeal, ophthalmopathy and hydrophobia. It is also used in heart disease. Berries are used to posses tonic, diuretic and cathartic properties. They are also useful in inflammations and skin diseases. The roots are useful in osteopathy, ophthalmopathy, rhinopathy and hepatitis. The whole plant used as antiseptic, anti-inflammatory, expectorant, cardiotonic, digestive, diuretic, laxative, diaphoretic, sedative,

swelling, cough, asthma. The plant is also effective in curing cardiopathy, leprosy, hemorrhoids, nephropathy, ophthalmopathy, dropsy and general debility. Decoction of the plant depresses the CNS and reflexes of the spinal cord [6-10].

Fig 1: Leafs and fruits of *Solanum nigrum*

Phytoconstituents

Phytochemical investigation of whole plant reported that which contain alkaloids, flavonoids, tannins, saponins, glycosides, proteins, carbohydrates, coumarins & phytosterols. It has been found that Solanum nigrum contains the substances, such as total alkaloid [11], steroid alkaloid [12], steroidal saponins [13] and glycoprotein [14], exhibiting anti-tumor activity [15]. Researchers studied the chemical characterization of osmotin – like protein from this plant [16]. New glycoprotein (150 KDa) has been isolated from this plant which consist carbohydrate content (69.74%) and protein content (30.26%) which contain more than 50% hydrophobic aminoacids such as glycine and proline [17]. Small unripe fruits of *Solanum nigrum* had a high concentration of solasodine, but both the concentration and the absolute amount per fruit decreases with fruit maturation [18]. The berries of *Solanum nigrum* from New Zealand have recently been studied and found to contain 4 steroidal alkaloid glycosides, Solamargine, Solasonine, α and β-solanigrine. The berries of *Solanum nigrum* have been found to contain a saturated steroidal genin, which has been identified as tigogenin by mixed melting point and IR spectroscopy [19]. One spirosestanol glycoside and two furostanol glycosides have been isolated from a methanol extract of the stems and roots of Solanum nigrum [20]. Some researchers found the presence of ascorbic acid in the fruits of Solanum nigrum and the concentration of ascorbic acid is more in fruit than root [21]. Six new steroidal saponins, solanigrosides C-H, and one known saponin, degalactotigonin, were isolated from the whole plant of Solanum nigrum [22]. Some researchers isolated two new steroidal saponins, named nigrumnins I and II, together with two known saponins were obtained from the whole plant of Solanum nigrum [23]. Recently phytochemical analysis of Solanum nigrum has resulted in the isolation of two novel disaccharides. Their structures were determined as ethyl b - D -thevetopyranosyl-(1-4)- b- D -oleandropyranoside and ethyl b- D -thevetopyranosyl-(1-4)- a - D-oleandropyranoside, respectively, by chemical and spectroscopic methods [24]. *Solanum nigrum* seeds have high lipid content. Their protein content and minerals elements (Mg being prominent) are considerable and Solanum nigrum oil is an important source of linoleic acid [25]. Chemical structures of some phytoconstituents from *Solanum nigrum* present in Fig 2.

