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Solanum nigrum: A review study with anti-cancer and antitumor perspective

Sepide Miraj

M.D., Gynecologist, Fellowship of Infertility, Assistant Professor, Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran

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ABSTRACT

Solanum nigrum or locally just black nightshade is a species in the Solanum genus, native to Eurasia and introduced in the Americas, Australasia, and South Africa. While this plant has lots of properties, the aim of this study is to overview its therapeutic effects of Solanum nigrum. This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases from 1998 to 2016.totally, of 93 found articles, 60 articles were included. The search terms were "Solanum nigrum", "therapeutic", "pharmacological", Various studies have shown that Solanum nigrum Possess Anti-Tumor effect, Anti-Cancer Activity, Hepatoprotective Effect, Anti-fungal effect, Anti -larvicidal effect, Anti-Stress effect, Antioxidative effect, Antiallergic effect, Estrogenic activity. Although Solanum nigrum have a long history of medicinal use within the traditional Chinese system, it has been only recently in the West that we have begun to understand their pharmacological possibilities. Solanum nigrum has a wide range of potential therapeutic applications in anti-cancer and anti-tumor activities.

Keywords: *Solanum nigrum*, "therapeutic", "pharmacological",

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INTRODUCTION

It is proved that herbal medicine is effective in the treatment of many diseases[1-20].European black nightshade (*Solanum nigrum*) or locally just black nightshade) is a species in the Solanum genus, native to Eurasia and introduced in the Americas, Australasia, and South Africa. Parts of this plant can be toxic to livestock and humans. Nonetheless, ripe berries and cooked leaves of edible strains are used as food in some locales, and plant parts are used as a traditional medicine. A tendency exists in literature to incorrectly refer to many of the other "black nightshade" species as "*Solanum nigrum*"[21].

Solanum nigrum has been recorded from deposits of the Paleolithic and Mesolithic era of ancient Britain and it is suggested by the botanist and ecologist Edward Salisbury that it was part of the native flora there before Neolithicagriculture emerged. The species was mentioned by Pliny the Elder in the first century AD and by the great herbalists, including Dioscorides. In 1753, Carl Linnaeus described six varieties of *Solanum nigrum* in Species Plantarum[22].

Black nightshade is a common herb or short-lived perennial shrub, found in many wooded areas, as well as disturbed habitats. It reaches a height of 30 to 120 cm (12 to 47 in), leaves 4.0 to 7.5 cm (1.6 to 3.0 in) long and 2 to 5 cm (1 to 2 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 (0.24 to 0.31 in) in diam., dull black or purple-black. In India, another strain is found with berries that turn red when ripe[23].

Sometimes *Solanum nigrum* is confused for the more toxic deadly nightshade, Atropa belladonna, in a different Solanaceae genus altogether. A comparison of the fruit shows that the black nightshade berries grow in bunches, the deadly nightshade berries grow individually.

The plant has a long history of medicinal usage, dating back to ancient Greece. "... In the fourteenth century, we hear of the plant under the name of Petty Morel being used for canker and with Horehound and wine taken for dropsy." It was a traditional European medicine used as a strong sudorific, analgesic and sedative with powerful narcotic properties, but was considered a "somewhat dangerous remedy". Internal use has fallen out of favor in Westernherbalism due to its variable chemistry and toxicity, but it is used topically as a treatment for herpes zoster[24].

Solanum nigrum is an important ingredient in traditional Indian medicines. Infusions are used in dysentery, stomach complaints, and fever. The juice of the plant is used on ulcers and other skin diseases. The fruits are used as a tonic, laxative, appetite stimulant, and for treating asthma and "excessive thirst". Traditionally the plant was used to treat tuberculosis. It is known as peddakashapandlakoora in the Telangana region. This plant's leaves are used to treat mouth ulcers that happen during winter periods of Tamil Nadu, India. It is known as manathakkalikeerai in Tamil Nadu and kaagesoppu in Karnataka, and apart from its use as a home remedy for mouth ulcers, is used in cooking like spinach. 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[24-27].

