Original Article

A Sneak peek (1970-2021) Into Phytochemistry and Ethnomedical Properties of Solanum Nigrum Linn (Makoi)

Kirti Goel[1], Md Sohel Ahmed[2], Randhir Singh[3], Vipin Saini[4], Seema Bansal[5]

[1] Research Scholar, Department of Pharmaceutical Science, M.M. College of Pharmacy, Maharishi Markandeshwar (Deemed to be University), Mullana, Ambala, India, kirtijain2727@gmail.com
[2] Student, Department of Pharmaceutical Sciences, M.M. College of Pharmacy, Maharishi Markandeshwar (Deemed to be University), Mullana, Ambala, India, gazisohel0914@gmail.com
[3]Associate Professor, Central University of Punjab, Bhatinda, Punjab, India, randhirsingh.dahiya@gmail.com
[4]Director, RAAC, Maharishi Markandeshwar College of Pharmacy, MM (DU), Mullana, Ambala, Haryana, India vipinsaini31@rediffmail.com
[5]Professor, Department of Pharmacology, Maharishi Markandeshwar College of Pharmacy, MM (DU), Mullana, Ambala, Haryana, India, seema.bansal@mmumullana.org

***Corresponding author:** Dr. Seema Bansal

*Professor, Department of Pharmacology, Maharishi Markandeshwar (Deemed to be University), Mullana, Ambala, India, 133207,E-mail: seema.bansal@mmumullana.org,Contact: +91-7696017167
DOI: 10.47750/pnr.2022.13.S05.95

Abstract

Introduction: Plants have always played a substantial role in the traditional medicine system worldwide. In India and other parts of the world, *Solanum Nigrum Linn.* is one of the most promising and reliable sources of medicine in the traditional medicine system. It is well known for its dynamic therapeutic properties. The concrete objective of selecting this plant is to consolidate its bioactive elements and possibly medicinal qualities. So that future scientists and researchers may progress novel pharmaceuticals for pre-clinical and clinical trials, which could be launched as new targeted therapeutic options.

Method: This review summarized the previous three decades' worth of scientific publications from online databases such as Google Scholar, PubMed, ScienceDirect, Web of Science, and library books to assemble their possible phytopharmacological and therapeutic potentials.

Results: From the ongoing research database, *S. Nigrum* possesses a plethora of active phytoconstituents like glycoproteins, polysaccharides, polyphenolic compounds, and glycoalkaloids which are responsible for various pharmacological activities such as antioxidant, anticancer, antitumor, hepatoprotective, antidiabetic, and anti-asthmatic etc.

Conclusion: This mystic herb has exhibited numerous ethnomedical properties in humans. Our research findings provide clear evidence that *S. Nigrum* could be a potential natural source of several ailments and might be marketed as an alternative to contemporary medicines. The stem, flower, root, and seed contain numerous dynamic bioactive constituents that are unexplored. Future researchers have an excellent opportunity to investigate them and elucidate their biomedical scientific activities and mechanisms in different diseases.

Keywords: European black nightshade**,** traditional medicine, therapeutic properties, phytoconstituents, phytopharmacological activities etc

INTRODUCTION

Solanum Nigrum Linn. is a commonly used traditional herbal plant used for various ailments, and it is well known for its therapeutic properties and traditional Indian medicine. *Solanum Nigrum* belongs to the Solanaceae family (Oh et al., 2016), also known by Black nightshade or Makoi(Kumar et al., 2019; Shivappa et al., 2019; Mohamed Saleem et al., 2009), is an annual, branched, short-lived herb found in forested areas and disturbed habitats(Chauhan et al., 2012; Teklehaimanot et al., 2015). The height of the plant is between 30-120 cm. The roots are fibrous and have a shallow taproot. The stem is round to angular and surrounded by tiny multicellular hairs. The leaves are dull to dark green, 2–8 cm in length, and 1–5.5 cm in width. The flowers are bell-shaped white with a 4–18 mm diameter. Fruits or berries are round, fleshy, and dull purple to black or yellowish-green in colour and 6-8 mm in size. Some other fruit variants reported in India become red after they are ripe (Miraj, 2016; Karmakar et al., 1970; Venkateswarlu & Krishna Rao, 1971).*Solanum Nigrum* has long been used in traditional therapy to cure illnesses such as hepatitis, irritation, and fever (Heo & Lim, 2004; Jain et al., 2011; Zakaria et al., 2006). It can use in the treatment of sexually transmitted diseases (Ebiloma & Ajayi, 2011). A wide range of chemicals has shown a broad range of activities. *Solanum Nigrum has* been used for a long time in traditional therapy to relieve symptoms (Jain et al., 2011). It is an

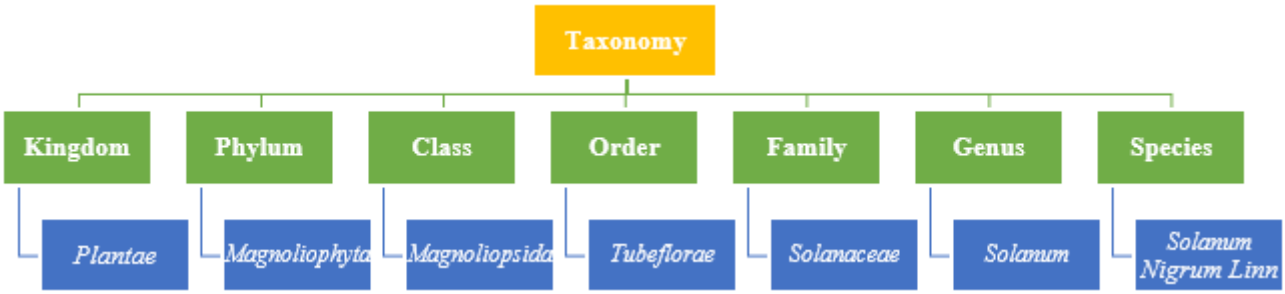
African pediatric herb used to treat various disorders that cause infant death, including feverish convulsions, eye problems, hydrophobia, and chronic skin ailments. It is a potent natural alternative with anticancer properties(Rani et al., 2017; Rajathi et al., 2015). However, it has not received much attention as a modern therapeutic potential (Abu et al., 2017).

"Figure 1: Different parts of Solanum Nigrum Linn (Leaves, Flower, Berries, and whole plant)(Edmonds & Chweya, 1997) "

MATERIALS AND METHODS

Taxonomical classification

Solanum Nigrum Linn. is the largest species of genus *Solanum,* and *Solanum* is the largest genus(Edmonds & Chweya, 1997) in the family *Solanaceae*. It contains approximately 84 genera and 3000 species (Mohy-Ud-Din et al., 2010). The science-based representation of taxonomy is shown below in figure 2.



