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Revisão

Plants with anticonvulsant properties - a review

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RESUMO: "Uma revisão de plantas com propriedades anticonvulsivantes". Cerca de um terço dos pacientes epilépticos não conseguem ter um tratamento adequado com as drogas anticonvulsivantes atuais. Nesse sentido, as plantas medicinais surgem como uma fonte promissora de novas moléculas químicas com propriedades biológicas apreciáveis. Muitas plantas ou produtos de origem naturais têm sido propostos para o tratamento de várias patologias, tais como: epilepsia, diabetes, ansiedade, depressão, dentre outras. O presente trabalho realizou um extenso levantamento na literatura especializada de plantas medicinais com propriedades anticonvulsivantes. Um total de 355 espécies vegetais foi identificado, sendo 16 plantas encontradas na flora brasileira, com indicação para o tratamento de quadros convulsivos. Características como nome da espécie, família, partes utilizadas, país do estudo e /ou publicação, métodos e referências foram sumarizados. Além disso, os principais apectos dos modelos animais mais utilizados no estudo de plantas/substâncias com propriedades anticonvulsivantes foram revisados. Mais de 170 referências foram consultadas.

Unitermos: Plantas medicinais, Produtos naturais, convulsão, atividade anticonvulsivante, modelos animais, revisão.

ABSTRACT: Seizures are resistant to treatment with currently available anticonvulsant drugs in about 1 out of 3 patients with epilepsy. Thus, there is a need for new, more effective anticonvulsant drugs for intractable epilepsy. However, nature is a rich source of biological and chemical diversity and a number of plants in the world have been used in traditional medicine remedies, i.e., anticonvulsant, anxiolytic, analgesic, antidepressant. This work constitutes a literature review on medicinal plants showing anticonvulsant properties. The review refers to 16 Brazilian plants and a total 355 species, their families, geographical distribution, the utilized parts, method and references. Some aspects of research on medicinal plants and a brief review of the most common animal models to discover antiepileptic drugs are discussed. For this purpose over 170 references were consulted.

Keywords: Medicinal plants, Natural products, convulsion, anticonvulsant properties, animal models, review.

INTRODUCTION

Epilepsy is one of the most common diseases of the brain, affecting at least 50 million persons worldwide (Scheuer & Pedley, 1990). Epilepsy is a chronic and often progressive disorder characterized by the periodic and unpredictable occurrence of epileptic seizures which are caused by an abnormal discharge of cerebral neurons. Many different types of seizures can be identified on the basis of their clinical phenomena (Löscher, 1998). Seizures are fundamentally divided into two major groups: partial and generalized. Partial (focal, local) seizures are those in which clinical or electrographic evidence exists to suggest that the attacks have a localized onset in the brain, usually in a portion of one hemisphere, while generalized seizures are those in which evidence for a localized onset is lacking. Partial seizures are further subdivided into simple partial, complex partial and partial seizures evolving to secondarily generalized seizures, while generalized seizures are categorized into absence (nonconvulsive), myoclonic, clonic, tonic, tonic-clonic and atonic seizures. In addition to classifying the seizures that occur in patients with epilepsy, patients are classified into appropriate types of epilepsy or epileptic syndromes characterized by different seizure types, etiologies, ages

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of onset and electroencephalographic (EEG) features (Commission, 2003).

The discovery of novel antiepileptic drugs (AEDs) relies upon the preclinical employment of animal models to establish efficacy and safety prior to the introduction of the AEDs in human volunteers (Löscher & Schmidt, 2006). Clearly, the more predictive the animal model for any given seizure type or syndrome, the greater the likelihood that an investigational AED will demonstrate efficacy in human clinical trials (Smith et al., 2007).

Mind-altering drugs, especially plants, have always fascinated human beings. Surrounded by mystic superstitions, magic thoughts and religious rituals, they have always occupied man's attention. Among the plants used by humans, those able to alter the conscience and the sensorium have drawn special consideration. However, the challenge of trying to unravel the mechanisms of action on mood, humor, cognition, ensorium, etc., led to an inconvenience: to ignore, or to face as low priority, the fact that plants could also have beneficial properties to treat mental disease and some psychic ailments (Carlini, 2003; Carlini et al., 2006).

Furthermore, as most of the plants were first used by the so-called primitive cultures, their occasional use by the White occidental culture was relegated to a second plan, being considered as sorcerer's therapeutics. Until recently, very little attention was given by the scientific community to the benefits, as accepted by folk medicine and the medicinal properties of the natural product (Barbosa-Filho et al., 2006a). In addition, nature is a rich source of biological and chemical diversity. The unique and complex structures of natural products cannot be obtained easily by chemical synthesis. A number of plants in the world have been used in traditional medicine remedies (Barbosa-Filho et al., 2006b; Funke & Melzig, 2006; Saúde-Guimarães & Faria, 2007; Agra et al., 2007 and 2008; Veiga-Junior, 2008).

Thus, many plants were known for their anticonvulsant activity. Various phytochemical and pharmacological studies have been carried out on these anticonvulsant plants (Chauhan et al., 1988; Nsour et al., 2000).