Solanum nigrum is a widely used plant in oriental medicine where it is considered to be antitumorigenic, antioxidant, anti-inflammatory, hepatoprotective, diuretic, and antipyretic[28].

Anti-Tumor effect

A polysaccharide fraction from *Solanum nigrum*, SN-ppF3 was examined regarding to immunomodulatory activity .These results suggested that tumor suppression mechanisms observed in SN-ppF3-treated mice were most probably due through enhancing the host immune response [29].

Effects of crude polysaccharides isolated from *Solanum nigrum* L. on erythrocyte membranes of tumor-bearing S180 and H22 in mice was investigated. *Solanum nigrum* L.-type mice transplanted tumor can affect the red blood cell membrane fluidity and re-closed, through the red cell membrane of red blood cells to enhance the immune function of the possibility of erythrocyte immunity against tumor formation garland provide experimental basis [30]. The anti-tumour effect of polysaccharides from *Solanum nigrum* Linne, and its relationship with the immune function of tumour-bearing organisms was investigated. 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[31].

The effects of *Solanum nigrum* fractions in mouse peritoneal macrophages were determined. The results indicate that the anti-inflammatory compounds of *Solanum nigrum* exist preferentially in the nonpolar fraction, ruling out the possibility that diosgenin and α-solanine are the likely candidates. The inhibition of iNOS, TNF-α and IL-6 by the chloroform fraction may be partly due to the suppression of p38, JNK and ERK1/2. Further study is required to identify the active compounds of *Solanum nigrum*[32].

The effects of the crude polysaccharides isolated from *Solanum nigrum* Linne (SNL-P) in vitro and in vivo against U14 cervical cancerwas examined. The data showed that SNL-P possess potent antitumor activity and SNL-P might exert antitumor activity via activation of different immune responses in the host rather than by directly attacking cancer cells on the U14 cervical cancer bearing mice. Thus, SNL-P could be used as an immunomodulatory and an anticancer agent [33].

The anti-tumor active compound of polysaccharides isolated from *Solanum nigrum* Linne (SNL-P) and the thymus protective effects of this active compound were evaluated.SNL-P1a had significant growth inhibition effect on U14 cervical cancer and protective effect on thymus tissue of tumor-bearing mice [34].

Anti-Cancer Activity

The suppression of EMT in MCF-7 breast cancer cells treated with AESN was evaluated. The results suggested that AESN could inhibit EMT of MCF-7 breast cancer cells mediated by attenuation of mitochondrial function. AESN could be potentially beneficial in treating breast cancer cells, and may be of interest for future studies in developing integrative cancer therapy against proliferation, metastasis, and migration of breast cancer cells[35].

the antitumor effects of AE-SN was evaluated and the synergistic effects of AE-SN with docetaxel On the human endometrial cancer cell lines was assessed and result showed that AE-SN treatment was effective in suppressing endometrial cancer cells via the autophagic pathway and was also capable of enhancing the cytotoxicity of docetaxel in human endometrial cancer cells. Our results provide meaningful evidence for integrative cancer therapy in the future[36].

the inhibitory effect of solamargine (SM), a major steroidal alkaloid glycoside purified from SNL, on human hepatoma SMMC-7721 cells and investigate the possible mechanism of SM was evaluated. Result indicated that SM exerted potential anticancer activity on SMMC-7721 cells in vitro through the activation of caspase-3 and the regulation of the cell cycle progression to induce apoptosis and inhibit hepatoma cells proliferation[37].

the growth-inhibitory effects of the SN extract was evaluated. a polyphenolic extract of *Solanum nigrum* (SN)demonstrated differentially causes cell cycle arrest and apoptosis in various human prostate cancer cells without affecting normal prostate epithelial cells. Results showed that the SN extract is capable of selectively inhibiting cellular proliferation and accelerating apoptotic events in prostate cancer cells. SN may be developed as a promising therapeutic and/or preventive agent against prostate cancer[38].

the tumor-suppression efficiency of AE-SN integrated with a standard chemotherapeutic drugwas examined. The results suggested that the integrated treatment with AE-SN-potentiated cisplatin and doxorubicin induced cytotoxicity through the cleavage of caspase-7 and accumulation of microtubule-associated protein-1 light .AE-SN can potentially be used in novel integrated chemotherapy with cisplatin or doxorubicin to treat HCC patients [39].