"Figure 2: Taxonomical classification of *Solanum nigrum.* (Choudhary Bhagirath, 2021; Potawale et al., 2008; Agarwal et al., 2014)"

Ethnomedical Properties and traditional uses

S. Nigrum is a vital ingredient in traditional Indian remedies, and humans have used it since the ancient Greek era. In the 14th century, it was known as "Petty morel" and was used to cure canker and dropsy. In the European healthcare system, it was employed as an analgesic and sedative with strong narcotic qualities, although it was classified as a "somewhat dangerous remedy." It has been used topically to treat shingles (Miraj, 2016; Jain et al., 2011).

Aside from the other parts of the plant, in the Ayurvedic system, the leaves and berries are generally used for therapeutic purposes(Abu et al., 2017). The leaves are utilized for treating mouth ulcers in this winter season throughout Tamil Nadu, India (Miraj, 2016; Jainu & Devi, 2006). The leaves are employed in oral health care to relieve toothaches(Hebbar et al., 2004). The decoction made from flowers and berries can be beneficial in treating cough. They are remedies for bronchitis, pulmonary tuberculosis, and diuretics. The berry juice effectively treats dysentery, eye disease, liver disease, and hydrophobia(Mohamed Saleem et al., 2009). It can also treat anasarca, cardiac disease(Mohamed Saleem et al., 2009), piles, fever, diuretic, hydragogue, expectorant, sedative(Rastogi et al., 2001). Fruits contain tropeine alkaloid and solanine, with mydriatic action(Ghosh et al., 2008). They are also beneficial in treating inflammations and skin diseases(Abu et al., 2017; Chopra et al., 1992). The seeds are good for giddiness or dips. Boiling extracts of the leaf and fruit are used in North India to cure liver-related conditions such as jaundice(Abu et al., 2017). They can also use to cook spinach, apart from being used as a home remedy in mouth ulcers(Miraj, 2016; Wickens & Ambasta, 1988). Young fruits and leaves of farmed varieties are consumed in Indonesia. The fruit and leaves are either eaten raw as a traditional salad or cooked(Shivappa et al., 2019).

The juice extracted from its roots is used to treat asthma and whooping cough(Abu et al., 2017) in Assam(Miraj, 2016; Kirtikar KR, 1935). In Jordan, Jordanians use the fruit of *Solanum Nigrum* as antispasmodics and antirheumatics(Al-Qura'n, 2009). *Solanum Nigrum* fruits have long been used as skin antiseptics, diarrhoea medicines, expectorants, and laxatives in Yemen(Al-Fatimi et al., 2007). In India, the plant was utilized for treating tuberculosis(Kaushik et al., 2009). In Europe and South Africa, it is used to treat convulsions(Grieve, 1995). The Rappahannock is used as a weak infusion to cure insomnia(Vogel, 1970). The roots are beneficial for treating otopathy, ophthalmopathy, rhinopathy, and hepatitis (Mohamed Saleem et al., 2009; Mukhopadhyay et al., 2018). The CNS and reflexes within the spinal cord can be depressed by decocting the plant *(Mohamed Saleem et al., 2009; Abu et al., 2017)*. The juice of whole plants was used as sedative, hydragogue, diaphoretic, diuretic, chronic liver enlargement, blood-spitting, piles, and

dysentery symptoms in India (Karmakar et al., 1970; Ghani, 2003). Reported traditional activities of Solanum *Nigrum* are given in the below table 1.

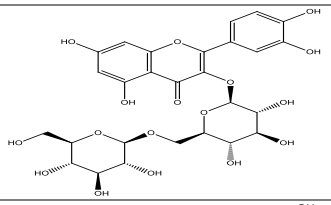
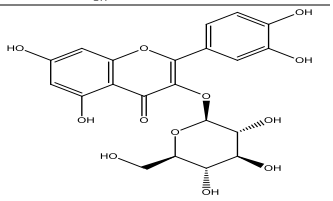
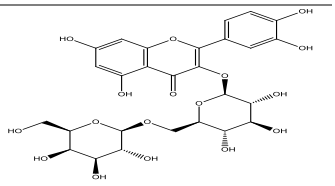
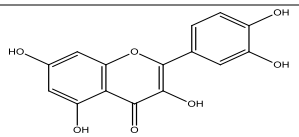
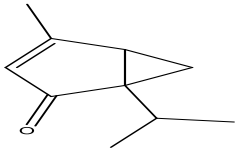
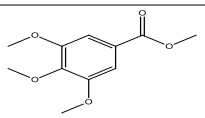
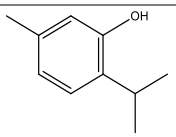
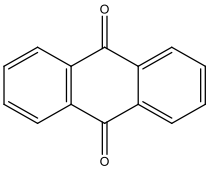
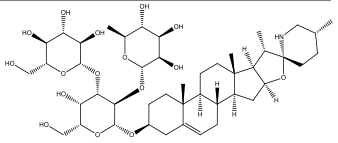
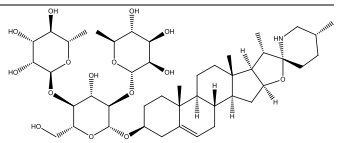
Table 1. Ethnomedical and traditional uses of Solanum nigrum

