

Review Article

MEDICINAL PLANTS WITH NEUROPHARMACOLOGICAL PROPERTIES FROM INDIAN ORIGIN

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ABSTRACT

Neuropharmacology is the scientific study of the effects of drugs on the central nervous system. Its primary focus is actions of medications for psychiatric and neurologic disorders as well as those of drugs of abuse. The goal of Neuropharmacology is to apply information about drugs and their mechanisms of action, develop safer and more effective treatments and eventually curative and preventive measures for a host of nervous system abnormalities. There are a number of drugs being used in the traditional medicine for treatment of various CNS disorders and presently many of these drugs are being explored scientifically to ascertain their CNS activities. Significant number of studies has been performed to find alternative treatment for diseases of the nervous system by identifying structures with activity at the central nervous system. However, most of the screenings are usually conducted on an ad hoc basis and not systematically. The initial purpose of this review is to summarize plants with neuropharmacological activities, in particular, those that have not been fully studied and that have molecular mechanisms whose active constituents are responsible for the activities remained to be identified. The second purpose was to identify potential target plants for future studies of new and alternative therapies for the treatment of neurological disorders and neurodegenerative diseases.

Keywords: Neuropharmacology, Medicinal plants, CNS.

INTRODUCTION

Drugs acting on central nervous system were among the first to be discovered by primitive human and are still the most widely used group of pharmacological agents. The CNS acting drugs are invaluable therapeutic, because they can produce specific physiological and psychological effects from the vast array of material medica of the indigenous system, so many plants have been reported to have activities against CNS disorders and thus act as very useful remedies for the alleviation of human suffering [1]. Search for new molecules that act on the central nervous system and that can be used for therapeutic purposes started with several studies in the 19th century. In fact, first drugs used to treat pathologic conditions of the CNS were based on natural resources, specifically on plants [2]. The present review is focused on various medicinal plants having CNS or neuropharmacological activities in animals.

Adiantum capillus veneris linn. (Adiantaceae)

The fresh or dried leaves fronds are antitussive, astringent, demulcent, depurative, emetic, laxative, stimulant, sudorific, tonic and used in skin diseases. The ethanolic extract of *Adiantum capillus veneris* (L) at dose 400 mg/kg body weight showed anticonvulsant activity by prolonging the onset of seizures and reducing the duration of seizures in a significant manner when compared with a control group in PTZ induced convulsion model, also by reducing time for various phases of seizure in MES induced seizures test. Significant increase in onset of paw licking to heat stimuli in Eddy's hot plate method and increase in reaction time to tail withdrawal in the tail immersion test showed analgesic activity of extract [3].

Anacyclus pyrethrum (Asteraceae)

It is used traditionally as a tonic to the nervous system. The roots of *Anacyclus pyrethrum* are reported to possess anti-inflammatory, immune stimulating, anabolic, aphrodisiac activities. The ethanolic extract of roots (50mg, 100mg and 200 mg/kg body wt) possesses potential neuropharmacological activity and antidepressant activity, evaluated by behavioural studies and sedative, muscle relaxant, anxiolytic, no-tropic and antidepressant activity in rats [4].

Argemone mexicana (Papaveraceae)

Papaveraceae family is known to have CNS depressant activity. The methanolic and ethyl acetate extract (100mg, 200 mg and 400

mg/kg body wt) orally, showed significant decrease in motor activity and fall off time of animals on rotating rod, along with sedative effect by potentiating phenobarbitone-induced sleeping time in Swiss albino mice, for locomotor activity, Muscle relaxant activity, and Effect on Phenobarbitone sodium induced sleeping model [5].

Argyrea speciosa Sweet (Convolvulaceae)

It is commonly known as 'Elephant creeper'. The roots are regarded as a tonic, aphrodisiac, bitter and used in rheumatism, gonorrhoea, chronic ulcer and diseases of the nervous system. The hydro-alcoholic extract of roots of *Argyrea speciosa Sweet* (100mg, 200mg and 500 mg/kg, p.o.) showed reduced spontaneous motor activity and potentiated pentobarbital induced hypnosis in pentobarbital-induced sleep model in mice [6].

Avicennia officinalis (Avicenniaceae)

The crude methanolic extract of the leaves potentiate the pentobarbital induced sleeping time in mice, decreased the open field score in open field test, decreased the number of holes crossed from one chamber in the hole cross test and decreased the head dip responses in hole board test [7].