Tumor suppression efficacy was determined using the ES-2, SKOV-3, and OVCAR-3 human ovarian cancer cell lines. Result suggested that the AE-SN exhibited tumor suppression efficacy and improved the tumor suppression efficiency of cisplatin, doxorubicin, and docetaxel in human ovarian cancer cells. Therefore, the AE-SN is a candidate antitumor ingredient that can be used in developing future integrated chemotherapy for managing ovarian cancer[40].

Cytotoxicity of specific concentrations of hydro-alcoholic extracts of C. pepo and *Solanum nigrum* was studied on normal rat fibroblast and cancer (HepG2 and CT26) cell lines. It is concluded that the extract of *Solanum nigrum* has almost similar cytotoxicity to the extract of T. baccata on cancer cells [41].

It was demonstrated that 12-o-tetradecanoylphobor-13-acetate (TPA) and constitutively activated PKC alpha significantly increased migration and invasion of HepG2 cells, while treatment with water or polyphenol extracts of SN attenuated TPA-induced migration and invasion. Results revealed the antimigration and anti-invasion effects of both extracts derived from SN, which may act as a promising therapeutic agent for the treatment of hepatocellular carcinoma [42].

the inhibitive effect of *Solanum nigrum* Linn. water extract (SNWE) on melanoma metastasis and dissect the underlying mechanisms of SNWE actions was evaluated. The results indicated SNWE significantly inhibited B16-F1 cell migration and invasion. Meanwhile, decreased Akt activity and PKCα, Ras, and NF-κB protein expressions were detected in dose-dependent manners. In line with this notion, >50% reduced tumor weight and lung metastatic nodules were observed in 1% SNWE fed mice. This was associated with reduced serum MMP-9 as well as Akt activity and PKCα, Ras, and NF-κB protein expressions [43].

Inhibitive effect on hepatocarcinoma cell growth of a polyphenolic extract of *Solanum nigrum* L. was evaluated. This study shows that SNPE is a potent agent for HCC treatment through targeting G(2)/M arrest and apoptosis induction, achieving cell growth inhibition[44].

The bioactive properties of lunasin from *Solanum nigrum* L. (SNL) was reported. Result illustrated that Lunasin isolated from autoclaved SNL inhibited core histone H3 and H4 acetylation, the activities of the HATs, and the phosphorylation of the Rb protein. Lunasin in the crude protein and in the autoclaved crude protein was very stable to pepsin and pancreatin in vitro digestion, while the synthetic pure lunasin was digested at 2 min after the reaction. We conclude that lunasin is a bioactive and bioavailable component in SNL and that consumption of SNL may play an important role in cancer prevention [45].

Strong cytotoxic effect of the extract of SN (SNE) was demonstrated a toward HepG2 cells. The findings indicate that SNE induced cell death in hepatoma cells via two distinct antineoplastic activities of SNE, the ability to induce apoptosis and autophagocytosis, therefore suggesting that it may provide leverage to treat liver cancer[46].

the tumor suppression efficacy of AE-SN using DLD-1 and HT-29 human colorectal carcinoma cells was evaluated and The results indicated that AE-SN induced autophagy via microtubule-associated protein 1 light chain 3 A/B II accumulation but not caspase-3-dependent apoptosis in both cell lines. AE-SN also demonstrated a combined drug effect with all tested drugs by enhancing cytotoxicity in tumor cells. Our results suggest that AE-SN has potential in the development of complementary chemotherapy for colorectal cancer[47].

Organic solvent and aqueous extracts obtained from berries of *Solanum nigrum* for antiproliferative activity on leukemic cell lines was evaluated. Results indicated increased cytotoxicity with increasing extract concentrations. Comparative analysis indicated that 50% inhibitory concentration value of methanol extract is the lowest on both cell lines[48].