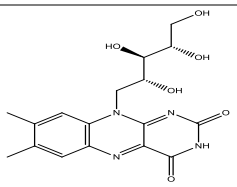
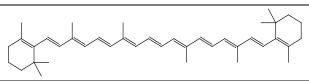
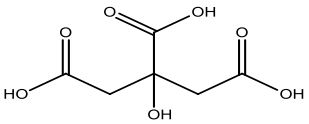
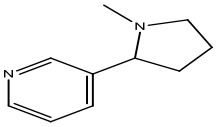
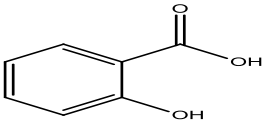
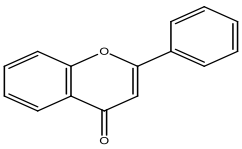
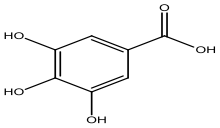
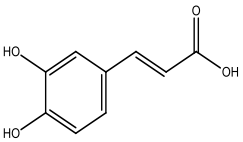
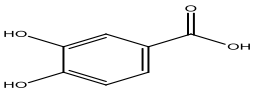
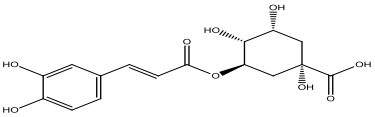
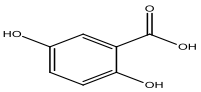
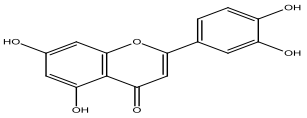
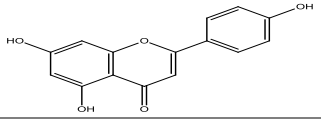
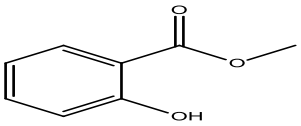
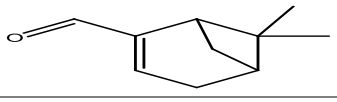
Reported traditional activities				
Parts of plants	**Method of preparation**	**Uses/ Application**	**Country/ State**	**References**
Leaves	Topically applied pounded leaf	Ringworm, Dressing of warts	Tanzania, Africa	(Moshi et al., 2009)
	Fresh leaves boiled with onion bulbs and cumin seeds	Stomachache, stomach ulcer	Tamil Nadu, India	(Jain et al., 2011; Ramya & Jayakumararaj, 2009)
	Topically applied paste	Wound healing		
	Paste	Liver tonic, indigestion	The Himalayan region, India	(Kala, 2005)
Fruits/ Berries	Juice	Gastric ulcer, gastritis, and other gastric problem	South India	(Rajeswari, 2013)
	Edible ripe fruits	Given kids to stop bed-wetting	Tanzania, Africa	(Moshi et al., 2009)
	Diluted infusion of berries	Blindness, conjunctivitis, Glaucoma, trachoma	Algeria, Africa	(Schultes, 1984)
Whole plants	Maceration	Snakebite/sting by a venomous animal	Congo, Africa	(Chifundera, 1998)
	Decoction of plants	Burns and dermal affections	Algeria, Africa	(Schultes, 1984)
Roots	Boiled with a pinch of sugar	Increase fertility in women	Thar Desert, India	(Parveen et al., 2007)

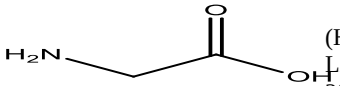
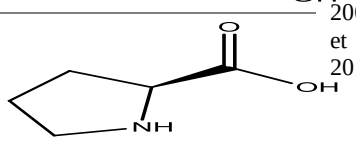
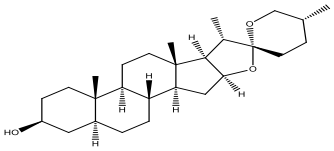
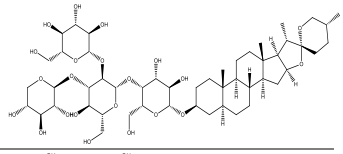
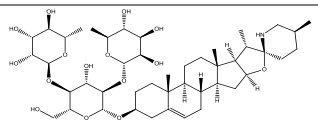
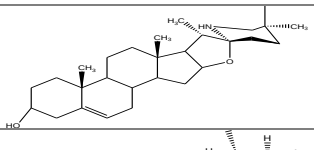
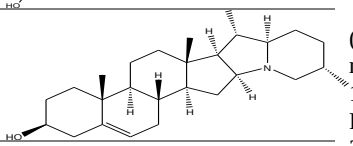
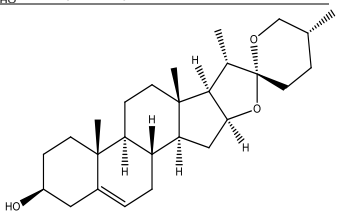
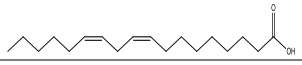
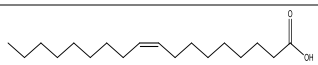
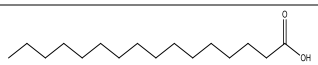
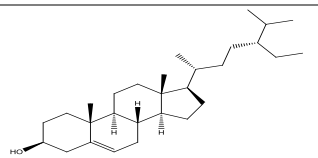
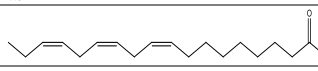
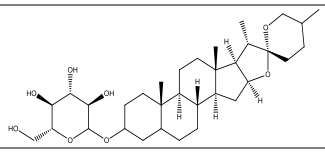
Phytochemical constituents

