WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 8, 353-367. Review Article ISSN 2277– 7105

ANTIEPILEPTIC ACTIVITY OF SOME MEDICINAL PLANTS OF SOLANACEAE FAMILY-A REVIEW

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Article Received on
21 May 2016,

Revised on 12 June 2016,
Accepted on 03 July 2016

DOI: 10.20959/wjpr20168-6652

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ABSTRACT

The Solanaceae family consists of about 98 genera and 2,700 species with a great diversity of habitats and morphology. This family is known for having a diverse range of alkaloids. To humans, these alkaloids can be desirable, toxic, or both. The many species contain a variety of alkaloids that can be more or less active or poisonous, such as scopolamine, atropine, nicotine and hyoscyamine. Herbal preparations are used in the management of various forms of epilepsy is very common in many parts of the world. They have been scientifically shown to possess promising anticonvulsant activities in animal models. Present review covers some important alkaoids like tropanes, solanine and solasodine present in the family. Also an attempt was taken to compile the Anti-epileptic activity of some important medicinal plants of the Solanaceae family that have antiepileptic activity like *Solanum nigrum, Solanum pubescens, Hyoscyamus niger and Withania somnifera.*

KEY WORDS: Epilepsy, Solanaceae, *Solanum nigrum, Solanum pubescens, Hyoscyamus niger, Withania somnifera.*

INTRODUCTION

Psychological, health and social problems are an increasing worldwide. 2001 has declared as the year for mental health by the World Health Organization in recognition of the burden that mental and brain disorders imposed on people and families. Last ten years of the 20th century

is called in neuroscience "decade of the brain".[1] Epilepsy is among the disorders that are strongly associated with significant psychological and social consequences for everyday living.

Epilepsy is a collective term for a group of chronic seizure disorders that have common, sudden, and transient episodes or seizures with loss or disturbance of consciousness that have usually, but not always with the characteristic body movements(convulsions) and sometimes with autonomic hyperactivity. It always correlates with disordered and rhythmic high frequency discharge of impulses by a group of neurons in the brain.[2] The disease affects approximately 1% of the world population. There is no doubt that epilepsy is the most encountered neurological conditions worldwide. Prolonged and sometimes life-long drug therapy is required.[3] The prevalence of epilepsy in developing countries is usually higher than in developed countries.[4] However, the problem of adverse effects has also not been solved completely and approximately 30% of the patients continue to have seizures with current Antiepileptic drugs therapy.[5]

Herbal preparations are used in the management of various forms of epilepsies is very common in many parts of the world. They have been scientifically shown to possess promising anticonvulsant activities in animal models for screening for anticonvulsant activity.[6] Herbal medicine is still the mainstay for primary health care about 75-80 % of the world population, mainly in the developing countries, because of better cultural acceptability, better compatibility with the human body and lesser side effects. Global estimates indicate that 80% of about 4 billion population cannot afford the products of the Western Pharmaceutical Industry and have to rely upon the use of traditional medicines which are mainly derived from plant material.[7] Considering the great reliance on traditional medicinal plants for treatment of diseases and the potential for drug discovery; it becomes relevant to search for potent, effective and relatively safe plant medicines. Hence, search should continue to develop newer, more effective, and safer herbal neuro protective agents for treatment of epilepsy.

THE SOLANACEAE FAMILY

The Solanaceae or nightshade family consists of about 98 genera and some 2,700 species with a great diversity of habitats and morphology. Solanaceae family belongs to the order Solanales, in the asterid group dicotyledons (Magnoliopsida). This family has a worldwide distribution, being present on all continents except Antarctica. The greatest diversity in

species is found in South America and Central America. Most members of the Solanaceae are erect or climbing, annual or perennial herbs, but shrubs are not uncommon and there are a few trees. The Solanaceae contain 98 genera and some 2,700 species.[8]

Solanaceae family is known for having a diverse range of alkaloids. Alkaloids are nitrogenous organic substances produced by plants as a secondary metabolite that have an intense physiological action on animals even at low doses. To humans, these alkaloids can be desirable, toxic, or both. The plants that contain these substances have been used for centuries as poisons. However, despite being recognized as poisons, many of these substances have invaluable pharmaceutical properties. Glycoalkaloids are nitrogen containing secondary metabolites found in plants belonging to Solanaceae and Liliaceae family. More than 100 different types of glycoalkaloids have been isolated from more than 350 Solanum species.[9]