The effect of *Solanum nigrum* on adhesion, migration and invasion in human colon carcinoma RKO cells was evaluated. *Solanum nigrum* may inhibit the proliferation, adhesion, migration and invasive abilities in RKO cells. The present study provides new insight into the application of *Solanum nigrum* for colon carcinoma treatment that are worthy of further study[49].

Hepatoprotective Effect

the protective effects of *Solanum nigrum* against alcoholic liver damage in primary hepatocytes and mice, using glutathione S-transferase alpha 1 (GSTA1) as an indicator was investigated. The results suggested that *Solanum 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 [50].

The ethnopharmacological use of a traditional formulation in hepatoprotection against paracetamol-induced hepatotoxicity was examined and the result showed that The polyherbal extract exhibits a significant hepatoprotective effect in vivo. The study contributes to its use in traditional Ayurveda system for the management of liver diseases.

The ethnopharmacological use of a traditional formulation in hepatoprotection against paracetamol induced hepatotoxicity was evaluated and The finding demonstrated its usefulness in traditional Ayurveda system for the management of liver diseases [51].

The inhibitory effect of aqueous extracts from *Solanum nigrum* (AESN) on AGEs-induced RAGE signaling and activation of hepatic stellate cells (HSCs) and hyperglycemia induced by high-fat diet with ethanol was investigated. The results suggest that AESN may be further explored as a novel anti-fibrotic strategy for the prevention of liver disease[52].

The hepatoprotective effect of *Solanum nigrum* Linn (SN) dried fruits and their ethanolic extract against $CdCl_2$ toxicity was determined. The treatment with dried fruits and their ethanolic extract in $CdCl_2$-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 *Solanum nigrum* against liver injury happened by CdCl2 which may be attributed to its hepatoprotective activity and thereby[53].

Anti-fungal effect

Anti-fungal effect of *Solanum nigrum* L. was investigated and result showed that the production of solamargine by a cultivable fungal endophyte at a significant yield is a new observation. Further experiments such as media optimization, OSMAC (One Strain Many Compounds) or epigenetic modifiers could be applied to enhance the fungal solamargine production[54].

Anti-larvicidal effect

The biocontrol potentiality of active ingredient isolated from ethyl acetate extract of mature leaves of *Solanum nigrum* L. (Solanaceae) was investigated. The findings indicated that there is a clear dose-dependent mortality, as the rate of mortality (Y) was positively correlated with the concentrations of the compound (X); having regression coefficient value close to 1[55].

Anti-Stress effect

The prophylactic or curative antioxidant efficacy of crude extract and the active constituent of *Solanum nigrum* leaves were evaluated .result suggested that Brain is vulnerable to stress induced prooxidant insult due to high levels of fat content. Thus, as a safe herbal medication the *Solanum 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[56].

Antioxidative effect

Effects of endophytic bacterium inoculation on plant growth was evaluated. The beneficial effect was more obvious at relatively low Cd concentration (10 μM). Based on the alteration of nutrient uptake and activated oxygen metabolism in infected plants, the possible mechanisms of endophytic bacterium in Cd phytotoxicity reduction can be concluded as uptake enhancement of essential mineral nutrition and improvement in the antioxidative enzymes activities in infected plant(57).

The protective effect of lunasin purified from *Solanum nigrum* L. against oxidative DNA was investigated. Result showed 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[58].

Antiallergic effect

Potential of the plant berries in the treatment of asthma was evaluated. The petroleum ether extract of *Solanum nigrum* berries can inhibits parameters linked to the asthma disease [59].

Estrogenic activity

The estrogenic potential of *Solanum nigrum* fruits by in vitro and in vivo assays was evaluated. Result demonstrate the hormone like activity of Solanum glycosides both in vitro and in vivo in mouse, which needs to be further explored to evaluate the possible mechanism and clinical implications[60].

CONCLUSION

Although *Solanum nigrum* have a long history of medicinal use within the traditional Chinese system, it has been only recently in the West that we have begun to understand their pharmacological possibilities. *Solanum nigrum* has a wide range of potential therapeutic applications in anti-cancer and anti-tumor activities.

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