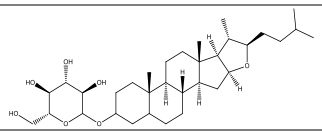
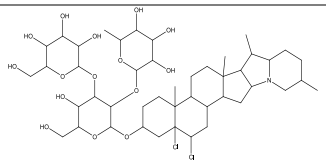
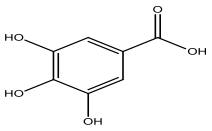
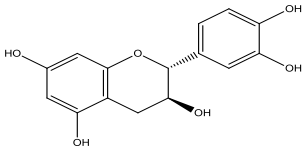
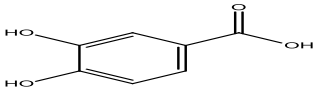
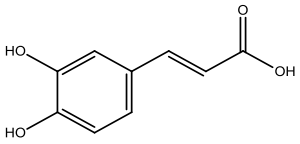
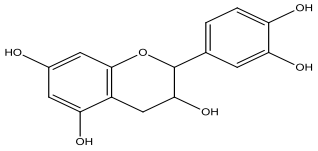
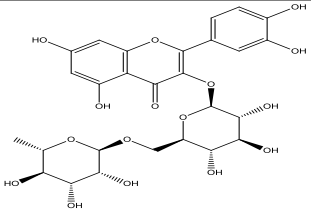
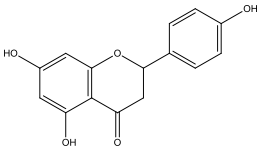
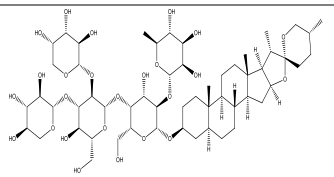
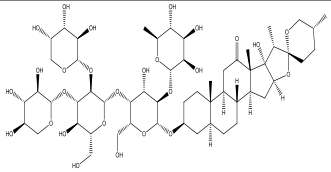
Solanum nigrum has a wide range of chemicals responsible for numerous activities. The most active ingredients are glycoalkaloids, glycoproteins, polysaccharides, and polyphenolic compounds that contain gallic acid, catechin, protocatechuic acid (PCA), caffeic acid, epicatechin, rutin, and naringenin (Sikdar, 2008). Glycoalkaloids are composed of solamargine, solasonine, and solanine, which are part of the tropane class of compounds (Jain et al., 2011). The presence of carbohydrates, alkaloids, tannins, saponins, steroids, glycosides, and gums was discovered during the phytochemical screening of the ethanolic extract of *Solanum nigrum* (Karmakar et al., 1970). Saponin, phytosterols, tannins, fixed oils, and lipids were found in hexane and benzene extracts, whereas carbohydrates, coumarins, phytosterols, and flavonoids were found in alcoholic extracts (Ravi, Saleem, Maiti, et al., 2009). Phytochemical screening of the aqueous extracts of *Solanum Nigrum* dried leaf powder confirms the presence of anthraquinones, resins, flavonoids, saponins, tannins, and alkaloids (A. Patel et al., 2014; Kokate et al., 1996). Riboflavin is abundant in the leaf, and it also has nicotine, vitamin C, beta-carotene, citric acid, protein, fat, steroidal glycol-alkaloids, solasonine, and solamargine(Karmakar et al., 1970; Ghani, 2003). It has a high concentration of polyphenols, mainly phenolic acid and flavones(Huang et al., 2010). Methanolic extracts of *Solanum Nigrum* dried leaf powder confirm the presence of five phenolic acids determination (gallic, protocatechuic, chlorogenic, gentisic, and caffeic) and two flavones: luteolin and apigenin. (Campisi et al., 2019). The fruits are rich sources of saponins and steroidal glycol-alkaloids (solanine, solamargine, solasonine, a and b-solanigrine) and the aglycone, solasodine, steroidal genin, trigogenin(Karmakar et al., 1970; Ghani, 2003), and two new disaccharides, as well as protein, minerals such as magnesium, phosphorus, and vitamins C, B, and folic acid. These disaccharides are ethyl beta-d-thevetopyranosyl -(1-4) -beta -D-oleandropyranoside and ethyl beta -d-thevetopyranosyl-(1-4) -alpha -D-oleandro- pyranoside isolated by chemical and spectroscopic methods(R. Chen et al., 2009). Seeds consist of solanine, protein, greenish-yellow oil consisting of linoleic, oleic, palmitic, stearic acids, and sitosterol(Karmakar et al., 1970). The seed oil of SN consists of palmitic acid (10.19%), stearic acid (4.6%), oleic acid (16%), linoleic acid (67.6%), and linolenic acid (0.85%)(Dhellot et al., 2006). Tartaric acid and citric acid are important for adaptive environmental stress(Sun et al., 2006). From methanolic extract of stems and roots of *S. Nigrum*, one spirostanol glycoside and two furostanol have been separated(Sharma et al., 1983). The entire plant of *Solanum Nigrum Linn.* yielded two new steroidal saponins, *nigrum*nin I and II, and two predominant saponins(Ikeda et al., 2000). The phytochemical constituents of *Solanum Nigrum* are listed in detail in table 2, and the structure is generated using the PubChem website and ChemDraw software.

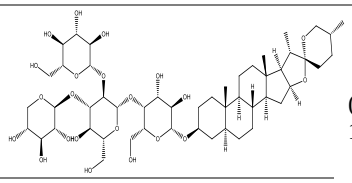
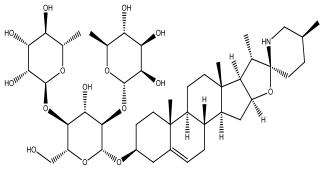
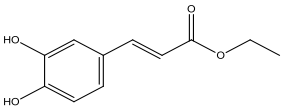
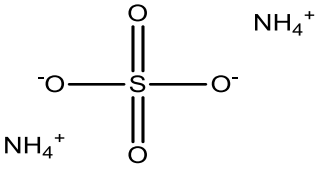
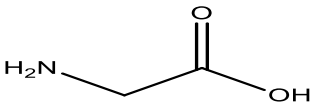
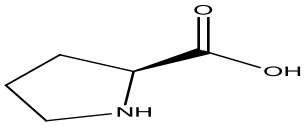
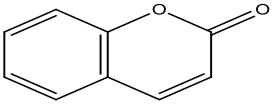
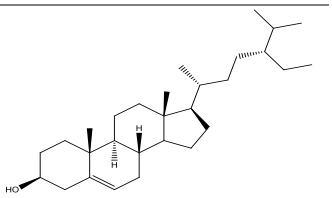
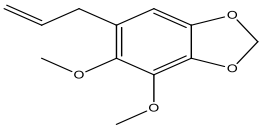
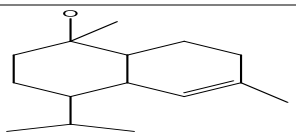
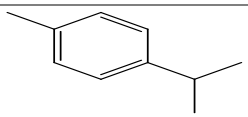
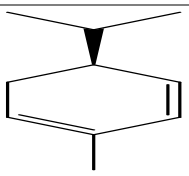
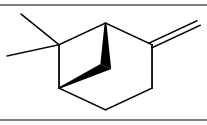
Table 2. Phytochemical Constituents

