Review on Effect of Solanumnigrum L. on Histopathology of Kidneys of Rats

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Summery

Solanumnigrum is commonly called black night shade that belongs to Solanaceae (potato) family. It is a fairly common herb or short-lived perennial shrub, found in many wooded areas, as well as disturbed habitats. Various experimental based scientific studies were conducted in order to investigate the efficacy and safety of S. nigrum extract. The scientific investigation from many research findings shows that this plant has various bioactive ingredients such as alkaloids, solanins, saponins, flavonoids, tannins, steroidal glycoalkaloids, steroidal genin and vitamins. These constituents are responsible for diverse activities including: anti-inflammatory, anti-bacterial, anti-diabetic, anti-fungal, anti-oxidant, hepatoprotective, nephroprotective and cytoprotective effects. In addition, these bioactive constituents in the S. nigrum have free radical scavenging capacity and anti-lipid peroxidation activities by stabilization of plasma membranes as well as repair of liver and kidney tissue damage. Moreover, the result of this review showed that S. nigrum whole plant extract and SNFEt have the capacity to reverse kidney damages to near normal levels if pathological change occurs. The S. nigrum whole plant extract and SNFEt were found to be safe for kidney parameters up to 5ml/kg doses. But this extract would have been toxic above 5ml/kg which is considered to be elevated dose. So that safe dosage needs to be identified for children and pregnant women because the children have less body resistance and the pregnant women may susceptible to abort since it may induce uterine contraction. Therefore, further studies required to isolate the active ingredients from the extract of S. nigrum for proper drug development to treat the above mentioned health problems by conducting further clinical trials.

1. Introduction

More than 3.5 billion people in the developing world rely on traditional medicinal plants as components of their healthcare (Balick and Cox, 1996). This global utilization of medicinal plants has considerably increased in the last two decades. As elsewhere in Africa, local people in Ethiopia, by large employed plant based traditional medicine to treat ailments arising from worms, fungi, virus and protozoa (Abebe, 2001).

In Ethiopia, about 80% of the human population and 90% of the livestock rely on traditional medicine and the medicinal plants have shown very effective medicinal value for some ailments of humans and livestock. In addition, the acquisition and transfer of indigenous knowledge on traditional medicine, in most developing countries including Ethiopia, is passed from one generation to the next by word of mouth. Nowadays, more than ever, researchers of natural products-based drugs are going back to nature for the search of more effective and safe new drugs. About one thousand identified medicinal plant species are reported in the Ethiopian Flora. Although plant based natural medicines are popularly acclaimed to be safe, scientists advocate the proper toxicological studies in order to ensure safety in the use of herbal medicines (Endashaw, 2007).

According to Schiefer et al. (1997), toxicology encompasses the study of the adverse effects of chemical and physical agents on living organisms and groups of organisms. This deals with adverse effects ranging from acute to (chronic) long term i.e. acute toxicity testing is done by using single or repeated doses with observation for 14 days (typically tests for lethality or skin irritancy); subacute toxicity testing is done by using repeated doses for up to 90 days whereas chronic toxicity testing is done by using repeated doses for up to 2 years (including carcinogenicity testing).

Most species in the Solanaceae family are poisonous to humans as well as to livestock. The toxic effects of the plants are mainly reported in the older literature. For instance, deadly nightshade contains tropane alkaloids. The toxin, when ingested by humans in large quantities, causes anticholinergic effects. Although S. nigrum is considered to be an edible plant, its toxicity is mainly due to the presence of solanine, a glycoalkaloid causing varying degrees of toxicity in a dose-dependent manner. The symptoms of poisoning in humans due to solanine are reported to include nausea, vomiting, diarrhea, headache, dizziness, loss of speech, fever, sweating, tachycardia, pupil dilation, blindness, mental confusion, convulsions, coma, and death (Jain et al., 2011).

The amount of toxic compound in a plant depends on the climate, soil type, season, and maturity. The green unripe berries are generally considered more toxic than the ripe berries. It is probable that by boiling the plant, the toxic components are destroyed as the plant is reported to be edible after cooking. Traditionally,

consumption of nightshade vegetables like tomato, potato, and eggplant has been considered to be problematic for arthritic patients. It has been reported that solanine present in the green parts of these vegetables is probably responsible for joint pain. Most toxic effects of drugs occur at a predictable time after administration, and such toxic effects caused by a drug are similar in human and some other animals. This fact serves as a principle for use of animal models in toxicological studies. Thus, continuous use and the growing demand for herbal therapies have restored the quest for validating the efficacy and safety or toxic implications of medicinal plants (Erasto et al., 2007; Jain et al., 2011).