Balanites roxburghii planch (Zygophyllaceae)

The fruit pulp mixed with goat milk, rubs on the chest to cure pneumonia in children. The methanolic extract of pericardium of *Balanites roxburghii* affected locomotor activity, reduced spontaneous motility, produced pro-depressant activity, produced relaxation of skeletal muscle, significantly prolonged pentobarbital-induced sleeping time and reduced Spatial learning on various animal models. The most significant depressant effect was observed with extract at a dose of 300mg/kg than 100mg/kg [8].

Barleria lupulina (Acanthaceae)

It is commonly known as 'Vishellakarani' (Bengali). The methanolic extract of aerial parts of *Barleria lupulina* (at doses 100mg, 200mg and 300 mg/kg) showed reduction in general behavioural pattern (spontaneous activity, alertness, awareness, pain response and touch response) in a dose dependent manner.

The methanolic extract was found to produce a significant reduction of the exploratory behavioural profile (Y-maze test, head dip test), conditioned avoidance response, significant motor in co-ordination

and muscle relaxant activity. The extract also potentiate phenol barbitone sodium induced sleeping time [9].

Bixa Orellana L. (Bixaceae)

It is known as the anode plant. An infusion of the leaves and roots is useful in epilepsy, dysentery, fever and jaundice. The methanolic extract of *Bixa Orellana L.* Leaves at doses of 125mg, 250mg and 500 mg/kg body weight statistically reduced the time for the onset of sleep at 500 mg/kg dose and (dose-dependently) increased the total sleeping time at 250mg and 500 mg/kg dose in the pentobarbitone-induced hypnosis test. A statistically significant decrease in locomotor activity was observed at all doses in the open-field and hole-cross tests. In the strychnine-induced anticonvulsant test, the extract increased the average survival time of the test animals (statistically significant at 250mg and 500 mg/kg) [10].

Bryophyllum pinnatum (Lam.) (Crassulaceae)

The aqueous leaf extract of *Bryophyllum pinnatum* at doses (50mg, 100mg and 200 mg/kg) was found to produce a profound decrease in exploratory activity in a dose-dependent manner. It also showed a marked sedative effect by a significant reduction in gross behaviour and potentiation of pentobarbitone-induced sleeping time. It delayed onset in strychnine and picrotoxin-induced convulsion (seizures) respectively, with the protective effect being significantly higher in picrotoxin than strychnine-induced convulsion [11].

Caesalpinia pulcherrima (L.) (Fabaceae)

It is used in the treatment of ulcer, fever, tumours and asthma and skin diseases. The crude methanolic extract of bark of *Caesalpinia pulcherrima* was evaluated for neuropharmacological activities. The extract of the bark potentiate the pentobarbital induced sleeping time in mice and decreased the open field score in open field test, decreased the number of holes crossed from one chamber in the hole cross test and decreased the head dip responses in hole board test [12].

Calotropis gigantea R.Br. (Asclepiadaceae)

The plant is used as an analgesic in toothache and earache, used in sprain, anxiety, epilepsy and in mental disorders. Alcoholic extract of peeled roots of *Calotropis gigantea R.Br.* was tested in albino rats at the dose level of 250 mg and 500 mg/kg bodyweight orally for CNS activity. Significant anticonvulsant activity in PTZ induced convulsions, intensity activity in elevated plus maze model, decreased locomotor activity and potentiation of the pentobarbitone induced sleep effect of the extract was observed [13].

Camellia sinensis (Theaceae)

Camellia sinensis commonly known as green tea, traditionally used to treat asthma, angina pectoris, peripheral vascular disease and coronary artery disease. The neuropharmacological study of *camellia sinensis* for anxiolytic activity was assessed by whole board test, Y maze test, social interaction test, foot shock induced aggression test, for aqueous extract at two doses of 200 mg/ Kg and 400 mg/ kg. The result from this study strongly suggests that *camellia sinensis* possess varied effects on the CNS including anxiolytic activity [14].

Cissus quadrangularis Linn (Vitaceae)

It is commonly called as Hadjoda, most widely used ingredients in alternative medicine for treatment of piles, anorexia, indigestion, chronic ulcers, asthma, otorrhoea, wounds and in augmenting fracture healing process. The effects of extracts on CNS were studied by using spontaneous motor activity, exploratory behaviour, Rota-rod performance and potentiation of pentobarbitone sleeping time in mice. The extract (50 mg, 100 mg and 200 mg/kg i.p.) produced a reduction in spontaneous motor activity, exploratory behaviour and motor coordination and prolonged pentobarbitone induced sleeping time [15].