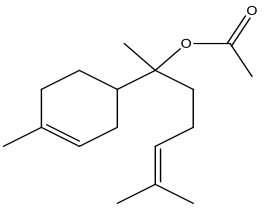
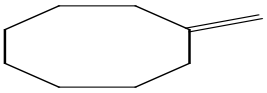
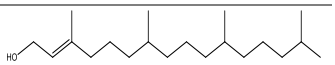
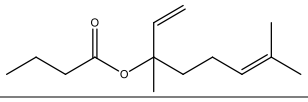
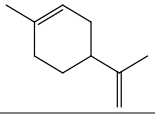
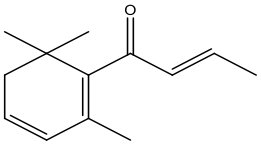
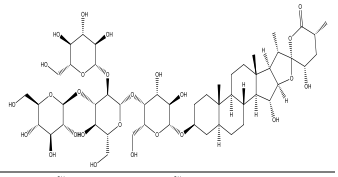
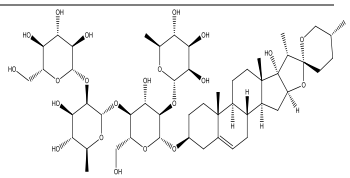
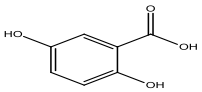
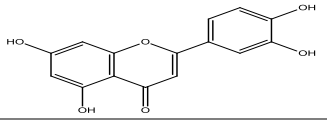
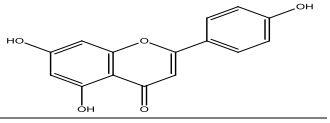
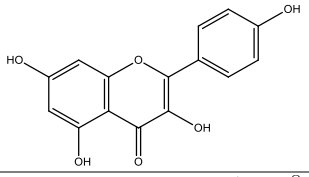
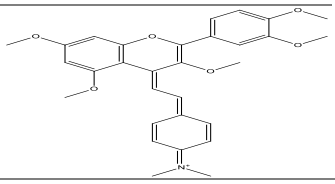
Parts of plant	Extracts/ compounds	Active constituents	Chemical Structure	References
Leaves	Isolated quercetin glycosides	3-gentiobioside		(A.M. Nawwar et al., 1989)
		3-glucoside		
		Quercetin 3-*O*-glucosyl galactoside		
		Quercetin		
	Crude leaf E.	Umbellulone		(Aburjai et al., 2014)
		Methyl eudesmate		
		Thymol		
	Aqueous E.	Anthraquinones		(A. Patel et al., 2014)
		Solasonine		
		Solamargine		

	Riboflavin		
	Beta-carotene		
	Citric acid		
	Nicotine		
	Polyphenols (phenolic acid)		(Huang et al., 2010)
	Flavones		
Methanolic E.	Gallic acid		(Campisi et al., 2019)
	Caffeic acid		
	Protocatechuic acid		
	Chlorogenic acid		
	Gentisic acid		
	Luteolin		
	Apigenin		
Crude fruit oil	Methyl salicylate		(Aburjai et al., 2014)
	Myrtenal		

	Glycoproteins (Hydrophobic amino acids)	Glycine		(Heo & Lim, 2004; Jain et al., 2011)
		Proline		
	Steroidal genin	Tigogenin		(Shivappa et al., 2019)
	Ethanolic E.	Degalactotigonin		(Lin et al., 2007)
		Beta-2 solamargine		
	Steroidal glycol-alkaloids	Solasodine		(Karmakar et al., 1970; Rani et al., 2017; Ghani, 2003)
		Solanidine		
		Steroidal genin (Diosgenin)		
Seeds	Isolated Seed oil	Linoleic acid		(Karmakar et al., 1970; Dhellot et al., 2006)
		Oleic acid		
		Palmitic acid		
		Stearic acid		
		Sitosterol		
		Linolenic acid		
		Spirostanol glycoside		(Sharma et al., 1983)

Stems and Roots	Methanolic E.	Furostanol glycoside		
	Steroid alkaloid	Solanine		(Ji et al., 2008)
	Polyphenolic compounds	Gallic acid		(Jain et al., 2011; S. J. Lee et al., 2004; Sikdar, 2008)
		Catechin		
		Protocatechuic acid (PCA)		
		Caffeic acid		
		Epicatechin		
		Rutin		
		Naringenin		
	Methanolic E.	*Nigrum*nin I		(Ikeda et al., 2000)
		*Nigrum*nin II		

Whole plant	Glycoalkaloids	β-2 Solamargine		(Hu et al., 1999)
		Degalactotigonin		
	Ethanolic E.	(E)-ethyl caffeate		(Jain et al., 2011)
	Glycoprotein	Ammonium sulfate		(Heo & Lim, 2004)
		Glycine		(K. R. Lee et al., 2004)
		Proline		
	Alcoholic E.	Coumarin		(Ravi et al., 2009)
		Phytosterol		
	Volatile constituents of the essential oil	Dillapiole		(Taherpour et al., 2017)
		α-Cadinol		
		Para-Cymene		
		α-Phellandrene		
		β-Pinene		

	α-Bisabolol acetate		
	8-methylene tricyclooctane		
	Phytol		
	Linalyl butanoate		
	Limonene		
	β-damascenone		
Steroidal saponins	solanigrosides C		(Abu et al., 2017; Zhou et al., 2006)
	solanigrosides H		
Isolated crude E.	Gentisic acid		(Rani et al., 2017)
	Luteolin		
	Apigenin		
	Kaempferol		
	Anthocyanidin		

Reported Pharmacological activities

Solanum Nigrum Linn. is a traditional medicinal plants and famous for its anti-cancer(S. Patel et al., 2009), anti-microbial(Kavishankar et al., 2011), antioxidant(Karmakar et al., 1970**;** Rani et al., 2017), anti-inflammatory(Abu et al., 2017), antipyretic, antinociceptive(Jain et al., 2011**;** Zakaria et al., 2012)**,** anti-diabetic(Sathya Meonah et al., 2012; Aali et al., 2011), cytotoxic(Karmakar et al., 1970) cardio-protective (Varshney et al., 2016)**,** hepatoprotective(Raju et al.,

2003**;** Drotman & Lawhorn, 1978)**,** anti-tumor(H. Chen & Qi, 2013)**,** Anticonvulsant(Eva González-Trujano et al., 2006**;** Wannang et al., 2008), and neuro-pharmacological properties(Sathya Meonah et al., 2012). The plants possess numerous pharmacological activities. The significant phytoconstituents responsible for pharmacological activities are listed below in the table 3.