Taxonomy of Solanumnigrum L

Solanumnigrum (S. nigrum) is a worldwide weed of arable land, gardens, rubbish tips, soils rich in nitrogen, in moderately light and warm situations which occur from sea to montane levels (Jennifer and James, 1997). It has vernacular name, black nightshade (English), Tikur-awitt (Amharic) and Muiulo (Afan Oromo). S. nigrum belongs to the kingdom Plantae (plants); subkingdom Tracheobionta (vascular plants); superdivision of Spermatophyta (seed plants); division of Magnoliophyta (flowering plants); class of Magnoliopsida (dicotyledons); subclass of Asteridae; order of Solanales; Family of Solanaceae (Potato family); genus of Solanum (nightshade) and species of Solanumnigrum L. (black nightshade) (Edmonds and Chewya, 2002).

1. S. nigrum L. subsp. nigrum: glabrous to slightly hairy with appressed non-glandular hairs. 2. S. nigrum L. subsp. schultesii (Opiz) Wessley: densely hairy with patent, glandular hairs.

Botanical description of Solanumnigrum L.

S. nigrum is a fairly common herb or short-lived perennial shrub, found in many wooded areas, as well as disturbed habitats. It is characterized by their lack of prickles and stellate hairs, their white flowers and their green or black fruits arranged in an umbelliform fashion. It has a height of 30 to 120 cm (12 to 48 in), leaves 4 to 7.5 cm (1.5 to 3 in) long and 2 to 5 cm (1 to 2.5 in) wide; ovate to heart-shaped, with wavy or large-toothed edges; both surfaces hairy or hairless; petiole 1 to 3 cm (0.5 to 1 in) long with a winged upper portion. The flowers have petals greenish to whitish, recurved when aged and surround prominent bright yellow anthers. The berry is mostly 6 to 8 mm (0.3 to 0.8 in) diameter, dull black or purple-black (Venkateswarlu and Krishna, 2007).

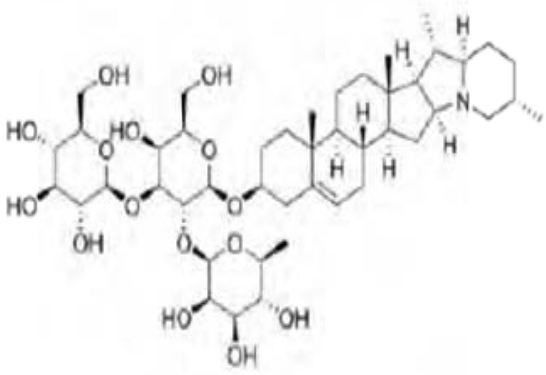
The toxicity of S. nigrum varies widely depending on the variety, and poisonous plant experts advise to avoid eating the berries unless they are a known edible strain (Turner and Aderka, 1997). Toxin levels may also be affected by the plant's growing conditions (Edmonds and Chewya, 2002)

Source: Edmonds and Chewya (2002)

Phytochemical property of Solanumnigrum

Phytochemicals are the secondary metabolites that have several subgroups, possessing various bioactivities such as antioxidant, antimicrobial, antivirus and anticancer. Even today, because of the belief that medicinal plants are safe and effective, most of the plant products are being used in local conventional systems of medicine. The unripe fruit of S. nigrum contain the highest concentration of toxin particularly solanine, a glycoalkaloid is found in most parts of this plant. The level of toxin in the berries is greatly reduced by ripening and when ripe, the berries are the least toxic and are sometimes eaten without ill effects. In addition, the ripe berries are eaten raw as fruits and are used in pies and preservative in many regions of the world (Aali et al., 2010; Din et al., 2012).

All parts of the plant can be poisonous, containing toxic glycoalkaloids at 0.524% (dry weight), including solamargine, solasonine and solanine. The toxins are most concentrated in the unripe green berries, but also occur in ripe berries. Solanine levels in S. nigrum can be extremely toxic and potentially fatal (Schep et al., 2009). Its toxicity is mainly due to the presence of active ingredient solanine, a glycoalkaloid causing varying degrees of toxicity in a dose-dependent manner (Jain et al., 2011).