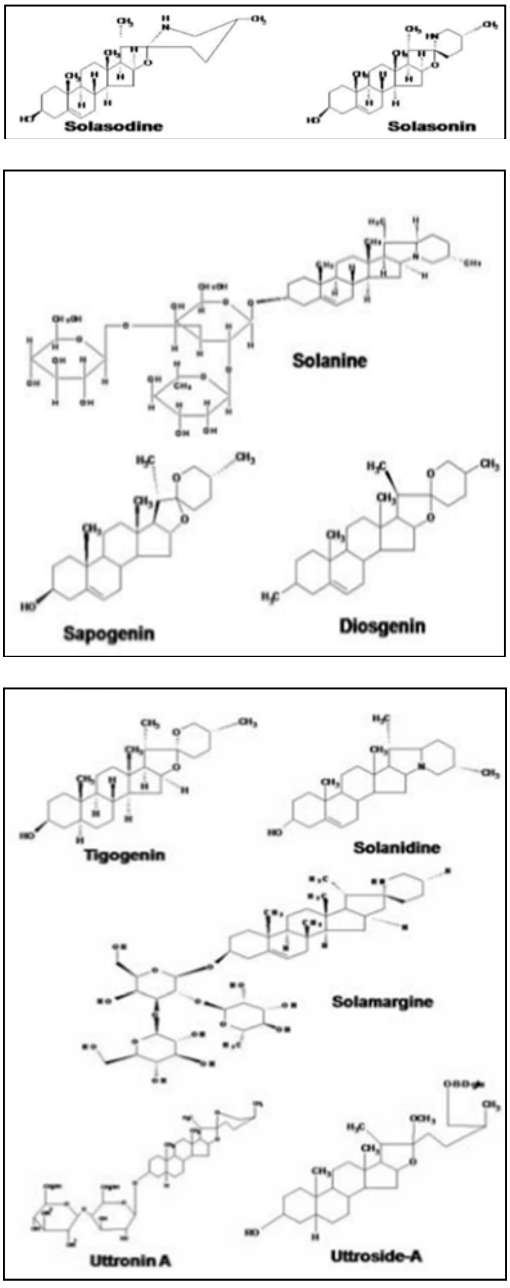

Fig 2: Phytoconstituents of *Solanum nigrum*

Pharmacological Activity

Hepatoprotective activity

Solanum nigrum aqueous and methanolic extracts were studied for hepatoprotective activity in rats injected with 0.2 ml/kg carbon tetrachloride (CCl4) for 10 consecutive days. *S. nigrum* aqueous extract (250 to 500 mg/kg) was administered to rats injected with carbon tetrachloride (CCl4) for 10 days. The water extracts showed a hepatoprotective effect against CCl4-induced liver damage, which was evident by the decrease in serum aspartate amino transferase (AST), alanine amino transferase (ALT) and alkaline phosphates (ALP) activities bilirubin concentration and by mild histopathological lesions when compared with the group of rats injected with CCl4 alone. The methanolic extracts of *S. nigrum* (250 to 500 mg/kg) also had hepatoprotective effects with levels of serum AST, ALT, ALP and bilirubin decreasing significantly in animals treated with S. nigrum methanolic extract compared to an untreated group [26].

Ethanol extract of *Solanum nigrum* was investigated for its hepatoprotective activity against CCl4-induced hepatic damage in rats. The ethanol extract showed remarkable hepatoprotective activity. 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 sample in treated animals were compared with respect to control [27].

Immunostimulant activity

In this investigation found immunostimulant potential plants being an alternative for preventing fish diseases. Six groups of experimental fishes (E. suratensis) were immunized with 0.2ml (4ppm) of five different extracts of Solanum nigrum through intra-peritoneal injection and challenged with heat killed Aphanomyces invadans. Blood collected from immunized and normal fish were analyzed such as, radial immunodiffusion, antibody titration, nitro blue tetrazolium assay, determination of IgG concentration and host resistance test. In both control and the experimental groups the peak antibody response was on day 21 after immunization and decreased towards 28th day. The methanol extract treated group, the antibody response was significantly enhanced on the day 14 and day 21 ($p<0.05$). The highest IgG level was on day 21 and decreased towards day 28. In Chloroform extract treated group the neutrophil activity was significantly enhanced on day 6 ($p<0.05$). In toluene extract treated group the neutrophil activity was significantly enhanced on day 6 ($p<0.05$). The ethanol and methanol extract treated group showed less mortality rate when compared to chloroform toluene and water extract treated group. Plants extracts have great potential as immunostimulant against microorganisms and that they can be used in the treatment of infectious diseases caused by microorganisms [28].

Antimicrobial activity

The methanol and aqueous extracts of leaves of *Solanum nigrum* L. were used for the investigation of antibacterial studies. In antibacterial screening performed by disc diffusion method against two gram negative bacteria namely *Xanthomonas campestris* (plant pathogen) and *Aeromonas hydrophila* (animal pathogen), it was found that the methanol extracts of all the plant samples showed significant activity against the two tested bacteria. The methanol extracts of S. nigrum exhibited clear zone of inhibition against the tested microorganisms [29].

Solanum nigrum was subjected to preliminary phytochemical screening activity against gram negative organism of Escherichia coli (NCIM: 2065) and gram positive organism of Staphylococcus aureus (NCIM: 2079) and they were compared with control drug Penicillin at different concentrations at 0.5, 1.0, 1.5, 2.0, and 2.5 mg/ml by disc diffusion method. In case of Escherichia coli, *Solanum nigrum* exhibits maximum zone of inhibition of about 30.1mm and control drug penicillin shows less activity compared to the *Solanum nigrum* plant extracts [30].