ACTIVE CONSTITUENTS OF SOLANACEAE FAMILY

Plant such as *Solanum tuberosum* contains glycoalkaloids. Glycoalkaloids concentration depends upon species as well as part of plant such as leaf, root, flower and stem. The amount of glycoalkaloids increases due to injury and exposure to light.[10] The many species contain a variety of alkaloids that can be more or less active or poisonous, such as scopolamine, atropine, hyoscyamine, and nicotine. Most well-known alkaloids found in the Solanaceae family are the tropanes.

Tropanes

Tropanes are bicyclic organic nitrogen compounds with the chemical formula of $C_8H_{15}N$ (Fig.1). These alkaloids include, atropine, cocaine, scopolamine, and hyoscyamine. *Hyoscyamus muticus* and *Scopolia atropioides* contain scopolamine which is used as an antiemetic against motion sickness or for people suffering from nausea as a result of receiving chemotherapy.[11] Scopolamine and hyoscyamine are the most widely used tropane alkaloids in pharmacology and medicine due to their effects on the parasympathetic nervous system. Atropine has a stimulant effect on the central nervous system and heart, whereas scopolamine has a sedative effect. These alkaloids cannot be substituted by any other class of compounds, so they are still in demand. Pharmacologically, they are the most powerful known anticholinergics in existence, meaning they inhibit the neurological signals transmitted by the endogenous neurotransmitter, acetylcholine. Atropine, which is a commonly used ophthalmological agent, dilates the pupils and thus facilitates examination of the interior of the eye. Despite the extreme toxicity of the tropanes, they are useful drugs

when administered in extremely small dosages. They can reverse cholinergic poisoning, which can be caused by overexposure to organophosphate insecticides and chemical warfare agents such as sarin and VX. Overdose may include dry mouth, dilated pupils, ataxia, urinary retention, hallucinations, convulsions, coma, and death. They are found in various species, such as mandrake *(Mandragora autumnalis)*, black henbane or stinking nightshade *(Hyoscyamus niger)*, belladonna *(Atropa belladonna)* the Stramonium *(Datura stramonium*) and *Brugmansia* species, as well as many others in the Solanaceae family.[12]

Fig.1: Tropane Ring

Solanine: Solanine is a toxic glycoalkaloid found in leaves, fruit, and tubers of various plants in Solanaceae family(Fig.2). The amount of these glycoalkaloids in plants like potatoes, for example, varies significantly depending of environmental conditions during their cultivation, the length of storage, and the variety. Solanine has the formula $C_{45}H_{73}NO_{15}$ and is formed by the alkaloid solanidine with a carbohydrate side chain. Its production is thought to be an adaptive defence strategy against herbivores. Substance intoxication from solanine is characterized by gastrointestinal disorders like abdominal pain diarrhoea, vomiting and neurological disorders headache and hallucinations. After ingestion symptoms become manifest 8 to 12 hr. The median lethal dose is between 2 and 5 mg per kg of body weight. The average glycoalkaloid concentration is 0.075 mg/g of potato.[13] Berries from species such as *Solanum nigrum* or *Solanum dulcamara*, or green potatoes are responsible for poisonings in people due to Solanine.[14]

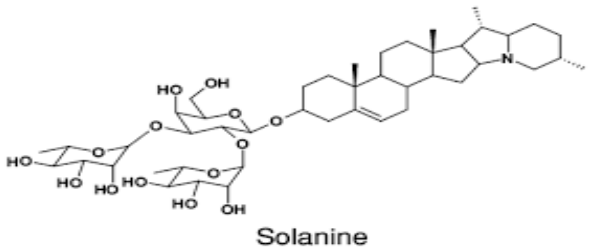
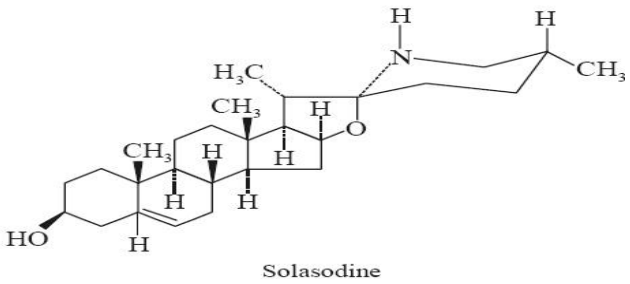