Table 3: Reported Pharmacological Activities of Solanum nigrum

Parts of plant	Extracts / active constituents	Model used	Therapeutic dose	Reported uses	References
Leaves	***In-vivo* activities of leaves**				
	Aqueous E.	picrotoxin, pentylenetetrazole induced seizure in rat and mice	30-60 mg/Kg of body weight	Anticonvulsant, Anti-seizure	(Eva González-Trujano et al., 2006; Wannang et al., 2008)
	Chloroform E.	*In-vivo* rat and mice model	20-200 mg/Kg	Anti-inflammatory antipyretic, anti-nociceptive	(Jain et al., 2011**;** Zakaria et al., 2012)
	Aqueous E.	Oral glucose-induced diabetic rat	200 mg and 400 mg/Kg	Hypoglycemic, Anti-diabetic	(Sathya Meonah et al., 2012; Aali et al., 2011)
	Aqueous E.	Busulfan plus infrared radiation and Methotrexate induced oral mucositis in rats	100 mg and 200 mg/Kg	Oral mucositis	(A. Patel et al., 2014)
	Ethyl acetate E. (Glucosinolate)	Against Culex quinquefasciatus	25 mg/L	Anti-larvicidal	(Rawani et al., 2014)
	Aqueous E.	Immobilization stress-induced pro-oxidant in rats	100 mg/Kg	Anti-stress	(Zaidi et al., 2014)
	Aqueous E.	Lead acetate induced toxicity in brains of mice	200mg/Kg	Protective Effects	(Chinthana et al., 2012)
	Aqueous E.	Ethanol-induced gastritis pylorus ligated rats	250mg/Kg	Anti-gastritis and anti-ulcerogenic	(Rajeswari, 2013)
	Alkaloids	Patients in the age group of 35 – 60 years for 90 days	Dose dependently	Anti-diabetic	(Sugunabai et al., 2014)
	Glycoprotein	Patients in the age group of 35 – 60 years for 90 days	Dose dependently	Antihyperlipidemic	
	***In-vitro* activities of leaves**				
	Methanol: water (80:20)	Sunflower oil model	2%	Anti-oxygenic Effects	(Padmashree et al., 2014)
	Ethanolic E.	Free radical mediated DNA sugar damage	5-25µg/ml	Hepato-protective	(Sultana et al., 1995)
	Aqueous E.	Against adult L. acuminata and larvae of Cx. vishnui group.	1, 2, and 3%	Molluscicidal & mosquito larvicidal activities	(Rawani, Ghosh, & Chandra, 2014)
	Phytosterol isolated from chloroform: methanol (1:1 v/v) extract	*In-vitro* against early 3rd instar larvae of the Cx. vishnui group and An. subpictus.	25, 45, and 60 mg/L	Anti-larvicidal, mosquitocidal agents	(Rawani et al., 2017)
	Ethyl acetate E.	Against Culex quinquefasciatus Say	Dose dependently	Mosquito larvicidal agents	(Rawani et al., 2010)
	Methanol And Aqueous E.	Agar well disc diffusion method	100µg/ml per disc	Anti-bacterial	(A. John de Britto & Plant, 2011)
	Methanol, ethanol and ethyl acetate E.	Agar well disc diffusion method against fungal strain	500µg/ml	Anti-fungal	(Sridhar et al., 2011)
	Methanol E.	Agar well disc diffusion method	Dose-dependently	Antimicrobial	(Kavishankar et al., 2011)
	Ethanol, methanol, ethyl acetate, diethyl ether, chloroform and hexane E.	Agar well disc diffusion method	500µg/ml	Anti-bacterial and anti-fungal	(Sridhar & Naidu, 2011)
	***In-vivo* activities of fruits**				
	Ethanolic E.	CCl4-induced hepatic damage rat Model	250mg/Kg	Hepatoprotective or liver disease	(Raju et al., 2003**;** Drotman & Lawhorn, 1978)
		$CdCl_2$ induced hepatotoxic albino rat	200mg/kg	Hepatoprotective	(Abdel-Rahim et al., 2014)
	Aqueous E.	Alloxan induced diabetic rat	200mg/kg, 400mg/kg	Anti-diabetic	(Umamageswari et al., 2017)
	Ethanolic E.	Carrageenan induced oedema in the hind paw rat model	500mg/Kg	Anti-inflammatory	(Jain et al., 2011**;** Li et al., 2010)
	Methanolic and Aqueous E.	Oral glucose induced diabetic rat	200mg/kg and 400mg/kg	Anti-diabetic effects	(Sathya Meonah et al., 2012)
	Methanol E	Carrageenan induced rat paw oedema model	375Mg/Kg	Anti-inflammatory	(Arunachalam et al., 2009**;** Ravi, et al., 2009)

Fruits/ Berries	Petroleum ether, ethanol, and aqueous E.	Effect on clonidine-induced catalepsy	50, 100 and 200 mg/kg, i.p.	Anti-allergic, anti-histaminic, anti-asthmatic	(Nirmal et al., 2012)(Yerukali Sudha Rani, V. Jayasankar Reddy, Shaik Jilani Basha, Mallapu Koshma, 2017)
		Milk-induced leukocytosis in mice			
		Milk-induced eosinophilia in mice			
		In-vivo albino mice	1300mg/kg	Acute toxicity	
	Ethanol E.	PTZ induced seizure in mice	300 mg/kg p.o.	Anticonvulsant	(H. Le Son & Yen, 2014)
	Ethanolic E.	Acetic acid-induced writhing in mice model	500mg/kg	Analgesic activity	(Kaushik et al., 2009; Karmakar et al., 1970)
		Castor oil-induced diarrhea in mice	250mg/kg and 500mg/kg	Anti-diarrheal	
	Aqueous E.	U14 cervical-cancer induced mice	200mg/Kg and 500mg/Kg	Anti-tumour or anti-proliferative effects	(Li et al., 2008)
	Aqueous E.	Acute Oral Toxicity test by up-and-down procedure on mice	3129 mg/kg	Acute oral toxicity	(H. Le Son & Yen, 2014)
	Methanol E	Uterotrophic assay in ovariectomized mouse model	100mg/kg	Estrogenic activity	(Jisha et al., 2011)
	Ethanolic E.	Serum sex hormone and testis of male Wister rat	500mg/kg for 60 days	Anti-spermatogenic and anti-androgenic activity	(Meerwal & Jain, 2019)
	Methanolic E.	Doxorubicin-induced cardio-toxicity in rat	1gm/Kg/day for 30 days	Cardio-protective	(Varshney et al., 2016)
	Aqueous E.	Aspirin-induced gastric ulcers of pylorus ligated rats	50mg/kg	Anti-gastritis and anti-ulcerogenic	(Rajeswari, 2013)
	Methanolic E.	Aspirin induced ulceration in rats	400,500 and 1000 mg/kg for 7 days	Anti-ulcerogenic	(Jainu & Devi, 2006)
	Ethanolic E.	Eddy's hot plate and acetic acid-induced writhing rat	250mg/kg and 500mg/kg	Analgesic	(Kaushik et al., 2009)
	Ethanolic E.	Carrageenan-induced rat paw edema	500mg/kg	Anti-inflammatory	(Kaushik et al., 2009)
	SNL Glycoprotein (150 kDa)	DSS-induced colitis in A/J Mouse	10 and 20 mg/kg	Preventive effect	(Joo et al., 2009)
	Steroidal glycoside (Glucosinolate)	Ovariectomized mouse model using Uterotropic assay	100mg/kg	Estrogenic activity	(Jisha et al., 2011)
	β -sitosterol	Clonidine-induced catalepsy	200mg/kg	Anti-asthmatic and anti-cataleptic	(Rani et al., 2017; Nirmal et al., 2012)
	***In-vitro* activities of fruits**				
	Petroleum ether, ethanol, and aqueous E.	Histamine-induce contraction on guinea pig ileum	100µg/ml	Anti-allergic, anti-histaminic, anti-asthmatic	(Rani et al., 2017; Nirmal et al., 2012)
	Methanol E.	HAP binding assay on MCF-7 cell line	80-320µg/ ml	Estrogenic activity	(Jisha et al., 2011)
	Ethanolic E.	Pentobarbital induced sleeping time in rat	510mg/kg	Neuropharmacological activity	(Perez G. et al., 1998)
	Ethanolic E.	DPPH radical scavenging assay	200µg/ml	Antioxidant	(Rani et al., 2017; Karmakar et al., 1970)
		Brine shrimp lethality bioassay	160µg/ml	Cytotoxic activity	
	Methanolic E.	*In-vitro* ischemia-reperfusion injury	2.5 and 5.0 mg/kg for 6 days per week for 30 days.	Cardio-protective	(Chauhan et al., 2012; BHATIA NITISH , MAITI PARTHA PRATIM, KUMAR ABHINIT, 2011)
	Ethanolic E.	Agar well disc diffusion method	25,50,75, 100mg/kg	Anti-microbial	(Kaushik et al., 2009)
	Methanolic E.	HeLa cell line by SRB and MTT assay	10 mg/ml to 0.0196 mg/ml	Anti-cancer	(S. Patel et al., 2009)
	Ethanolic E.	Disc diffusion method	500µg/disc	Anti-bacterial	(Kaushik et al., 2009; Karmakar et al., 1970)