Solanine

Source: Edmonds and Chewya (2002)

Poisoning symptoms are typically delayed for 6 to 12 hours after ingestion. The symptoms of poisoning in humans due to toxicity of solanine are reported include fever, headache, sweating, nausea, vomiting, abdominal pain, diarrhea, drowsiness, dizziness, loss of speech, tachycardia, pupil dilation, blindness, mental confusion, convulsions, coma, and death. Death from ingesting plant parts results from cardiac arrhythmias and respiratory failure. Children have died after eating unripe berries, and consumption has caused livestock fatalities. Livestock have also been poisoned from nitrate toxicity by grazing the leaves of S. nigrum (Schep et al., 2009).

Although numerous texts state that the cooked ripe fruit of black nightshade is safe to eat, detoxification cannot be attributed to normal cooking temperatures because the decomposition temperature of solanine is much higher at about 243°C. There are ethnobotanical accounts of S. nigrum leaves and shoots being boiled as a vegetable with the cooking water being discarded and replaced several times to remove toxins (Tull, 1999; Edmonds and Chewya, 2002).

S. nigrum has been widely used as a food since early times, and the fruit was recorded as a famine food in 15thC in China. Despite toxicity issues with some forms, the ripe berries and boiled leaves of edible strains are eaten. The thoroughly boiled leaves although strong and slightly bitter flavoured are used like spinach as horta, in fataya pies and quiches. The ripe black berries are described as sweet and salty, with hints of liquorice and melon (Irving, 2009).

In Ethiopia, the ripe berries are picked and eaten by children in normal times, while during famines all affected people would eat berries. In addition the leaves are collected by women and children, who cook the leaves in salty water and consumed like any other vegetable. Farmers in the Konso Special Woreda report that because S. nigrum matures before the maize is ready for harvesting; it is used as a food source until their crops are ready. The Welayta people in the nearby Wolayita Zone do not weed out S. nigrum that appear in their gardens since they likewise cook and eat the leaves (Zemede, 1995).

S. nigrum is an important ingredient in traditional Indian medicines. Infusions are used in dysentery, stomach complaints and fever. The leaves are known to be used to treat headache and diseases of nose, ringworm, heart liver and kidney ailments, wounds, burns and toothache. The ethnomedicinal information reveals that the juice

of dried leaves of S. nigrum is used for lowering blood sugar level. The juice of the plant is used on ulcers and other skin diseases. The fruits are used as a tonic, laxative, appetite stimulant and also for treating asthma and "excessive thirst". In North India, the boiled extracts of leaves and berries are also used to alleviate liver-related ailments, including jaundice. In Assam, the juice from its roots is used against asthma and whooping cough (Kaushik et al., 2009; Maharana et al., 2010).

S. nigrum is a widely used plant in oriental medicine where it is considered to be anti-tumorigenic, anti-oxidant, anti-inflammatory, hepatoprotective, diuretic, and antipyretic. Chinese experiments confirm that the plant inhibits growth of cervical carcinoma in mice (Jian et al., 2011b; Senthilnath et al., 2013).

Histopathology effect of S. nigrum on Kidneys

Kidney is an important organ actively involved in maintaining homeostasis of the body by reabsorbing important material and excreting waste products. It has been reported that habitual consumption of large amount of alcohol was associated with an increased risk of kidney failure in the general populations (Parekh and Klag, 2001). Kidney functional markers such as urea, uric acid, creatinine and CAT are the main indicators of renal dysfunction (Mirunalini et al., 2012).

According to Shaheen et al. (2014) in normal control group the serum creatinine (0.65 + 0.01mg/dl) and urea (60.63 + 1.27mg/dl) were significantly increased to 1.06 + 0.07mg/dl and 85.67 + 3.73mg/dl respectively while CAT was reduced from 48.14 + 0.84mg/dl to 28.23 + 2.10mg/dl in GM treated renal injury. When the GM treated renal injury further treated with S. nigrum extract resulted in reduction of serum creatinine (0.71 + 0.02mg/dl) and urea (67.58 + 1.60mg/dl). However, the level of CAT was elevated to 34.01 + 1.55mg/dl (Table 11).

This is in agreement with Mirunalini et al. (2012) the normal control levels of urea (25.38 ± 1.69mg/dl), uric acid (1.30 ± 0.06mg/dl) and creatinine (0.86 ± 0.06mg/dl) in ethanol-induced rats were significantly increased to 45.26 ± 2.96mg/dl, 2.63 ± 0.35mg/dl, 1.88 ± 0.07mg/dl respectively whereas treatment with SNFEt (250mg/kg b.wt) significantly decreased 30.51 ± 2.13mg/dl, 2.01 ± 0.16mg/dl, 0.99 ± 0.08mg/dl the levels to near normal values (Table 7). This may indicate the extract of S. nigrum and SNFEt improved nephroprotective activity.