Fig.2

Solasodine

Solanaceae family (Genus Solanum) is rich in steroidal glycoalkloids,which is an important group of plant secondary metabolites. These compounds are used as starting material for the synthesis of steroidal drugs(Fig.3). In majority of solanaceous plants, solasodine occurs as aglycone part of glycoalkloids, which is a nitrogen analogue of sapogenins. Solasodine has C27 cholestane skeleton. It can be readily converted to 16-dehydropregnenolone, which is a key intermediate in the synthesis of steroidal drugs such as progesterone and cortisone.[15] Solasodine is obtained by chemical or microbial hydrolysis of solamargine. It is a potent moiety to be used as a substitute for diosgenin in the semi-synthetic production of steroidal hormones in pharmaceuticals. Therefore, steroidal glycoalkaloid from Solanaceae plants have become increasingly important as the starting material for the production of steroidal hormones.[16] An anticonvulsant and CNS depressant effect of solasodine isolated from *S. sisymbriifolium* using several experimental models was investigated. The results showed that in the PCT-induced convulsions intraperitoneal injection of solasodine significantly delayed latency of hind limb tonic extensor phase. In the MES model, solasodine significantly reduced duration of HLTE in a dose-dependent manner. Prior treatment of solasodine significantly potentiated thiopental-provoked sleep in a dose-dependent manner.[17]



Solasodine

Fig.3

ANTI EPILEPTIC PLANTS OF SOLANACEAE FAMILY

Medicinally, as well as in terms of poisoning and psychotropic effects, members of Solanaceae have been prized for their alkaloid content and used throughout history. Some of the medicinally important plants of Solanaceae family which have anti-epileptic activity are *Solanum nigrum* (black nightshade), *Solanum pubescens, Hyoscyamus niger* and *Withania somnifera* (Ashwaganda).

Solanum nigrum (black nightshade): *Solanum nigrum* commonly known as Makoi or black nightshade of Solanaceae family usually grows as a weed in moist habitats in different kinds

of soils, including dry, stony, shallow or deep soil(Fig.4)s. It can be cultivated by sowing the seeds in well-fertilized nursery beds in tropical and subtropical agro climatic regions during April-May.[18]

Fig. 4: *Solanum nigrum*

S. nigrum has been extensively used traditionally to treat various ailments such as inflammation, pain and fever.[19] This plant is also used for various purposes – as an antioxidant, antitumor, anti-inflammatory, hepatoprotective, diuretic and antipyretic agent. *S. nigrum* is widely used in many traditional systems of medicine worldwide. Leaves are used for the treatment of ring worm, dressing of warts, indigestion, liver tonic, stomach ache and stomache ulcer. Fruits are used for the treatment of blindness, glaucoma,cataract and given to kids to stop bed wetting. Roots are used to treat asthma, cough and to increase the fertility in women. Whole plant is used against snake bite,burns dermal infection and cough.[20,21,22]

S. nigrum contain various compounds that are responsible for diverse activities and major active components are glycoproteins, glycoalkaloids, and polysaccharides, polyphenolic compounds such as catechin, gallic acid, protocatechuic acid (PCA), epicatechin, caffeic acid, naringenin and rutin.[23] Glycoalkaloids include solamargine, solanine and solasonine that belong to the tropane group of compounds. Solanine's function and activity has been extensively studied. It comprises 95 percent of the total alkaloid concentration present in the plant and is found naturally in any part. It is one of the plant's major natural defenses as it is toxic even in small quantities. With a molecular weight of 868.04 and formula C45H73NO15 it consists of an aglycone, solanidine (alkaloidal portion), and three sugar moieties.[24]