Clitoria ternatea Linn (Fabaceae)

It is commonly known as "Butterfly pea." The roots are useful in dementia, hemiparesis, burning sensation, leprosy, inflammation, leucoderma, bronchitis, asthma, pulmonary tuberculosis and fever.

The spectrum of activity of the methanolic extract of *Clitoria ternatea* with the doses 100mg, 200mg and 400 mg/kg body weight on the CNS was determined. The extract was found to possess no-tropic, anxiolytic, antidepressant, anticonvulsant and anti-stress activity [16].

Couroupita guianensis Aubl. (Lecythidaceae)

The methanolic extract of *Couroupita guianensis* was studied on spontaneous motor activity, Rota-rod performance and phenobarbital sleeping time with doses 100mg, 250mg and 500 mg/kg in mice. The extract in a dose dependent manner showed a significant reduction in spontaneous motor activity and the onset and duration of pentobarbitone induced hypnosis but had no effect on motor coordination [17].

Eclipta alba (Linn.) (Asteraceae)

It has been mentioned to be a nervine tonic in addition to possessing hepato-protective, hair growth promoting and anti-aging properties. Aqueous and hydro-alcoholic extracts of the plant were evaluated for sedative, muscle-relaxant, anxiolytic, no-tropic and anti-stress activities. The aqueous and hydro-alcoholic extracts were administered in a dose of 150mg and 300 mg/kg p.o., while the hydrolysed fraction was administered in a dose of 30 mg/kg, p.o. The findings indicated no-tropical activity of the aqueous extract (300 mg/kg, p.o.) and its hydrolysed fraction (30 mg/kg, p.o.) [18].

Fumaria indica Linn. (Fumariaceae)

It is commonly known as geometry. Traditionally it is used as anti-dyspeptic, blood purifier, cholagogue, diaphoretic, diuretic, laxative, stomachic, sedative and tonic. Pentobarbital induced sleeping time, locomotor activity, effect on muscle grip performance of mice, maximal electroshock seizures in rats and pentylenetetrazole induced convulsions in mice were used as behavioural models to evaluate CNS effects of the extract with 100 mg, 200 mg and 400 mg/kg doses (p. o.). The animals treated with *Fumaria indica Linn* extract showed significant and dose dependent increase in pentobarbital-induced sleeping time and marked decrease in the onset of sleeping time in rats. *The Fumaria indica Linn extract* has shown a significant decrease in locomotor activity. *The Fumaria indica Linn extract* did not show any muscle relaxant effect in the Rota-rod test in mice. *The Fumaria indica Linn extract* showed significant anticonvulsant activity in MES in rats and PTZ induced convulsions in mice respectively [19].

Hedychium coronarium Koen (Zingiberaceae)

The rhizome of the plant is used in the treatment of type 2 diabetes. It is also used as anti-rheumatic, excitant, febrifuge and tonic. The extract with doses of 100mg, 200mg and 400 mg/kg body wt. investigated for its neuropharmacological activities using Hole-cross and Open field test in mice. The extract displayed dose dependent suppression of motor activity and exploratory behaviour in the tested animal models [20].

Jatropha gossypifolia Linn. (Euphorbiaceae)

It is popularly known as bellyache bush (English). The neuropharmacological activities were evaluated by Hole cross test, whole board test, and Elevated plus maze test, of methanolic extract at doses 200mg and 400 mg/kg body weight. The extract at both doses showed a significant sedative effect in whole cross test. In whole board test, the extract showed highly significant anxiolytic activity at lower dose, whereas this activity was observed at higher doses in EPM test [21].

Leptadenia reticulata (Asclepiadaceae)

It is known as "jivanti" is considered to have the ability to bestow health and vigour. It is well known for its tonic, restorative and stimulant property in traditional medicines. The methanolic extract of *Leptadenia reticulata* was evaluated for antiepileptic and neuropharmacological activities with doses of 250mg, 500mg and 1000 mg/kg body wt. The methanolic extract was found to be significant against maximum electro shock and Pentylenetetrazol. The extract has no significant effect on haloperidol induced

cataplexy, but it possessed significant decrease in locomotor activity and increase in phenobarbitone induced sleeping time and no significant change in motor coordination [22].