In a previous paper this research group has reviewed crude plant extracts and chemically defined molecules with potential antitumor activity for mammary (Moura et al., 2001), cervical (Moura et al., 2002) and ovarian neoplasias (Silva et al., 2003), as inhibitors of HMG CoA reductase (Gonçalves et al., 2000), central analgesic activity (Almeida et al., 2001), employed in prevention of osteoporosis (Pereira et al., 2002), for the treatment of Parkinson's disease (Morais et al., 2003), with antileishmanial (Rocha et al., 2005), hypoglycemic (Barbosa-Filho et al., 2005), and antiinflammatory activity (Falcão et al., 2005, Barbosa-Filho et al., 2006c), inhibitors of the enzyme acetylcholinesterase (Barbosa-Filho et al., 2006a), inhibitors of the angiotensin converting enzymes (Barbosa-Filho et al., 2006b), giardicidal (Amaral et al., 2006), and antileprotic activity (Barbosa-Filho et al., 2007).

The aim of this article is to given an up-to-date review on plants with anticonvulsant properties and realized a brief review of the most common animal models to discover antiepileptic drugs.

MATERIAL AND METHODS

The keywords used for this review were Epilepsy, Plants, Animal models, Anticonvulsant, Natural product and antiepileptic. The search perfound using Chemical Abstracts, Biological Abstracts, Web of Science, ScienceDirect and the data bank of the University of Illinois at Chicago, NAPRALERT (Acronym for NAtural PRoducts ALERT), updated to December 2006. From the literature search, all plants/herbal preparations that are used ethnomedically to treat epilepsy or those which have been tested for anticonvulsant activity are included in this review. The references obtained were later consulted.

RESULTS AND DISCUSSION

Over 170 references were found in which plants have been tested for their anticonvulsant activity in *in vivo/in vitro* studies or clinical studies. Review refers to 355 species, their families, geographical distribution, the utilized parts and methods (see Table 1).

The 20th century has witnessed considerable progress in anticonvulsant drug development (Loscher & Schmidt, 1994). The major drugs in clinical use, i.e. phenytoin, carbamazepine, valproate, benzodiazepines, ethosuximide, phenobarbital and primidone, were developed and introduced between 1910 and 1970 and will be referred to as 'old drugs' or 'first generation' drugs in the following. After a hiatus of over 20 years, several new anticonvulsant drugs, i.e., vigabatrin, gabapentin, felbamate, lamotrigine, oxcarbazepine, tiagabine and topiramate, have been introduced into clinical practice, referred to as 'new drugs' or 'second generation' drugs in the following. More recent anticonvulsants which are in preclinical or clinical development will be referred to as 'third generation' drugs (Löscher, 1998).

In the other hand, approximately 70% of patients with epilepsy are well controlled by monotherapy with currently available antiepileptic drugs. Another 5-10% of patients are stabilized by the addition of another antiepileptic drug but there remains over 20% of patients whose seizures are not controlled (Richens & Perucca, 1993). Therefore, phytomedicines can potentially play an important role in the development of new antiepileptic drugs to pharmacoresistent patients (Nsour et al., 2000).

Many plants were known for their anticonvulsant activity. Reviews articles (Athanassova et al., 1965 and 1969; Dhar et al., 1968 and 1973; Adesina, 1982a; Chauhan et al., 1988 and Nsour et al., 2000) were previously published with regards to plants with anticonvulsant properties.

In fact, current world-wide interest in traditional medicine has led to rapid development and studies of many remedies employed by various ethnic groups of the world. The information is recorded in alphabetical order of plant scientific name, family, part used, route of administration, dose, method and reference, as showed in Table 1 that summary of the plants which have been tested or reported for anticonvulsant properties.

Among those medicinal plants are found to possess anticonvulsant activity in animal models and/or folk medicine, include: *Abelmoschus angulosus*, *Allium sativum, Artemisia* spp, *Cannabis sativa, Cinchona officinalis, Egletes viscosa*, *Icacina trichantha, Magnolia grandiflora, Plumbago zeylanica* and others. However, a recent study with Brazilian Northeastern plants showed proexcellent results for the species *Bauhinia outimouta, Rauvolfia ligustrina* and *Ximenia americana* (Quintans-Júnior et al., 2002). In our review 13 Brazilian plants were cited: *Acosmium subelegans, Artemisia verlotorum, Centella asiatica*, *Cymbopogon citratus, Erythrina velutina, Erythrina mulungu, Hippeastrum vittatum, Lanata microphylla, Licaria puchury-major, Lippia alba, Nepeta cataria, Passiflora alata* and *Xylopia* spp.

Among those plants tested, a number of them (from different families) are found to possess anticonvulsant activity. While in most cases, the active constituents are yet to be found, for those where the active components are known, they belong to different chemical classes. However, previous studies showed that some natural plant coumarins and triterpenoids exhibit anticonvulsant properties (Chaturvedi et al., 1974; Nsour et al., 2000).

In addition, the history of drug discovery showed that plants are highly rich sources in the search for new active compounds and they have become a challenge to modern pharmaceutical industry. Many synthetic drugs owe their origin to plant-based complementary medicine (Howes et al., 2003; Orhan et al., 2004).

A number of animal models have demonstrated utility in the search for more efficacious and more tolerable AEDs. In fact, the models employed in the early phase of AED discovery are highly predictive of subsequent efficacy in easy-to-manage generalized and partial epilepsy (Smith et al., 2007). Thus, animal models more employed were leptazole-induced seizure (LIS), maximal electroshock seizure (MES), metrazole-induced seizures (MIS), picrotoxin-induced convulsions (PIC), pilocarpine (PILO), pentylenetetrazole (PTZ) and strychnine-induced seizures (SIS). However, MES, PIC and PTZ seizure models continue to represent the three most widely used animal seizure models employed in the search for new AEDs (While et al., 2002).