S. nigrum and many more used in traditional medicine have proven anticonvulsant properties in animal models and may be a source of new antiepileptic drugs. Experimentally, in *S. nigrum* seizures were induced by picrotoxin, pentylenetetrazole or electric shock in the adult albino rats. Aqueous extract of *S.nigrum* leaves provided protection against induced seizures

in rats and a significant dose-dependent protection in chicken. Mechanism of action of the extract still needs to be elucidated.[25]

Solanum pubescens: *Solanum pubescens* belong to the family Solanaceae commonly also called as pajarito (Fig.5). It is commonly used by the tribal people in India for the treatment of diarrhoeal diseases, liver disorders and cancer disorders.[26]

Fig.5: *Solanum pubescens*

Phytochemical studies showed the presence of alkaloids, resins, glycosides, carbohydrates, reducing sugar, fats and oils, flavonoids and terpenoids.[27] The percentage composition of various compounds within this species is total alkaloid content (0.12%) total glycoalkaloids (0.038%), and glycosylated compounds derived from solasodine, namely solasonine (0.0043%) and solamargine (0.0028%).[28] Kusirisin et al. (2009) recorded polyphenolic compounds that included phenol, flavonoids and tannin. The concentrations of these compounds were recorded as 160.30, 104.36 and 65.91 mg/g, respectively.[29] Antiviral isoflavonoid sulfate and steroidal glycosides were also isolated from the fruits of S. torvum. Arthan et al., investigated MeOH extracts of fruit and found one new isoflavonoid sulfate named as torvanol A, and a new steroidal glycoside, named torvoside H, together with the already-known glycoside, torvoside A. Compounds isolated from aerial parts. Aerial parts of S. torvum are rich sources of steroid and saponins.[30]

Anti convulsant activity of *Solanum pubescens* was screened using Pentylene tetrazole-induced convulsion test and Phenobarbitone induced sleeping time. The methanolic extract of *Solanum pubescens* significantly prolonged the onset of both tonic-clonic phases of seizures and myoclonic spasms induced by pentylenetetrazole. Using phenobarbitone induced sleeping time, methanolic extract of *Solanum pubescens* offered 60 percent protection against seizures induced death at 300 mg/kg. Results indicated *Solanum pubescens* methanolic extract of significantly reduced the latency for the onset of sleep. It potentiated the duration

of sleep at all the doses tested when compared with the control. The results obtained in the study showed that the extract and fraction of *Solanum pubescens* possesses anticonvulsant and sedative activity. The extract significantly prolonged the onset of both myoclonic spasms as well as tonic–clonic phases of seizure in mice. The effect of pentylenetetrazole induced seizures is an indication of possible effectiveness of the methanolic extract of *Solanum pubescens* against absence seizures as drugs that inhibit pentylenetetrazole-induced convulsions are generally effective against absence seizures.[31, 32, 33]

Flavonoids was implicated in various pharmacological actions like anticonvulsant and CNS depressant activity. Here flavonoids are the only Phytochemical that is found present in the active extract and fractions. Flavonoids have central inhibitory and neuromodulatory effects.[34] The leaf of Solanum pubesencs exhibited significant anticonvulsant and sedative effects that support the evidence for its folkloric use, while these neuropharmacological effects might possibly be due to the presence of flavonoids.

Hyoscyamus niger: *Hyoscyamus niger* is an annual or biennial which grows up to three feet tall(Fig.6). The stems of mature plant is erect, leafy, branched, and densely covered with long glandular hairs. It has been distributed in Europe and Asia. In ancient Iranian medicine, the plant has been used for diarrhea, stomach pain and some central nervous system disorders such as parkinsonism, hysteric patients and seizures [35]