Six solvent extracts from leaf, seed and roots of *Solanum nigrum* were assayed for *in vitro* antibacterial activity against pathogenic bacteria such as Bacillus subtilis, Bacillus megaterium, Staphylococcus aureus, klebsiella pneumonia E.coli, Proteous vulgaris, Pseudomonas putrida, and the zone of inhibition were compared with different standard antibiotics. Phytochemical screening of the crude extracts revealed the presence of secondary compounds such as alkaloids, flavonoids, steroids, tannins, and phenols. The organic solvent extracts (ethanol, methanol, ethyl acetate, diethyl ether, chloroform and hexane) of seeds were exhibited strong antibacterial activity against different pathogenic bacteria compared to leaf and root solvent extracts. The ethyl acetate seed extracts of *Solanum nigrum* exhibited strong activity against Pseudomonas, Proteous vulgaris, Klebsiella (20.5 – 21.0mm of zone of inhibition). Among different types of extracts tested ethyl acetate seed extract showed lowest MIC values (1.50-4.50 µg/m) against all the bacterial isolates tested. A lowest MIC value was recorded against pseudomonas putrida, Proteus vulgaris, Klebsiella pneumonia [31].

The ethanolic extract of the dried fruit of *Solanum nigrum* L. was assessed for its possible antimicrobial activity. The ethanolic extract showed moderate antibacterial activity against both gram-positive and gram-negative bacteria [32].

The antibacterial activity of *Solanum nigrum* was detected against Bacillus subtilis, Escherichia coli, Klebsiella pneumonia and Pseudomonas aeruginosa. Solanum nigrum plant extracts of, 10ìg, 50ìg and 100ìg were taken as per CLSI standards. The zones of inhibitions obtained were recorded and analyzed against standard control streptomycin. The methanolic extracts were showed highest antibacterial activity than ethanolic extracts. In both extracts, whole plant extract showed potential anti-bacterial activity than stem and berries. The results indicate that the whole plant extracts of *Solanum nigrum* may recommend to use in preparation of herbal drugs [33].

Anti-HCV activity

Methanol and chloroform extracts of *Solanum nigrum* (SN) seeds exhibited 37% and more than 50% inhibition of HCV respectively at nontoxic concentration. Moreover, antiviral effect of Solanum nigrum seeds extract was also analyzed against HCV NS3 protease by transecting HCV NS3 protease plasmid into liver cells. The results demonstrated that chloroform extract of Solanum extracts decreased the expression or function of HCV NS3 protease in a dose-dependent manner and GAPDH remained constant. These results suggests that SN extract contains potential antiviral agents against HCV and combination of SN extract with interferon will be better option to treat chronic HCV [34].

Anti gastritis and antiulcerogenic effects

Leaves and berries of *Solanum nigrum* are commonly used in South India for the treatment of gastric ulcers, gastritis and other gastric problems. The present study investigated the *Solanum nigrum* leaf and berry extracts for their protective effect on ethanol induced gastritis and aspirin induced gastric ulcers of pylorus ligated rats. Sucralfate and Ranitidine were used as standard Drugs. Oral administration of aqueous extract of leaf (80 mg/kg and 250 mg/kg respectively) and berry (50 mg/kg) significantly reduced the concentration of Evans blue in both gastric contents and glandular tissue indicating decreased vascular permeability and mucosal damage with respect to that of control. The berry aqueous extract offered more protection against gastritis than the leaf extracts. Pretreatment with aqueous extracts of Leaf (250 mg/kg) and berry (50 mg/kg) significantly reduced the Ulcer Index [35].

Cardioprotective activity

The cardioprotective activity of methanolic extract of berries of the plant *Solanum nigrum* was evaluated by using global *in vitro* ischemia-reperfusion injury carried out using doses of 2.5 and 5.0 mg/kg for 6 days per week for 30 days. The results indicate that the extract exhibited significant ($p<0.001$) cardioprotective activity against global in-vitro ischemia-reperfusion injury. The activity occurred in a dose-independent manner. The methanolic extract of berries of the plant *Solanum nigrum* possessed cardioprotective activity [36].

Analgesic activity

Ethanolic extracts of *Solanum nigrum* for analgesic activity was evaluated. analgesic activity of the extract was evaluated for its central and peripheral pharmacological actions by using Eddy's hot plate and acetic acid induced writhing respectively. The study was carried out using doses of 100, 250 & 500 mg/kg orally. The extract showed significant analgesic activity at the dose of 500 mg/kg ($P<0.01$) as compare to standard drug Diclofenac sodium (50 mg/kg) [38].