This review only briefly mention the most common animal methods for evaluating of the plants with anticonvulsant properties and medicinal plants studies to epilepsy described in literature. More information, seen an excellence reviews by Mello et al. (1986), Fisher (1989), Meldrum (1997), Nsour et al. (2000) and Smith et al. (2007).

Animals models for testing anticonvulsant drugs (Screening)

Since the Landmark identification of the anticonvulsant properties of phenytoin in 1936 by virtue of its ability to protect against electroshock-induced convulsions in the cat (Putman & Merritt, 1937) the majority of novel AEDs have been identified through screening in animal models of epilepsy.

The National Institutes of Health (NIH)/ American Epilepsy Society (AES) Models II Workshop, held in 2002, described the "ideal" epilepsy model as one that reflects similar pathophysiology and phenomenology to human epilepsy. Seizures should evolve spontaneousl after a postinsult latent period or in a developmental time frame consistent with the human condition. Furthermore, the ideal model should display a pharmacological profile that is resistant to at least two of the existing AEDs (Stables et al., 2003). Finally, the ideal model would be amenable to high-throughput screening. Given the highly heterogeneous nature of seizure disorders in humans, the complexity of the seizure phenotypes, and the syndromes involved, the reality is that it is highly unlikely that any one animal model will ever predict the full therapeutic potential of an investigational AED. Therefore, investigational AEDs are currently evaluated in a battery of syndrome-specific model systems. As specific models are developed (and the drugs they identify are validated clinically), they are integrated into the existing discovery process to better identify more effective antiseizure and potentially antiepileptic therapies. Moving beyond the symptomatic treatment of epilepsy, the goal of most basic and clinical scientists in epilepsy research is to identify therapies capable of preventing, delaying, or modifying the disorder (Smith et al., 2007).

The fact that preclinical models used for identification and development of novel drugs have been originally validated by 'old' drugs, i.e. conventional anticonvulsants, may explain that several of the new drugs possess mechanisms which do not differ from those of the standard drugs .

The MES and PTZ tests

The most commonly employed animal models in the search for new anticonvulsant drugs are the maximal electroshock seizure (MES) test and the pentylenetetrazole (PTZ) seizure test (Löscher &

Schmidt, 1988). The maximal electroshock seizure test, in which tonic hindlimb seizures are induced by bilateral corneal or transauricular electrical stimulation, is thought to be predictive of anticonvulsant drug efficacy against generalized tonic-clonic seizures, while the pentylenetetrazole test, in which generalized myoclonic and clonic seizures are induced by systemic (usually s.c. or i.p.) administration of convulsant doses of PTZ, is thought to represent a valid model for generalized absence and/or myoclonic seizures in humans (Löscher, 1998).

Everett and Richards (1944) demonstrated that both trimethadione and phenobarbital, but not phenytoin (PHT), were able to block seizures induced by the $GABA_A$-receptor antagonist PTZ. Soon thereafter, Lennox (1945) demonstrated that trimethadione was effective at attenuating petit mal (i.e., absence epilepsy) attacks but was ineffective intreating or worsening grand mal seizures (i.e., generalized tonic-clonic seizures).

The positive results obtained in the PTZ seizure test were historically considered suggestive of potential clinical utility against generalized absence epilepsy, based largely on the finding that drugs active in the clinic against spike-wave seizures (e.g., ethosuximide, trimethadione, valproic acid, the benzodiazepines) were effective at blocking clonic seizures induced by PTZ (Smith et al., 2007).

MES and PTZ tests provide some insight into the ability of a given drug to penetrate the blood-brain barrier and exert a central nervous system (CNS) effect. Indeed, both models are nonselective with respect to mechanism and therefore are well suited for screening anticonvulsant activity, as neither model assumes that the pharmacodynamic activity of a particular drug is dependent on its molecular mechanism of action (Smith et al., 2007).

The pilocarpine (PILO) and kainate (KAI) test

Pilocarpine and kainate models replicate several phenomenological features of human temporal lobe epilepsy and can be used as animal preparations to understand the basic mechanisms of epileptogenesis (Turski et al., 1983; Ben-Ari, 1985; Turski et al., 1989). Local or systemic administration of PILO and KAI in rodents leads to a pattern of repetitive limbic seizures and status epilepticus, which can last for several hours (Cavalheiro et al., 1982; Leite et al., 2002).

The brain damage induced by status epilepticus in such preparations may be considered an equivalent of the initial precipitating injury event, usually a prolonged febrile convulsion, which is commonly found in patients with mesial temporal lobe epilepsy (Leite et al., 2002).

Indeed, neuropathological changes such as neuron loss in several hippocampal subfields and reorganization of mossy fibers into the molecular layer of the fascia dentata are observed in both models and are similar to hippocampi from patients with hippocampal sclerosis (Mello et al., 1993; Mathern et al., 1995). This abnormal synaptic reorganization has been suggested to be an anatomical substrate for epileptogenesis (Buckmaster & Dudek, 1997).

Thus, for AED studies in PILO and KAI models, sequential analysis will enable to build precise and reliable correlations between pharmacological effects on seizure behavior and involved brain substrates (Leite et al., 2002).

Chemical kindling model

Those animal models previously cited are convenient but does not mimic spontaneous seizures occurring in the epileptic brain (Meldrum & Rogawski, 2007). Indeed, kindling model has been widely studied both as a tool for understanding chronic epileptogenesis and as a model for testing AEDs with a potential for treating complex partial seizures. This model is too laborious for use as a primary screening procedure, yet it is clear that it consistently identifies compounds with therapeutic potential in complex partial seizures (Löscher & Schmidt, 2006).