Lucas longifolia Benth. (Lamiaceae)

It is commonly called 'Barumbi or Dudhani'. Crude petroleum ether, chloroform and methanol extracts of aerial parts of *Lucas longifolia* have been evaluated for central nervous system depressant activity (100mg, 200mg and 400 mg/kg i.p.). The methanolic extract significantly reduces spontaneous motor activity at higher doses than petroleum ether extract. The fall off time (motor coordination) was also decreased. A potentiation in the pentobarbitone-induced sleep due to the sedative effect of the methanolic extract was observed [23].

Lippia nodiflora (Verbanaceae)

It is commonly known as Poduthalai and is traditionally used as anodyne, antibacterial, diuretic etc. It has been shown that ethanolic extract of *Lippia nodiflora* at doses (250mg and 500 mg/kg p.o.) and its chloroform extract at higher dose of 500 mg/kg produced central inhibitory (sedative) effect, anticonvulsant effect and anxiolytic effect in mice [24].

Mikania scandens (L.) Wild. (Asteraceae)

It is known as climbing hemp weed (English). Aqueous leaf extracts of this plant have been used in folk medicine to treat stomach ulcers and applied to the affected area of body in the treatment of wounds and bruises. Neuropharmacological properties of hydro alcoholic extract of aerial parts of *Mikania scandens* (at 250mg and 500 mg/kg body weight i.p.) were evaluated. The results of this study revealed significant and dose-dependent central anti-nociceptive, locomotor and depressant, muscle relaxant and sedative potentiating effects, demonstrating its depressant action on the central nervous system [25].

Mimusops elengi (Sapotaceae)

It is commonly known as Bakul (Bengali). Several therapeutic uses such as catatonic, alexipharmic, stomachic, anthelmintic and astringent have been ascribed to bark of *Mimusops elengi*. The central nervous system depressant activity of extract at doses 100mg, 200mg and 400mg/kg body weight was evaluated using whole cross and open field test. The extract significantly decreased motor activity and exploratory behaviour of mice in whole cross and open field tests respectively [26].

Nigella sativa L. (Ranunculaceae)

The seed of *Nigella sativa L.* Used in the treatment of asthma and as anti-tumour, bactericidal, anti-chested, anti-nematode, anti-inflammatory, analgesic, anti-diabetic, anti-ulcerogenic, diuretic, lactagogue and vermifuge. The aqueous and methanol extracts of *Nigella sativa* seed at dose 100mg/kg body wt. produced an alteration in the general behaviour patterns, significant reduction of spontaneous motility, reduction in normal body temperature and significant analgesic action against hotplate and pressure tests. All of the above findings suggest a CNS-depressant action of both extracts [27].

Passiflora incarnata Linn (Passifloraceae)

The fresh or dried whole plant has been used as herbal medicine to treat nervous anxiety and insomnia. Methanolic extract of aerial parts of *Passiflora incarnata Linn* was investigated for anxiolytic (by Forced swimming test) and antioxidant activities at doses 100mg and 200 mg/kg body wt. in animal models. The results showed a significant anxiolytic effect comparable with diazepam in all the tested doses [28].

Peperomia pellucida (L.) (Piperaceae)

It is locally known as Luchi Pata. The leaves are used in the treatment of headache, fever, eczema, abdominal pains and convulsions. Petroleum ether and ethyl acetate soluble fractions of ethanolic extract of *Peperomia pellucida* leaves at doses (50mg, 200mg/kg) were administered to mice by intra-peritoneal route and their effects on the duration of diazepam-induced sleep,

nikethamide-induced toxicity, light-dark test and force swimming test were determined. The duration of diazepam-induced sleep was extended by administration of these fractions. Nikethamide at high doses causes death of mice and administration of these fractions delay the time that nikethamide causes the death of animals. In light-dark test and force swimming test these fractions showed diazepam type effects. These results suggest that both fractions of *Peperomia pellucida* leaves have dose dependent depressant effects [29].

Pistia stratiotes L. (Araceae)

It is also called water cabbage or water lettuce. Leaves are used in the treatment of ringworm infection of the scalp, syphilitic eruptions, skin infections, boils, wounds. The CNS activity evaluated at doses 850 mg/kg by hole cross test, open field test, beam walking test and thiopental sodium induced sedative test in mice. It significantly decreased the locomotor activity in mice. The extract showed significant anti-nociceptive activity when subjected to the hot plate, tail immersion and acetic acid-induced writhing test in mice [30].