	Ethanolic E.	Induces apoptosis in MCF-7 breast cancer cell line using MTT assay	50µg/ml	Cytotoxic effect	(Y. O. Son et al., 2003)
	Anthocyanin from Acetic acid and ethanol E.	DM130 macro- porous resin, Sephadex LH20, and a C18 column	Dose-dependently	Antiulcer, antioxidant	(Meng et al., 2020)
	Steroidal glycoside (Glucosinolate)	MCF-7 cell line by MTT assay	100mg/kg	Estrogenic activity	(Jisha et al., 2011)
	***In-vivo* activities of whole plants**				
	Ethanolic E.	Lipofundin induce hyperlipidemia in rabbits	300mg/kg	Anti-hyperlipidemic	(Ali, 2016)
	Ethanolic E.	Oral glucose-induced diabetic albino rat	250mg/kg for 5-7 days	Anti-diabetic	(Umamageswari et al., 2017**;** Aali et al., 2011)
	Aqueous E.	U14 cervical carcinoma bearing mice	250 and 500mg/kg	Anti-tumour	(Li et al., 2008)
	Aqueous E.	*In-vivo* C57BL/6 mice model	2mg/kg daily for 15 days	Metastatic melanoma cancer	(Wang et al., 2010)
	Aqueous E.	CCl_4 -induced chronic hepatotoxicity in rats	500 and 1000mg/kg for 6 weeks	Hepato-protective and liver disease	(Jain et al., 2011**;** Cai et al., 2010)
	Methanol E.	CCl_4 -induced chronic hepatotoxicity in rats	250 and 500mg/kg	Liver damage	(Elhag et al., 2011)
	Aqueous E.	CCl_4- and TAA-induced oxidative damage in rats.	200, 500, and 1000 mg/kg for 6 weeks	Hepatoprotective	(Lin et al., 2008)
	SNL- Polysaccharide	U14 cervical cancer-bearing mice	90, 180, 360 mg/kg	Immunomodulator and an anticancer, Antitumor agent	(Li et al., 2009)
	SNL- Polysaccharide-1a	U14 cervical cancer on thymus tissue of tumour-induced apoptosis on mice	25 and 50mg/kg for 12 days	Anti-cervical cancer and modulating properties	(Li et al., 2010**;** Li et al., 2007)
	Methanolic E.	Carrageenin and egg white induced hind paw oedema in rat	100 and 200mg/kg	Anti-inflammatory	(Arunachalam et al., 2009)
Whole plants	SNL- Polysaccharide	Lymphocyte proliferation in H22 tumor-bearing mice	30, 60, 120mg/kg	Anti-tumor	(H. Chen & Qi, 2013)
	***In-vitro* activities of whole plants**				
	SNL-glycoalkaloids solamargine and solasonine	Colon (HT29) and Liver (HepG2) Cancer Cells using MTT assay	0.1, 1, 10, and 100µg/ml	Anti-proliferative, anti-cancer	(K. R. Lee et al., 2004)
	SNL- glycol-alkaloids (Solanine)	MTT assay on HepG2, SGC-7901, and LS-174 cells line	100µl/well	Anti-tumor	(Ji et al., 2008)
	Ethanol E.	Gentamicin induced toxicity on Vero cell by MTT, hydroxyl radical scavenging activity assay, and trypan blue exclusion assay	10-1000µg / ml	Cytoprotective	(Mohamed Saleem et al., 2009**;** Prashanth Kumar et al., 2001)
	Aqueous E.	Mouse melanoma B16-F1 cells line through MTT assay	0.5gm/ml	Anti-metastatic effects	(Wang et al., 2010)
	Methanolic E. and phenolic compound (polyphenol)	DPPH radical scavenging activity	Dose-dependent	Anti-oxidant	(Jain et al., 2011**;** Akula & Odhav, 2013)
	SNL-glycoprotein	MCF-7 cell lines using DPPH, 2-deoxyribose oxidation, and superoxide anion scavenging assay.	20µg /mL	Anti-oxidative	(Heo & Lim, 2004)
	SNL-glycoprotein	Apoptosis-induced HCT-116 cells line	10, 20 and 40µg /ml	Apoptotic effects	(S. J. Lee et al., 2004)
	SNL-glycoprotein	Induced tumour promotion in HCT-116 cells through MTT, DNA fragmentation and H33342 and ethidium bromide staining assay	0–40µg /ml	Cytotoxic and apoptotic effects	(S. J. Lee et al., 2004)
	Solamargine	Induces apoptosis on human cholangiocarcinoma on QBC939 cell using MTT assay	Dose-dependent	Cholangiocarcinoma	(Zhang et al., 2018)