The kindling model of epileptogenesis, originally described by Goddard et al. (1969), is characterized by the development of persistent reduction in seizures threshold after a repeated administration of subconvulsant doses of stimulant drugs, such as cocaine, carbamylcholine and pentylenetetrazole (PTZ) (Fabisiak & Schwark, 1982). A well-established model in epilepsy research is PTZ-kindling of mice and rats.

PTZ may cause seizures by inhibitory chloride ion channel associated with $GABA_A$ receptors (Meldrum & Nilsson, 1976). The mechanism underlying kindling are nowadays still not completely understood (Rössler et al., 2000). As PTZ has been shown to interact with the GABA neurotransmitter and the GABA receptor complex (Löscher & Schmidt, 1988), On the other hand, investigations concerning the biochemistry of glutamate, especially modifications in glutamate binding after electrical kindling, showed increased glutamate release and increased receptor density in target neurons populations (Cincotta et al., 1991). Other studies provided evidence that AMPA and NMDA receptors are involved in the initiation of seizures and their propagation (Velisek et al., 1995) and that NMDA receptors antagonists retard the development of kindling (Becker et al., 2001). Although, little is known about the changes of the glutamatergic neuronal transmission after chemical kindling induced by repeated applications of initially subconvulsive doses of PTZ (Rauca et al., 2000), however, alters in glutamatergic system may not be the main factor but one of several possibilities.

Others methods

Summary of the common methods used to evaluation anticonvulsant properties of the medicinal plants and AED as showed in Table 2.

In fact, all currently available drugs are anticonvulsant (anti-seizure) rather than antiepileptic. The latter term should only be used for drugs which prevent or treat epilepsy and not solely its symptoms. The goal of therapy with an anticonvulsant drug is to keep the patient free of seizures without interfering with normal brain function (Löscher, 1998). The selection of an anticonvulsant drug is based primarily on its efficacy for specific types of seizures and epilepsy (Mattson, 1995).

CONCLUSION

It can be concluded that studies with species from a range of families have been shown anticonvulsant properties and understanding of the complex mechanism of epilepsy. Academic institutions should invest in this type of study with medicinal plants and contribute to the benefit of the populations needing this type of health care. Thus, it is the wish of the authors that this review article will stimulate the interests in further investigations into natural products for new antiepileptic agents.

Table 1. Plant showed anticonvulsant properties.

Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
Abelmoschus angulosus	Malvaceae	Aerial Parts	India	ip	-	ACV	Bhakuni et al., 1988
Abrus precatorius	Leguminosae	Root	India	-	-	LIS, SIS	Adesina, 1982a
Abrus precatorius	Fabaceae	Root	Nigeria	ip	-	MIS	Adesina, 1982a
Acanthus longifolius	Acanthaceae	Entire Plant	Bulgaria	ip	2-4 mg/ml	MIS, MES	Rousinov et al., 1966
Achillea millefolium	Asteraceae	Aerial Parts	Bulgaria	ip	2-4 mg/ml	ACV, MES	Athanassova et al., 1965
Aconitum species	Ranunculaceae	-	China	iv	-	AVC	Ameri, 1997