Portulaca oleracea L. (Portulacaceae)

It is used as antiseptic, anti-scorbutic, antispasmodic, diuretic, vermifuge and in oral ulcers and urinary tract disorders. The extract with doses 200mg and 400 mg/kg body wt., on intra-peritoneal administration, showed a significant reduction in the locomotor activity in mice, anti-nociceptive activity in rats using Tail flick method, an increase in the onset time of pentylenetetrazole-induced convulsions in mice and muscle relaxant activity in-vitro (rat hemi diaphragm) and in-vivo (grip strength) experiments [31].

Portulaca quadrifida Linn. (Portulacaceae)

It is useful in asthma, cough, urinary discharges, inflammations and ulcers. The effect of ethanolic extract of *Portulaca quadrifida Linn.* in central and peripheral nervous system were studied by using spontaneous motor activity, anti-nociceptive activity, in vivo muscle relaxant activity and anticonvulsant activity at doses of 400mg and 800mg /kg (i.p.). The extract showed a significant reduction in spontaneous motor activity, anti-nociceptive activity and also showed reduction in time to recover from the electrical shock induced convulsions. The effect of extracts on grip strength was found non-significant [32].

Ruta chalepensis (Rutaceae)

The ethanol extract of aerial parts of *Ruta chalepensis* was given systemically at doses (i.e. 10 – 1000) mg/kg body wt., results from experimental models showed a delay in the onset of seizures and a dose-dependent suppression in tonic phase and mortality induced by Pentylenetetrazole, a prolongation of time of sodium pentobarbital induced hypnosis, a significant attenuation in anxiety-response and a reduction in licking them and shaking behaviour in formalin-induced nociception test. The sedative-hypnotic potentiation, anxiolytic, anticonvulsant and anti-nociceptive effects suggest that *Ruta chalepensis* induces a depressant activity on the CNS [33].

Solanum nigrum L (Solanaceae)

The plant *Solanum nigrum L.* commonly known as 'hierba mora'. The ethanol extract of fruit at doses 51mg, 127.5mg and 255mg/kg body wt., was studied for its neuropharmacological properties in experimental animals. An intra-peritoneal injection of the extract significantly prolonged pentobarbital-induced sleeping time, produced an alteration in the general behaviour pattern, reduced exploratory behaviour pattern, suppressed the aggressive behaviour, affected locomotor activity and reduced spontaneous motility. The ethanol extract of fruit did not show any sedation and motor incoordination [34].

Strychnos nux-vomica Linn. (Loganiaceae)

It is mostly used in disorders of the gastro-hepatic tract. Effect of detoxification on *Strychnos Nux-vomica* seeds by traditional processing with aloe and ginger juices, by frying in cow ghee, and by boiling in cow milk was investigated. The ethanolic extracts of these samples were subjected to spontaneous motor activity,

pentobarbitone-induced hypnosis, PTZ induced convulsions, diazepam-assisted protection and morphine-induced catalepsy. All samples reduced SMA and inhibited catalepsy. Seeds processed into milk showed the lowest strychnine content, exhibited marked inhibition of PTZ induced convulsions and maximal potentiation of hypnosis [35].

Thuja occidentalis (L.) (Capressaceae)

It has been used to treat bronchial catarrh, enuresis, cystitis, psoriasis, uterine carcinomas, amenorrhoea and rheumatism. Oral administration of 100mg, 200mg and 400 mg/kg doses of aqueous extract of *Thuja occidentalis* Linn in rats and mice were evaluated for its anxiolytic, anticonvulsant and motor coordination activity. The extract in a dose dependent manner inhibits the incidence of convulsions in Pentylene-tetrazole induced seizures. Significant motor incoordination and increased in immobility time in case of Rota road test and Tail suspension test respectively indicate CNS depressant activity of the extract [36].

Trapa bispinosa (Trapaceae)

The fruits are used as intestinal astringent, aphrodisiac, anti-inflammatory and in leprosy, urinary discharges, fractures, sore throat, bronchitis and anaemia. Neuropharmacological activities of hydro alcoholic extract of *Trapa bispinosa* were evaluated by motor coordination, spontaneous locomotor activity, object recognition, transfer latency, anxiolytic activity, analgesic activity, sodium nitrite induced respiratory arrest and hypoxic stress etc. The extract (250 mg & 500 mg/kg) was found to decrease time required to occupy the central platform (transfer latency) in the elevated plus maze and to increase discrimination index in the object recognition test, indicating no-tropic activity. *Trapa bispinosa* extract (250 mg and 500mg/kg) showed the significant increase in reaction time in hot plate analgesic activity. Moreover it also showed significant reduction in spontaneous locomotor activity and latency to death in sodium nitrite induced respiratory arrest [37].