Fig.6: *Hyoscyamus niger*

The chemical characterization of plants shows the presence of different alkaloids such as hyocyamine, hyoscine (scopolamine) and atropine which are proved to have anticholinergic (parasympatholytic). Atropine and scopolamine are mainly present in leaves whereas apoatropine (atropamine) and cuscohygrine are the main alkaloids of the root. The main alkaloid of seeds are hyoscyamine. The plants also produces non-alkaloid secondary metabolites like withanolides, flavonoids, lignans, coumarinolignans, saponins, glycerides,

glycosides and phenolics [36] Hyoscyamine,which is levo-isomer of atropine, has the same action with twice power of atropine. Hyoscyamine almost mixed with atropine. L-hyoscyamine is formed in the plant is readily hydrolyzed to atropine in the plant cells and also in process of extraction. The major effect of Hyoscyamine is the central nervous system (CNS) depression. Atropine, which is (±)-hyoscyamine, has equal part of D and L hyosciamine. When atropine is hydrolyzed it forms (±)-tropic acid and tropine. Tropane alkaloids are derived from a combination of a piperidine and a pyrrolydine ring designated as a tropane [37] The plant also has Non-alkaloidal compounds including Canabisin D, Canabisin G, Grossamide, hyosmin, Hyosciamide, Hyoscyamal Balanophonin, Cleomiscosin A, Cleomiscosin B, Rutin Hyosgerin, Atroposide and Riboflavin.[34, Seeds contain non alkaloids include Lignans, coumarinolignans, lignanamides, saponin (, hyoscyamal, balanophonin, pongamoside D pongamoside C and withnaloides. have also found four coumarinolignans including cleomiscosin A, cleomiscosin B, cleomiscosin A-9'-acetate and cleomiscosin B-9'-acetate.[38,39]

Anticonvulsant activity of *Hyoscyamus niger* L seeds were screened using picrotoxin test using adult male mice. The results of the laboratory animal study provided evidence in favour of the anticonvulsant activity of the herb, and showed that aqueous extract of *H. niger* possesses anticonvulsant activity in the experimental animal model used. Picrotoxin, a potent, selective GABA-A receptor antagonist produces seizures by blocking the effect of GABA at central GABA-A receptors, which have been associated with epilepsy. Postsynaptic GABA-A receptors are functionally linked to benzodiazepine receptors, barbiturate receptors and chloride ion channels to form GABA-chloride ionophore complex, which is intimately involved in the modulation of GABAergic neurotransmission epilepsy. Picrotoxin, a GABA-A receptor antagonist, produces seizures by blocking the chloride-ion channels linked to GABA-A receptors, thus preventing the entry of chloride ions into the brain.[40] The experimental evidence obtained in the present laboratory animal study indicates that *H. niger* methanolic extract significantly delayed the onset of seizures induced by picrotoxin. Since picrotoxin-induced attenuation of GABAergic neurotransmission, it is not unreasonable to speculate that *H. niger* methanolic extract probably produces its anticonvulsant activity by enhancing GABAergic neurotransmission. The observed anticonvulsant activity of the plant's extract may also be due to its ability to depress the central nervous system (CNS) by one or more of the known mechanisms of anticonvulsant action.

***Withania somnifera* (Ashwaganda)**

Withania somnifera, known commonly as *ashwagandha*, Indian ginseng, poison winter cherry or gooseberry is a plant in the Solanaceae or nightshade family (Fig.7). The plant is long, brown, tuberous roots are used in traditional medicine. In Ayurveda, the berries and leaves are applied externally to tumors, tubercular glands, carbuncles, and ulcers.[41,42]

Fig.7:*Withania somnifera*

The biologically active chemical constituents of *Withania somnifera* include alkaloids like isopelletierine, anaferine, cuseohygrine, anahygrine, steroidal lactones like withanolides, withaferins and also saponins .[43] Ashwagandha contain anti-stress agents like Sitoindosides and acylsterylglucosides. Active principles of Ashwagandha, for instance the sitoindosides VII-X and Withaferin-A, have been shown to have significant anti-stress activity against acute models of experimental stress.[44] Many of its constituents support immunomodulatory actions.[45] The aerial parts of *Withania somnifera* yielded 5-dehydroxy withanolide-R and withasomniferin-A. Cuscohygrine usually comes with other, more potent alkaloids like atropine or cocaine. There are also the alkaloids ashwagandhine, ashwaganidhine, and somniferine.[46]