	Aqueous E.	Induced apoptotic death in HepG2 cells	100-5000µg /ml	Cytotoxic effects	(Lin et al., 2007)
		Induced apoptotic death of HepG2 cells	2 and 5 mg/ml	Apoptotic effects	
		Induced autophagic death in HepG2 cells.	50-1000µg/ml	Autophagy effects	
	Steroidal alkaloid glycoside (solamargine)	Human hepatoma SMMC-7721 and HepG2 cells and induced cell apoptosis using MTT assay	40µg //ml	Anticancer	(Ding et al., 2012)
	Crude E.	Modified disc diffusion method	1.0 mg/disc and 5.0 mg/disc	Anti-microbial	(Ramya et al., 2012)
Roots	***In-vitro* activities of roots**				
	Methanolic E.	*In-vitro* fungal and bacterial strain model	Dose-dependent	Antimicrobial	(Chauhan et al., 2012; Hameed et al., 2017)
	Ethanol, ethyl acetate, diethyl ether	Agar well disc diffusion method	100µg/ml	Anti-bacterial	(Sridhar & Naidu, 2011)
Seeds	***In-vitro* activities of seeds**				
	Methanol and chloroform E.	HCV NS3 protease into the liver cell	Dose-dependent	Anti-HCV, anti-viral activity	(Javed et al., 2011)
	Methanol, ethyl acetate, and ethanol E.	Agar well disc diffusion method	2.0-6.0µg/ml	Antimicrobial, anti-fungal	(Chauhan et al., 2012; Sridhar & Naidu, 2011)
	Lunasin peptide	Oxidative DNA damage caused by iron using DNA cleavage assay	Dose dependently	Anti-oxidant, Anticancer	(Jeong et al., 2010)

Toxicology profile

Certain portions of the Solanum *nigrum* plant may be deadly to humans and livestock(Miraj, 2016). Poisoning has killed children who ingested unripe berries. On the other hand, the ripe berries producing minor gastrointestinal aches, vomiting, and diarrhea. Nightshade poisoning may occur in various species, including cattle, sheep, poultry, and pigs(Edmonds & Chweya, 1997). Solanine, the poisonous glycol-alkaloids, is found in all plant sections except the mature fruit, and eating unripe fruits may cause poisoning with solanine-like symptoms. Symptoms of poisoning are usually delayed for 6 to 12 hours after intake(Schep et al., 2009). Fever, sweating, vomiting, stomach discomfort, diarrhea, disorientation, and sleepiness are the first signs of poisoning. Ingesting considerable amounts of the plant causes cardiac rhythms and respiratory collapse, which may lead to death(*Solanum Nigrum L. IPCS. INCHEM.*, n.d.). Grazing the leaves of S. *nigrum* has also poisoned livestock due to nitrate toxicity. The majority of poisoning incidents are thought to be caused by eating unripe fruit or leaves(Edmonds & Chweya, 1997). Black nightshade includes atropine and scopolamine in its stems, leaves, berries, and roots, which paralyze the body's involuntary muscles, including the heart. Even physical contact with the leaves might irritate the skin(*7 of the World's Deadliest Plants | Britannica*, n.d.). Toxins in S. *nigrum* are mostly contained in the unripe green berries; hence, immature fruit should be avoided(Schep et al., 2009; *Solanum Nigrum L. IPCS. INCHEM.*, n.d.; Edmonds & Chweya, 1997). The cooked ripe fruit of the black Solanum *nigrum* has been considered safe to consume. Since the breakdown temperature of solanine is substantially higher, at 243°C, detoxification cannot be ascribed to conventional cooking temperatures. Solanum *nigrum* leaves should be cooked like a vegetable with the cooking water removed and replenished numerous times to eliminate toxins(Kuete, 2014a; Kuete, 2014b; Knight, 2011). According to recent studies on animals done by some pharmacologists, up to 3100 mg/kg compound is safe but elevated dose from 3100mg/kg can cause different types of toxicity(Edmonds & Chweya, 1997).

RESULTS AND DISCUSSIONS

Solanum Nigrum Linn. (*European black Nightshade or Makoi*), a member of the *Solanaceae* family, is well-known in traditional Indian and Chinese medicine for its numerous pharmacological actions. In traditional medicine and the Ayurveda system, these plants were used in various treatments, such as eye disorders(Mohamed Saleem et al., 2009), ulcers(Rajeswari, 2013), liver tonics, skin diseases(Mohamed Saleem et al., 2009), asthma, whooping cough(Abu et al., 2017; Miraj, 2016; Kirtikar KR, 1935), and other inflammatory conditions. *S. Nigrum* was discovered to contain a variety of active phytoconstituents such as glycoproteins(Heo & Lim, 2004**;** K. R. Lee et al., 2004), polysaccharides, polyphenolic compounds(Jain et al., 2011**;** S. J. Lee et al., 2004), steroidal saponins(Ikeda et al., 2000) and glycol-alkaloids(Hu et al., 1999) such as solamargine, solasonine, and solanine, which are responsible for antimicrobial (Kaushik et al., 2009), anti-diabetic(Sathya Meonah et al., 2012), anti-inflammatory(Arunachalam et al., 2009**;** Ravi et al., 2009), antioxidant (Akula & Odhav, 2013), antitumor (Li et al., 2008), anticancer (S. Patel et al., 2009), antidiarrheal(Kaushik et al., 2009), cytotoxic(Y. O. Son et al., 2003**;** Huang et al., 2010), and cardioprotective activities. Various methods have been used to isolate and describe the significant compounds, and *In-vivo*, *In-vitro* activities have also been investigated.

CONCLUSIONS

Solanum Nigrum Linn. is an excellent candidate plant for constructing targeted medications, even though it is mentioned as a component in several prominent polyherbal formulations. In contrast, the specific mechanism of action in obesity, neuropharmacology, anti-emetics, immunomodulator or immunostimulant, and many other situations is unknown. To assess the usefulness of this plant with a wide range of therapeutic characteristics in whole organism systems, well-designed clinical investigations and human trials are needed. As per traditional claims, these plants are expected to be a significant source of novel compounds and raw materials for pharmaceutical manufacturing. Many of these plants are discovered in wild areas, so they must be grown locally and don't need any special care to grow. This plant is explored for its anticancer, antitumor, antioxidant, and hepatoprotective efficacy. In the future, it might be a potent drug for chemotherapeutic agents to treat cancer and tumours in the alternative to synthetic drugs, as synthetic drugs have more side effects on the human body. The stem, flower, root, and seed contain numerous vital bioactive constituents that are unexplored. Future researchers have an excellent opportunity to investigate them and elucidate their activities and mechanisms in different diseases.

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