Trigonella foenum-graecum Linn. (Fabaceae)

It is commonly known as Fenugreek. The crude extract possesses different activities such as anticancer, antiseptic, aphrodisiac, astringent, demulcent, emollient, expectorant, anthelmintic, wound healing and gastro protective effects. Neuropharmacological screening of methanolic extract was carried out by whole cross and Open field test at doses of 100mg, 200 mg and 400mg/kg of body weight in mice. The extracts significantly displayed a dose dependent suppression of motor activity, exploratory behaviour [38].

Viscum album L. (Loranthaceae)

It is also called as mistletoe. It has been reputed against cardiovascular diseases, i.e. hypertension and atherosclerosis; various bone and joint disorders including peri-arthritis, spondylitis and arthritis; for immune system stimulation; in nervous disorders as sedative or to combat epilepsy. The aqueous leaf extract of *Viscum album* L. at doses 50mg and 150 mg/kg body wt., prolonged the pentobarbital induced sleeping time and reduced the locomotor activity in actophotometer. In addition the extract reduced Maximal electro shock, Isoniazid and Pentylene-tetrazole-induced convulsions. The extract decreased the apomorphine-induced stereotyped behaviour and potentiates the HAL-induced cataleptic score which suggests extract possess anti dopaminergic activity [39].

Wedelia calendulacea Less (Asteracea)

Neuropharmacological activities of methanolic and aqueous extract of *Wedelia calendulacea* stem were screened using pentobarbital-induced sleeping time, pentylene-tetrazole and strychnine induced seizure, spontaneous motor activity, exploratory behaviour and rota-rod performance (motor coordination). The methanolic extract (20 mg and 50 mg/kg i.p.) and aqueous extract (200mg and 500 mg/kg i.p.) produced a significant prolongation of pentobarbital induced sleeping time and reduced the SMA and exploratory behaviour. The extract prolonged onset of the phases of seizure activity but did not protect mice against lethality induced by pentylene-tetrazole and strychnine. It also failed to affect the motor coordination test. These results suggest that extract contained an agent

with neuropharmacological activity that may be sedative in nature [40].

Xylocarpus moluccensis Lamk. M. Roem. (Meliaceae)

It is commonly known as 'Possur'. The bark is used as an astringent, febrifuge and has been used traditionally in the treatment of dysentery, diarrhoea and other abdominal problems. The methanolic extracts of the barks and pneumatophores of *Xylocarpus moluccensis* at doses 250 mg and 500 mg/kg b. wt., were assessed for their effects on central nervous system using pentobarbitone induced sleeping time, open field, hole cross, hole-board and evasions tests in mice. These extracts produced a dose-dependent reduction in the onset and duration of pentobarbitone induced hypnosis, reduction of locomotor and exploratory activities in the open field, whole cross, and head-dip and evasion tests. These results suggest that both bark and pneumatophore extracts possess CNS depressant activity [41].

CONCLUSION

Plants in the form of herbs, spices and foods constitute an unlimited source of molecules available for improving human health. However, a single plant contains hundreds or thousands of secondary bioactive metabolites. A chemical diversity that determined the evolutionary success of plants, favouring their adaptation to a changing environment. In this view, to ascribe health-promoting effects of a medicinal herb or a plant food only to a molecule or a single class of compounds, represents an inappropriate and inopportune task. It is likely that different phytochemicals produce *in vivo* additive and synergistic effects, thus amplifying (or reducing / inhibiting) their activities [42]. Plants have been used by human beings since immemorial times to cure diseases and to promote relief from ailments. There were times when they were most important sources of medicines for people. However, beginning in the late 1940s, this old form of therapeutics began to lose its importance, being more and more replaced by synthetic remedies. The lessons from millennia were forgotten and were considered "unscientific."

On the other hand, such ancient use of plants was a lead for scientists in their search for new substances endowed with therapeutic properties. It is estimated that nearly 25% of the modern drugs directly or indirectly originated from plants. Several are examples concerning the CNS: Caffeine, ephedrine, cannabinoids, opioids and reserpine are a few of them. However, for the majority of CNS active plants, the active principles are not yet known [43].

CONFLICT OF INTERESTS

Declared None

ABBREVIATIONS

CNS: Central nervous system; PTZ: Pentylene-tetrazole; MES: Maximal electro shock; EPM: Elevated plus maze; p.o.: per oral; i.p.: Intra-peritoneal

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