The antioxidants in normal control group such as SOD (11.30 + 1.36U*/mg protein), CAT (39.82 + 2.88U#/mg protein), GPx (8.50 + 0.50U$/mg protein) and GSH (113.52 + 9.14mg/100g) was remarkably declined to SOD (7.51 + 0.74U*/mg protein), CAT (23.93 + 2.03U#/mg protein), GPx (4.77 + 0.21U$/mg protein) and GSH (63.87 + 5.57mg/100g) in kidney of rats administered with ethanol when compared to experimental groups. In response to SNFEt the activities were brought back to near normal levels, SOD (9.77 + 0.94U*/mg protein), CAT (34.56 + 2.28U#/mg protein), GPx (6.43 + 0.29U$/mg protein) and GSH (96.41 + 7.81mg/100g) (Tables 11) (Mirunalini et al., 2012). This increase could be due to efficient scavenging of ROS

which might be implicated to oxidative activation of enzymes (Jayaraman et al., 2009). SNFEt preserves the functional capacity of the kidney against ethanol toxicity.

According to Shaheen et al. (2014) the histopathological features as seen in the kidney in the gentamicin induced resulted in severe effect of glomerular congestion, peritubular congestion, epithelial desquamation, blood vessel congestion, inflammatory cells, necrosis and connective tissue proliferation (Table 12). Increase in intracellular free oxygen radicals can initiate irreversible cellular injury process leading to tubular necrosis and tubular degeneration in renal tissues. Scavenging of free oxygen radicals prevent irreversible renal cell injury and necrosis. Many studies confirmed that mediation of ROS may have linked with degenerative tubular effects of gentamicin (Walker et al., 1999).

Various researchers like Ganguly et al. (2009) stated the S. nigrum total extract was found to be safe >5 g/kg body weight. This is presumably due to the fact that glycoalkaloids of S. nigrum contain appreciable amount of conjugated metal ions (except Cu2+). The increasing trend in toxicity of the metal ions depleted glycoalkaloids of S. nigrum was further manifested in the sub-acute toxicity study. The S. nigrum total extract was found to be safe the hematological and hepatic parameters, upto a dose of 4 gm/kg, p.o. administered for 21 days as compared to normal control animals. Whereas glycoalkaloids fraction of S. nigrum was found to be toxic at a dose of 200 and 400 mg/kg, p.o. treated for 21 days (Table 14).

This is analogous to Feroz et al. (2013), study on the dosage of S. nigrum extracts and stated the normal dose of S. nigrum (0.43 ml/kg) possesses hepatoprotective effects against CCl4 induced liver damage in rats. Further the microscopic examination of hepatic tissue in animals kept on normal and moderate dose (5ml/kg) of herbal drug showed inflammatory changes. Whereas animals kept on high dose (10ml/kg) show mild patchy necrosis as compared to control animals. This may be due to the toxicity effects of S. nigrum extract at high doses.

Conclusion

S. nigrum is commonly called black night shade that belongs to Solanaceae family. Traditionally it is frequently used to treat human health problems. This plant has various bioactive constituents such as alkaloids, solanins, saponins, flavonoids and tannins that are important for hepatoprotective and nephroprotective functions. These

constituents are responsible for diverse activities including anti-inflammatory, anti-microbial, anti-helminthic and antioxidant activities.

The result showed that S. nigrum whole plant extract and SNFEt were able to reverse the pathological parameters and serum levels of ALP, ALT, AST and bilirubin of liver and kidney damages to near normal levels. This plant also showed free radical scavenging capacity, liver and kidney regeneration which are very important for human health. This protecting and regeneration capacity may be due to having at least partially to the high content of polyphenols, alkaloids and saponins in S. nigrum extract.

The S. nigrum whole plant extract and SNFEt were found to be safe for the liver and kidney parameters up to 5ml/kg dose having good protective activities and it shown dose dependent activities. But this would have been toxic at the elevated doses. So that safe dosage needs to be identified for children and pregnant women because children have less body resistance and in the pregnant women may lead abortion since it may induce uterine contraction.

Therefore, further studies required to isolate the active ingredients from the extract of S. nigrum for proper drug development to treat the above mentioned health problems by conducting further clinical trials.

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