In a study administration of the *Withania somnifera*, root extract showed anticonvulsant action by increasing the PTZ seizure threshold for the onset of tonic extension phase in mice. Further, a sub-effective dose of the extract potentiated the actions of GABA (γ-gamma amino butyric acid), a GABA receptor agonist, and diazepam, a GABA receptor modulator against the PTZ seizure threshold. Besides monitoring the changes in latency of different phases of seizures, the computation of the PTZ dose (in mg/kg) required by the animal made a precise assessment of the role of different doses of *Withania somnifera*, in attenuating the seizures. Higher doses of the extract increased the PTZ seizure threshold for the onset of tonic extensor phase.[47] That established the role of the *Withania somnifera*, root extract in preventing seizure propagation. Antiepileptic drugs which increase the threshold for the onset of

myoclonic jerks and tonic extensor are known to prevent seizure generation and propagation, respectively.[48]

CONCLUSION

Search for herbal remedies can possibly act as therapeutic agents is an active area of research to combat these diseases. Natural products play a vital role in treatment of Epilepsy. This review reveals the therapeutic role of Solanaceae plants like are *Solanum nigrum* (black nightshade), *Solanum pubescens, Hyoscyamus niger* and *Withania somnifera* (Ashwaganda) and its chemical constituents in management of epileptic seizures. The findings of the laboratory animal studies also support the folkloric and ethnomedical uses of these plants.

REFERENCES

1. Varma G. G. , Mathai B. K. , Das K. , Gowda G. , Rammohan S. , Einstein J. W. Evaluation of antiepileptic activity of methanolic leaves extract of Tragia involucrata Linn. in mice . International letters of Natural Sciences, 2014; 12(2).
2. Mary J. Mjcek, Richard A. Harvey, Pamela C, Champe, Bruce D.Fisher, Lippincott's IIIustrated reviews:Pharmacology,6th edition,Lippincott Williams and wilkins a wolters Kluwer publishers, 2014; 171-73.
3. Rout, S.K. and D.M. Kar. A review on antiepileptic agents, current research and future prospectus on conventional and traditional drugs. Int. J. Pharm. Sci. Rev. Res., 2010; 3: 19-23.
4. Mac, T.L., D.S. Tran, F. Quet, P. Odermatt, P.M. Preux, and C.T. Tan.Epidemiology, aetiology, and clinical management of epilepsy in Asia: a systematic review. Lancet. Neurol., 2007; 6: 533-43.
5. Ezekiel, I., M.A. Mabrouk, J.O. Ayo, A.D. Goji, A.O. Okpanachi, A. Mohammed, and Y. Tanko,. Study of the Effect of Hydro-Ethanolic Extract of Commiphora Africana (Stem-bark) on Sleeping Time and Convulsion in Mice. Asian. J. Med. Sci., 2010; 2: 85-8.
6. Wannang, N.N., J.A. Anuka, H.O. Kwanashie, S.S. Gyang, and A. Auta,. Antiseizure activity of the aqueous leaf extract of Solanum nigrum linn (solanaceae) in experimental animal. Afr. Health. Sci., 2008; 8: 74-9.
7. Joy, P.P., J. Thomas, S. Mathew, and B.P. Skaria, 2001. Medicinal Plants Tropical Horticulture. Vol. 2, Calcutta: Naya Prokashan.