The ethanolic extract of the dried fruit of *Solanum nigrum* L. was assessed for analgesic activity. In acetic acid induced writhing in mice, the ethanolic extract (250 and 500mg/kg) exhibited significant ($p<0.05$ & $p<0.01$) inhibition of writhing reflex 51.39% and 66.67% respectively compared to standard Diclofenac sodium. It shows the positive result for analgesic activity [36].

Antidiarrhoeal activity

The ethanolic extract of the dried fruit of *Solanum nigrum* L. was assessed for antidiarrhoeal activity. The fruit extract showed a significant ($P<0.01$ and $P<0.001$) antidiarrhoeal activity against castor oil induce diarrhoea in mice in which it decreased the frequency of defecation and increased the mean latent period at the dose of 250mg/kg and 500mg/kg body weight[36].

Cytotoxic activity

The ethanolic extract of the dried fruit of *Solanum nigrum* L. cytotoxic activity. In the brine shrimp lethality test, the extract showed cytotoxicity significantly with LC50= 63.10µg/ml and LC90= 160µg/ml [36].

Anti-inflammatory activity

The methanolic extract of whole plants of Solanum nigrum L. was investigated for anti-inflammatory activity on the experimental animal models. The methanolic extract at a concentration of 100 mg/kg b.w and 200 mg/kg b.w showed the significant dose dependent antiinflammatory activity in carrageenin and egg white induced hind paw edema in rats. The standard drugs were Indomethacin (10 mg/kg) and Cyproheptadine (8 mg/kg) [37].

Ethanolic extracts of *Solanum nigrum* for anti-inflammatory was evaluated by using Carrageenan induced rat paw edema. The study was carried out using doses of 100, 250 & 500 mg/kg orally. Anti-inflammatory activity at the dose of 500 mg/kg ($P<0.01$) as compare to standard drug Diclofenac sodium (50 mg/kg) [37].

The effect of methanolic extracts of berries of *Solanum nigrum* were studied on carrageenan induced paw edema. The methanolic extract decreased the edema induced in hind paw. The methanolic extract of *Solanum nigrum* (375 mg/kg b.w.) has showed significant anti-inflammatory [38].

Anticancer activity

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 [39].

Anti hyperlipidemic activity

The ethanolic extract *Solanum nigrum* in lowering the cholesterol level in lipofundin treated hyperlipidemia rabbits *in vivo*. 20% lipofundin was used to induce hyperlipidemia in rabbits @ 2 ml/kg body weight through slow intravenous administration in the marginal ear vein for 7 days. For next 2 weeks the control group was placed at standard diet, whereas the test group was given the ethanolic crude extract of *Solanum nigrum* at the dose of 300 mg/kg body weight. On the completion of treatment blood samples were collected from both control and test groups and were analyzed for the lipid profile values. It was observed in the test group after treatment with ethanolic extract of *S. nigrum*, the raised level of serum total cholesterol, triglyceride, high density lipoprotein, low-density lipoprotein were decreased towards normal values. Thus the present study demonstrated that *S. nigrum* possessed significant anti-hyper lipidemic activity in lipofundin induced hyperlipidemia rabbits [40].

Antioxygenic Activity

The antioxygenic activity of *Solanum nigrum* L. leaves and its various solvent extracts were evaluated using sunflower oil model system. Leaf powder and its methanol/water (80:20) soluble fraction showed strong antioxygenic activity in refined sunflower oil. On the other hand, ethyl acetate fraction exhibited marginal antioxygenic activity, whereas the water soluble fraction was practically devoid of any activity in refined sunflower oil. Thermal stability of different extracts of *Solanum nigrum* L. leaves heated at 80˚C in refined sunflower oil also indicated the strong efficacy of methanol/water (80:20) extract to inhibit thermal oxidation. Solanum nigrum L. contain high levels of magnesium (239.0 mg/100g) and phosphorous (80.3

mg/100g). Fatty acid analysis of the lipid extracted from *Solanum nigrum* L. leaves indicated the presence of linoleic (59.1%) as a major fatty acid. The result of this study confirmed the presence of antioxygenic compounds in leaves; in particular its methanol/water (80:20) extracts showed great potential as a natural antioxidant to inhibit lipid peroxidation in foods [41].

Conclusions

We conclude from the literature study and experimental results analysis that Solanum nigrum is a traditional remedy for hepatitis, fever, ulcer, and various immunological applications in cancer and others. The plant is beneficial in preventing hepatotoxicity & cytotoxicity thus improving functions of liver and Kidney. It also finds in analgesic, anti inflammatory, antimicrobial, antidiabetic, immunostimulant, central nervous system and brain functioning. It can really contribute to medical and pharmaceutical practices.

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