8. Griffin W, Lin G. Chemotaxonomy and geographical distribution of tropane alkaloids. Phytochemistry 2002; 53(6): 623-37.
9. Sun F, Li S, He D, Cao G, Ni X, Tai G, et al. Effects of glycoalkaloids from Solanum plants on cucumber root growth. Phytochemistry 2010; 71(13): 1534-38.
10. Arnqvist L, Dutta PC, Jonsson L, Sitbon F. Reduction ofcholesterol and glycoalkaloid levels in transgenic potato plantsby overexpression of a type 1 sterol methyltransferase cDNA1. Plant Physiol 2003; 131(4): 1792-99.
11. Li J et al. Chemical & pharmacological researches on hyoscyamus niger. Chinese herbal medicines 2011; 3(2): 117-126.
12. Singh S, et al. Medicinal importance of Genus Atropa Royle -A review, International Journal of Advanced Research, 2014; 2(2): 48-54.
13. Fukuda T et al. Phylogeny & biogeography of genus Lycium (solanaceae): Inferences from chloroplast DNA sequences. Molecular phylogenetics & evolution, 2001; 19(2): 246-58.
14. Rocha P et al. Functional expression of tropinone reductase 1 (tr1) & hyoscyamine-6β-hydroxylase (h6h) from Hyoscyamus niger in Nicotiana tobacum. Plant science 2002; 162(6): 905-13.
15. Pawar Pankaj K, Borse Tushar P, Pinjari Rizwan Z, Maheshwari Vijay L. A simple technique for rapid quantitative determination of solasodine from cultured hairy roots of Solanum surattense. J Herb Med Toxicol 2008; 2(1): 7-10.
16. Solouki M, Hoshyar H, Ramroudi M, Tavassoli A. Comparison and evaluation of steroid alkaloid solasodine on in vivo and in vitro cultures of Solanum surattense Burm L. Afr J Microbiol Res 2011; 5(23): 3981-85.
17. Chauhan K, Sheth N, Ranpariya V, Parmar S. Anticonvulsant activity of solasodine isolated from Solanum sisymbriifolium fruits in rodents. Pharm Biol 2011; 49(2): 194-99.
18. Kiran, Kudesia R, Rani M, Pal A. Reclaiming degraded land in India through the cultivation of medicinal plants. Bot Res Int 2009; 2: 174-181.
19. Acharya E, Pokhrel B. Ethno-medicinal plants used by Bantar of Bhaudaha, Morang, Nepal. Our Nature 2006; 4: 96-103.
20. Zakaria ZA, Gopalan HK, Zainal H, et al. Antinociceptive, anti-inflammatory and antipyretic effects of Solanum nigrum chloroform extract in animal models. Yakugaku Zasshi 2006; 126: 1171-78.

21. Lee SJ, Lim KT. Antioxidative effects of glycoprotein isolated from Solanum nigrum Linne on oxygen radicals and its cytotoxic effects on the MCF-7 cell. J Food Sci 2003; 68: 466-70.
22. Raju K, Anbuganapathi G, Gokulakrishnan V, et al. Effect of dried fruits of Solanum nigrum LINN against CCl4-induced hepatic damage in rats. Biol Pharm Bull 2003; 26: 1618-1619.
23. Sikdar M, Dutta U. Traditional phytotherapy among the Nath people of Assam. Ethno-Med 2008; 2: 39-45.
24. Lin HM, Tseng HC, Wang CJ, et al. Induction of autophagy and apoptosis by the extract of Solanum nigrum Linn in HepG2 cells. J Agric Food Chem 2007; 55: 3620-3628.
25. Glossman-Mitnik D. CHIH-DFT determination of the molecular structure and IR and UV spectra of solanidine. J Mol Model 2007; 13: 43-46.
26. Eva González-Trujano M, Tapia E, López-Meraz L, et al. Anticonvulsanteffect of Annona diversifolia Saff. And palmitone on penicillin-induced convulsive activity. A behavioral and EEG study in rats. Epilepsia 2006; 47: 1810-1817.
27. Chah K.F., Muko K.N and Oboegbulem S.I. Antimicrobial activity of methanolic extract of Solanum torvumfruit. Fitoterapia 2000; 71: 187-89.
28. Pérez-Amador1 M.C., Muñoz Ocotero1 V., García J.M., Castañeda1 A.R and González E. Alkaloids in Solanum torvumSw (Solanaceae). International experimental Botany2007; 76: 39-45.
29. Kusirisin W., Jaikang C., Chaiyasut C and Narongchai P. Effect of polyphenolic compounds from Solanum torvum on plasma lipid peroxidation, superoxide anion and cytochrome P450 2E1 in human liver microsomes. Medicinal Chemistry 2009; 5: 583-88.
30. Arthan D., Svasti J., Kittakoop P., Pittayakhachonwut D., Tanticharoen M and Thebtaranonth Y. Antiviral isoflavonoid sulfate and steroidal glycosides from the fruits of Solanum torvum. Phytochemistry. 2002; 59: 459-63.
31. K. Hemamalini, P. Ashok, G. Sunny, S. Kumarreddy, G. Ganesh, K. Santhoshini, K. Rashmita, P.Priyanka, Y.Jayasri, T. Vishwanath, Uma Vasi Reddy, "Gastro protective activity of Gymnosporia emerginata, Solanum pubescens and Anigeissus accuminata leaf extract against ethanol induced gastric mucosal injury in rats". International Journal of Pharmacy Biomed. Res 2011; 2(1): 38-42.
32. Kasture, V.S., Chopde, C.T., Deshmukh, V.K. Anticonvulsive activity of Albizzia lebbeck, Hibiscus rosasicnensis and Butea monosperma in experimental animals. J. Ethanopharmacology. 2000; 71: 65-75.

33. Kiranmai AS, Hemamalini K, and Vasireddy U: Anticonvulsant and Sedative effects of leaf extract of Solanum pubescens. Int J Pharm Sci Res 2013; 4(4): 1424-27.
34. Gribel G, Perrault G Tan S Shoenaker H, Sanger DJ. Pharmacological studies on synthetic flavonoids: comparision with diazepam. Neuropharmacology. 1999; 38(7): 965-77.
35. Urkin J, Shalev H, Sofer S, Witztum A. [Henbane (Hyoscyamus reticulatus) poisoning in children in the Negev] Harefuah. 1991; 120: 714–6.
36. Zhang L, Yang B, Lu B, Kai G, Wang Z, et al. Tropane alkaloids production in transgenic Hyoscyamus niger hairy root cultures over-expressing putrescine N-methyltransferase is methyl jasmonate-dependent. Planta. 2007; 225: 887–896.
37. Begum AS. Bioactive Non-alkaloidal Secondary Metabolites of Hyoscyamus niger Linn. Seeds: A Review. Research Journal of Seed Science. 2010; 3: 210–217. 38. Zhang WN, Luo JG, Kong LY. Phytotoxicity of lignanamides isolated from the seeds of Hyoscyamus niger. J Agric Food Chem. 2012; 60: 1682–1687.
38. Graev M, Fallani M. [Collective poisoning caused by ingestion of Hyoscyamus niger (with a fatal case)] Minerva Medicoleg. 1960; 80: 225–30.
39. Nicoll RA. Introduction to the pharmacology of CNS drugs. San Fransisco: McGraw-Hill Medical; 2007; 333-46.
40. Mirjalili, M. H.; Moyano, E.; Bonfill, M.; Cusido, R. M.; Palazón, J.. "Steroidal Lactones from Withania somnifera, an Ancient Plant for Novel Medicine".Molecules, 2009; 14(7): 2373–2393.
41. Pandit, S.; Chang, K.-W.; Jeon, J.-G. "Effects of Withania somniferaon the growth and virulence properties of Streptococcus mutans and Streptococcus sobrinus at sub-MIC levels". Anaerobe 2013; 19: 1–8.
42. Mishra LC, Singh BB, Dagenais S. Scientific basis for the therapeutic use of Withania somnifera. (Ashwagandha): A review. Alternative Medicine Reviews. 2000; 5: 334–46.
43. Bhattacharya SK, Goel RK, Kaur R, Ghosal S. Anti - stress activity of Sitoindosides VII and VIII. New Acylsterylglucosides from Withania somnifera. Phytother Res. 1987; 1: 32–37.
44. Ghosal S, Srivastava RS, Bhattacharya SK, Upadhyay SN, Jaiswal AK, Chattopadhyay U. Immunomodulatory and CNS effects of sitoindosides IX and X, two new glycowithanolides form Withania somnifera. Phytother Res. 1989; 2: 201–06.
45. Atta-ur-Rahman, Samina-Abbas, Dur-e-Shahwar, Jamal SA, Choudhary MI, Abbas S. New withanolides from Withania spp. Journal of Natural Products, 1991; 56: 1000–1006.

46. S K Kulkarni, Kiran Kumar Akula & Ashish Dhir, Effect of Withania somnifera Dunal root extract against pentylenetetrazol seizure threshold in mice: Possible involvement of GABAergic system; Journal of Experimental Biology, 2008; 46: 465-469.
47. Löscher W, Hönack D, Fassbender C P & Nolting B. The role of technical, biological and pharmacological factors in the laboratory evaluation of anticonvulsant drugs. III. Pentylenetetrazol seizure models, Epilepsy Res, 1991; 8:171.