Acorus calamus	Araceae	-	-	-	-	MIS	Chauhan et al., 1988
Acosmium subelegans	Leguminosae	Aerial Parts	Brazil	ig	100, 500, 1000 mg/kg	MES, PTZ	Vieira et al., 2002
Adonis vernalis	Ranunculaceae	-	-	-	-	AVC	Chauhan et al., 1988
Afraegle paniculata	Rutaceae	Root, Stem	Nigeria	ip	-	LIS, ACV	Ameri, 1997
Albizia lebbek	Leguminosae	Leaf, Root	India	ip	-	PIC, PTZ, MIS	Kasture et al., 1996
Albizia zygia	Leguminosae	Leaf	Africa	po	-	LIS, SIS	Adesina, 1982a
Allium ascalonicum	Liliaceae	Shallot	India	-	-	LIS	Adesina, 1982a
Allium cepa	Liliaceae	Bulb	India	-	-	LIS, SIS	Adesina, 1982a
Allium sativum	Liliaceae	Bulb	India	-	-	LIS	Adesina, 1982a
Alstonia boonei	Apocynaceae	Stem	India	-	-	LIS	Adesina, 1982a
Alstonia schoaris	Apocynaceae	Stem	India	-	-	LIS	Adesina, 1982a
Annona muricata	Annonaceae	Flower	India	po	-	LIS, SIS	Adesina, 1982a
Apium graveolens	Umbelliferae	-	-	-	-	ACV	Chauhan et al., 1988
Acorus calamus	Araceae	Rhizome	Bulgaria	ip	2-4 mg/ml	ACV, MES, PTZ	Rousinov et al., 1966
Acorus gramineus	Araceae	Rhizome	Taiwan	ip	5 mg/kg	PTZ	Liao et al., 1998
Afraegle paniculata	Rutaceae	Rootbark	Nigeria	ip	150,250 mg/kg	ACV, MIS	Adesina & Ette 1982
Afrormosia laxiflora	Fabaceae	Root	Nigeria	ip	250 mg/kg	MES, PIC	Haruna, 2000
Akebia species	Lardizabalaceae	Dried Stem	South Korea	ip	1 mg/kg	ACV	Hong et al., 1988
Albizia lebbek	Fabaceae	Leaf	India	ip	10, 20, 40, 80 mg/kg	MES, PTZ, PIC	Kasture et al., 1996
Allium ascalonicum	Liliaceae	Flower	Nigeria	ip	-	MIS	Adesina, 1982a
Allium cepa	Liliaceae	Bulb	Nigeria	ip	-	MIS	Adesina, 1982a
Allium sativum	Liliaceae	Bulb	Nigeria	ip	-	ACV, MIS	Adesina, 1982a
Alstonia boonei	Apocynaceae	Stembark	Nigeria	ip	-	MIS	Adesina, 1982a
Altingia excelsa	Hamamelidaceae	Entire Plant	India	ip	-	ACV	Singh et al., 1985
Anagallis arvensis	Primulaceae	Entire Plant	Bulgaria	ip	2-4 ml/kg	MIS, SIS	Rousinov et al., 1966
Angelica pancicii	Apiaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MIS	Rousinov et al., 1966
Annona diversifolia	Annonaceae	Leaf	Mexico	ip	200 mg/kg	ACV, PTZ	Gonzalez-Trujano, 1998
Annona muricata	Annonaceae	Leaf	Gabon	ip	100, 250 mg/kg	PTZ	N'gouemo et al., 1997
Apium graveolens	Apiaceae	Seed	India	ip	0.73; 1 ml/kg-	PTZ, MES, MIS	Kulshrestha et al., 1970
Areca catechu	Palmae	-	-	sc, iv	-	ACV	Lodge et al., 1997
Armillaria mellea	Tricholomataceae	-	China	sc	10-20 ml/kg; 25 mg/kg	ACV	Junhua et al., 1990
Artemisia absinthium	Asteraceae	Aerial Parts	Bulgaria	ip	2-4 ml/kg	PTZ, MES, PILO	Athanassova et al., 1965
Artemisia verlotorum	Asteraceae	Whole Plant	Brazil	ip	-	MES, PILO, 3-MCAIC	Lima et al., 1993
Artemisia vulgaris	Asteraceae	Leaf, Stem	Israel	ip	0.2 ml/animal	PIC	Abdul-Ghani et al., 1987
Asarum heterotropoides	Aristolochiaceae	Whole Plant	China	-	-	ACV	Sun et al., 1991
Asarum himalaycum	Aristolochiaceae	Whole Plant	China	-	-	ACV	Sun et al., 1991
Asarum ichangense	Aristolochiaceae	Whole Plant	China	-	-	ACV	Sun et al., 1991
Asparagus officinalis	Liliaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	LIS, MIS	Chauhan et al., 1988
Asparagus verticillatus	Liliaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MIS, SIS	Athanassova et al., 1969
Asperula odorata	Rubiaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MIS, SIS	Athanassova et al., 1969
Asplenium trichomanes	Aspleniaceae	Entire Plant	Bulgaria	ip	2-4 ml/kg	MES, MIS, SIS	Athanassova et al., 1965

Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
Atractylodes lancea	Asteraceae	Rhizome	Japan	po	250, 500 mg/kg	MES	Yamahara et al., 1977
Astragalus centralpinus	Leguminosae	-	-	ip	-	HIC	Chauhan et al., 1988
Atractylodes lancea	Asteraceae	-	China	ip	500 mg/kg	MIN, PTZ, PIC	Chiou et al., 1997
Baccharis serraefolia	Asteraceae	Leaf	Mexico	ip	200 mg/kg	PIZ, SIS	Tortoriello et al., 1996
Basslla alba	Basellaceae	Leaf, Stem	India	po	-	LIS, SIS	Adesina, 1982a
Basslla ruba	Basellaceae	Leaf, Stem	India	po	-	LIS, SIS	Adesina, 1982a
Bauhinia outimouta	Fabaceae	Whole Plant	Brazil	ip	150 mg/kg	PTZ	Quintans-Júnior et al., 2002
Berberis lycium	Berberidaceae	Root	India	ip	25 mg/kg	MES	Dhar et al., 1968
Boerhavia diffusa	Nyctaginaceae	Leaf	Nigeria	ip	2 mg/kg	ACV, PTZ, MES, MIS	Akah & Nwambie, 1993
Bupleurum chinense	Apiaceae	Entire Plant	China	ip	-	ACV	Wu & Yu, 1984
Bupleurum falcatum	Apiaceae	Root	China/Japan	ip, po	1,5 mg/kg	ACV	Narita et al., 1982
Butea monosperma	Fabaceae	Flower	India	ip	50, 200 mg/kg	MES, PTZ, SIS	Kasture et al., 2000
Buthus martensii	Buthidae	Venom	China	-	-	ACV	Liu et al., 1989
Cadia rubra	Fabaceae	Leaf	Madagascar	ip	100 mg/kg	PTZ	Pieretti et al., 1993
Caesalpinia bonduc	Leguminosae	Root, Stem	-	-	-	LIS, SIS	Adesina, 1982a
Caesalpinia bonducella	Fabaceae	Leaf	Nigeria	ip	-	MES, MIS, SIS	Adesina, 1982a
Calliandra portoricensis	Leguminosae	Root, Stem	Nigeria	ip	100, 300 mg/kg	LIS, MIS, SIS	Akah & Nwaiwu 1988
Cannabis sativa	Cannabinaceae	Whole Plant	Bulgaria	ip,po, sc	2-4 ml/kg	ACV, PTZ, MES, KID	Dantas, 2005; Dwivedi & Harbison, 1975
Canscora decussata	Gentianaceae	Whole Plant	-	po	-	ACV	Dikshit et al., 1972
Capparis baduca	Capparaceae	-	-	-	-	ACV	Adesina, 1982a
Capsella bursa-pastoris	Brassicaceae	Entire Plant	Bulgaria	ip	2-4 ml/kg	MES, MIS	Rousinov et al., 1966
Capsicum annum	Solanaceae	Flower	-	-	-	LIS, SIS	Adesina, 1982a
Carica papaya	Caricaceae	Root	Nigeria	-	20, 100 mg/kg	MES, LIS, SIS	Chauhan et al., 1988
Carthamus tinctorius	Asteraceae	Flower	Japan	sc	10 mg/kg	MIS	Kasahara et al., 1989
Casimiroa edulis	Rutaceae	Leaf	Mexico	po, sc	10, 100 mg/kg	MES, MIS	Adesina 1982a; Ruiz et al., 1995
Cassia siamea	Fabaceae	Leaf	Thailand	ip	-	MIS, SIS	Arunlakshana, 1949
Centella asiatica	Apiaceae	Aerial Part, Entire Plant	Nigeria, India, Brazil	ip	-, 500 mg/kg	LIS, PTZ, SIS	Chauhan et al., 1988; Sudha et al. 2002; De Lucia et al., 1997
Cerbera odollam	Apocynaceae	Leaf	Vietnam	ip	10 mg/kg	PTZ	Hien et al., 1991
Chaerophyllum bulbosum	Apiaceae	Aerial Part	Bulgaria	ip	2-4 ml/kg	MES, MIS, SIS	Rousinov et al., 1966
Chelidonium majus	Papaveraceae	Aerial Part	França	ip	9.5 mg/kg	MES, PTZ	Mahe et al., 1978
Chrysanthemum indicum	Asteraceae	Flower, Stem	Bulgaria	ip	0.25 mg/kg	MÊS, SIS	Lashev et al., 1981
Cimicifuga dahurica	Ranunculaceae	Root	Russia	ip	-	SIS	Nikol-Skaya & Shreter, 1961
Cimicifuga simplex	Ranunculaceae	Rhizome	China	-	0.5, 1, 2 mg/kg	MIS, SIS	Shibata et al., 1980
Cinnamomum cassia	Lauraceae	Bark	China	po	2 mg	ACV	Narita et al., 1982
Cinnamomum loureirii	Lauraceae	Bark	China	po	0.3%	ACV, MIS	Sugaya et al., 1978
Cinnamomum zeylanicum	Lauraceae	Bark	China	po	1 mg/kg	ACV	Sugaya et al., 1988
Cinchona officinalis	Rubiaceae	-	-	-	-	ACV	Chauhan et al., 1988
Cissampelos pareira	Menispermaceae	Root	Nigeria	ip	-	MIS, LIS, SIS	Adesina, 1982a
Cistus villosus var.tauricus	Cistaceae	Aerial Part	Bulgaria	ip	4 ml/kg	MES, MIS, SIS	Athanassova et al., 1969
Citrus aurantifolia	Rutaceae	Peel, Flower	-	-	-	LIS, SIS	Adesina, 1982a
Citrus aurantium	Rutaceae	Peel	-	ip	800 mg/kg	LIS, SIS	Adesina, 1982a
Citrus bergamia ssp. *vulgaris*	Rutaceae	Flower	Italy	ip	20,40 mg/kg	PTZ	Occhiuto et al., 1995
Clausena anisata	Rutaceae	Root, Stem	Nigeria	ip	150, 250 mg/kg	MIS, PTZ, SIS	Makanju, 1983
Cleome cileata	Capparidaceae	Leaf	Nigeria	ip	55, 68 mg/kg	MES, PTZ	Akah et al., 1993; 1997
Clerodendrum colebrookianum	Verbenaceae	Leaf	India	ip	40 mg/kg	SIS	Gupta et al., 1998

Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
Cnestis ferruginea	Verbenaceae	Rootbark	Ivory Coast	ip	0.7 mg/kg	SIS	Declume et al., 1984
Cnestis glabra	Connaraceae	-	-	-	-	ACV	Chauhan et al., 1988
Cocculus hirsutus	Menispermaceae	Root, Stem	India	ip	100 mg/kg	MES, MIS	Das et al., 1964
Cola acuminata	Sterculiaceae	-	-	-	-	LIS, SIS	Adesina, 1982a
Connarus wightii	Connaraceae	Aerial Part	India	ip	165 mg/kg	SIS	Dhar et al., 1973
Consolida orientalis	Ranunculaceae	Aerial Part	Bulgaria	ip	4 ml/kg	MES, MIS, SIS	Athanassova et al., 1969
Convolvulus arvensis	Convolvulaceae	Aerial Part	Bulgaria	ip	4, 44 ml/kg	ACV, MIS, SIS	Chauhan et al., 1988,
Convolvulus hirsutus	Convolvulaceae	Aerial Part	Bulgaria	ip	4 ml/kg	MIS, SIS	Athanassova et al., 1969
Convolvulus pluricaulis	Convolvulaceae	Entire Plant	India	ip	-	ACV, MES	Sharmaxvn et al., 1965
Convolvulus suendermannii	Convolvulaceae	Aerial Part	Bulgaria	ip	4 ml/kg	MIS, SIS	Athanassova et al., 1969
Coptis chinensis	Ranunculaceae	Rhizome	South Korea	-	1 mg/kg	ACV	Hong et al., 1988
Corydalis cava	Papaveraceae	Aerial Part	Bulgaria	ip	2-4 ml/kg, 4 mg/kg	MES	Athanassova et al., 1965
Crassostrea gigas	Ostreidae	-	Japan	po	10%	ACV	Bac et al., 1998
Croton zehntneri	Euphorbiaceae	Branches	Brazil	-	20,80 mg/kg	ACV, PIC, SIS	Bernardi et al., 1991
Coyledon orbiculata	Crussalaceae	-	South Africa	ip	50-400 mg/kg	ACV, PIC, PTZ	Amabeoku et al., 2007
Cryptotympana atrata	Cicadidae	Skin	Taiwan	ig	0.5 mg/kg	PIC	Hsieh et al., 1991
Cucurbita pepo	Cucurbitaceae	-	Nigeria	-	-	LIS, SIS	Adesina, 1982a
Cuminum cyminum	Apiaceae	Fruit	Iran	ip	0.5 ml/mg	MES, PTZ	Sayyah et al., 2002
Curcuma amada	Zingiberaceae	Rhizome	India	ip	500 mg/kg	MES	Bhakuni et al., 1969
Curcuma aromatica	Zingiberaceae	Root	China	Ig, po	-, 2.5 mg	ACV	Li, 1987
Cuscuta chinensis	Convolvulaceae	Entire Plant	China	ig	1 mg/kg	ACV	Akbar et al., 1985a
Cyathea nilgirensis	Cyatheaceae	Aerial Part	India	ip	0.25 mg/kg	MES	Dhawan et al., 1977
Cylista scariosa	Fabaceae	Root	India	ip	500 mg/kg	SIS	Dhar et al., 1968
Cymbopogon citratus	Gramineae	Leaf	Brazil	po, ip	-	ACV	Carlini et al., 1986
Cynanchum otophyllum	Asclepiadaceae	Rhizome	China	ip	12.5 mg/kg	ACV	Pei et al., 1981
Cynodon dactylon	Gramineae	Leaf	Nigeria	ip	600 mg/kg	MES, MIS, PTZ	Akah et al., 1997
Cyperus articulatus	Cyperaceae	Rhizome	L. America	po	50-2000 mg/kg	AVC	Ngo Bum et al., 1996
Cyperus rotundus	Cyperaceae	Root	Nigeria	ip	-	LIS, SIS	Adesina, 1982a
Cystophora moniliformis	Cystoseiraceae	Thallus	Australia	-	-	ACV	Spence et al., 1979
Cystoseira usneoides	Cystoseiraceae	Thallus	Spain	ip	6.25 mg/kg	ACV	Vazquez-Freire et al., 1995
Delphinium consolida	Ranunculaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	AVC, MIS, SIS	Nsour et al., 2000
Delphinium denudatum	Ranunculaceae	Root	Pakistan	ip	400, 600, 800 mg/kg	ACV, PIC, PTZ, SIS	Raza et al., 2001
Desmodium adscendes	Leguminosae	Leaf	Africa	ip	300 mg/kg	PTZ	N'gouemo et al., 1996
Dictamnus albus	Rutaceae	Entire Plant	Bulgaria	sc	2-4ml/kg	ACV	Athanassova et al., 1965
Digitalis ferruginea	Scrophulariaceae	Entire Plant	Bulgaria	sc	2-4 ml/kg	ACV, MES	Athanassova et al., 1965
Digitalis lanata	Scrophulariaceae	Entire Plant	Bulgaria	sc	2-4 ml/kg	ACV, MES	Athanassova et al., 1965
Dillenia indica	Dillenciaceae	Leaf	India	ip	400 mg/kg	MES	Bhakuni et al., 1969
Diospyros kaki	Ebenaceae	Calix	Japan	-	-	ACV	Fukuda & Shibata, 1994
Diospyros peregrine	Ebenaceae	Entire Plant	India	-	-	ACV	Singh et al., 1985
Duboisia leichhardtii	Solanaceae	-	-	-	-	AVC	Nsour et al., 2000
Dunaliella tertilecta	Dunaliellaceae	-	Spain	-	-	ACV	Laguna et al., 1990
Echinacea purpurea	Asteraceae	-	-	-	-	AVC	Nsour et al., 2000
Echium vulgare	Boraginaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	ACV, MES, MIS, SIS	Nsour et al., 2000,
Egletes viscosa	Asteraceae	Flower	Brazil	ig	-	PTZ	Souza et al., 1998
Elaeocarpus ganitus	Elaeocarpaceae	Entire Plant/Fruit	India	ip	1.2, 100 mg/kg	MES, MIS	Bhattacharya et al., 1975 Dasgupta et al., 1984
Elettaria cardamomum	Zingiberaceae	Seed	India	ig	3, 10 mg/kg	ACV	Shukia et al., 1987
Eryngium foetidum	Apiaceae	Leaf	Jamaica	ip	3 ml/kg	PIC	Simon, 1986
Erythroxylum spp.	Erythroxylaceae	Leaf	-	-	-	MIS	Adesina, 1982a

Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
Erythraea centaurium	Gentianaceae	Aerial Parts	Bulgaria	ip	2-4 ml/kg	CZIZ	Athanassova et al., 1965
Erythrina velutina	Fabaceae	Stem Bark	Brazil	ip	200-400 mg/kg	PTZ, SIS	Vasconcelos et al., 2007
Erythrina mulungu	Fabaceae	Stem Bark	Brazil	ip	200-400 mg/kg	PTZ, SIS	Vasconcelos et al., 2007
Euphorbia antiquorum	Euphorbiaceae	Whole Plant	India	ip	40 mg/kg	MIS	Dey et al., 1968
Euphorbia dracunculoides	Euphorbiaceae	Entire Plant	India	ip	500 mg/kg	ACV, MES	Bhakuni et al., 1969
Euphorbia hirta	Euphorbiaceae	Whole Plant	-	ip	-	ACV	Lanhers et al., 1996
Euphorbia pilulifera	Euphorbiaceae	Whole Plant	-	-	-	ACV	Chauhan et al., 1988
Euphorbia tirucalli	Euphorbiaceae	Aerial Part	India	ip	250 mg/kg	ACV, MIS	Dhar et al., 1968
Evolvulus nummularius	Convolvulaceae	Entire Plant	India	ip	40, 100 mg/kg	MES, MIS	Dey et al., 1968; Chatterjee 1964
Ferula gummosa	Apiaceae	Seed	Iran	ip	55, 198.3 mg/kg	MES, PTZ	Sayyah et al., 2002
Galeopsis ladanum	Lamiaceae	Aerial parts	poland	ip	200 mg/kg	PTZ	Czarnecki et al., 1993
Galicia spp.	Galiaceae	-	-	-	-	ACV	Chauhan et al., 1988
Galium cruciata	Rubiaceae	-	-	-	-	ACV	Chauhan et al., 1988
Galium sylvaticum	Rubiaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MIS, SIS	Chauhan et al., 1988,
Galphimia glauca	Malpighiaceae	Aerial Parts	Mexico	ip	500 mg/kg	ACV, LIS, SIS	Tortoriello et al., 1992
Galphimia glauca	Malpighiaceae	Aerial Parts	Mexico	ip	-	ACV	Tortoriello, 1993
Ganoderma lucidum	Ganodermataceae	Fruit	Japan	sc	300 mg/kg	PTZ, SIS	Kasahara et al., 1987
Garcinia mangostana	Clusiaceae	Fruit	-	-	-	ACV	Kurukawa et al., 1997
Gastrodia elata	Orchidaceae	-	China		5, 10, 20, 500 mg/kg	ACV, KAI	Chen, 1977; Chauhan et al., 1988, Hsieh et al., 2001
Geranium rotundifolium	Geraniaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MES, MIS, SIS	Athanassova et al., 1969
Ginkgo biloba	Ginkgoaceae	Rhizome	Africa	po	-	ACV	Rodriguez, 1993
Gleditsia officinalis	Fabaceae	Fruit	China	ig	-	ACV	Yen, 1977
Glycyrrhiza glabra	Fabaceae	Rhizome	Korea	-	1 mg/kg	ACV	Hong et al., 1988
Grewia hirsuta	Tiliaceae	Entire Plant	India	ip	500 mg/kg	SIS	Bhakuni et al., 1971
Gymnosporia falconeri	Celastraceae	Aerial Parts	India	ip	500 mg/kg	MIS	Bhakuni et al., 1971
Haplophyllum perforatum	Rutaceae	Seed	-	-	-	CZIC, LIS	Chauhan et al., 1988
Haplophyllum locosum	Rutaceae	Seed	-	-	-	CZIC, LIS	Chauhan et al., 1988
Haplophyllum spp	Rutaceae	-	-	-	-	ACV	Chauhan et al., 1988
Hedera rhombea	Araliaceae	Leaf	South Korea	ip	0.1 mg/kg	SIS	Lee et al., 1992
Helianthus annuus	Asteraceae	Flower	Bulgaria	-	2-4 ml/kg	CZIZ, MES	Athanassova et al., 1965
Heracleum sibiricum	Umbelliferae	-	-	-	-	MES, PTZ, CZIC, SIS	Chauhan et al., 1988
Heracleum vericillatum	Umbelliferae	-	-	-	-	MES, PTZ, CZIC, SIS	Chauhan et al., 1988
Herpestris monniera	Scrophulariaceae	-	-	-	-	PTZ	Chauhan et al., 1988
Hippeastrum vittatum	Amarillydaceae	Bulbs	Brazil	ip	-		Silva et al., 2006
Holarrhena floribunda	Apocynaceae	Leaf	Nigeria	ip	-	MES, PTZ	Akah et al., 1997
Hoslundia opposita	Lamiaceae	Leaf	Nigeria	ip	50, 354, 398 mg/kg	MES, PTZ	Akah et al., 1993
Humulus lupulus	Cannabaceae	-	Switzerland	ip	250, 500 mg/kg	PTZ	Lee et al., 1993
Hypericum perforatum	Hypericaceae	Whole Plant	Greece	ip	-	PTZ	Ozturk et al., 1996
Icacina trichantha	Icacinaceae	Tuber	Nigeria	ip	80, 100, 400 mg/kg	ACV, PTZ, SIS	Asuzu et al., 1990
Ipomoea stans	Convolvulaceae	Wood	Mexico	iv	-	MES, PTZ	Contreras et al., 1996
Iris kamaonensis	Iridaceae	Entire Plant	India	ip	375 mg/kg	MES	Dhawan et al., 1977
Jatropha curcas	Euphorbiaceae	Root	-	-	-	LIS, SIS	Adesina, 1982a
Jatropha gossypiifolia	Euphorbiaceae	Root, Leaf	-	-	-	LIS, SIS	Adesina, 1982a
Juniperus macropoda	Cupressaceae	Fruit	India	ip	100 mg/kg	ACV	Mishra et al., 1989
Kalanchoe crenata	Crussalaceae	Leaf	Cameroon	ip	150, 300 mg/kg	PTZ, SIS	Nguelefack et al., 2006
Khaya grandifoliola	Meliaceae	Stembark	Nigeria	ip	50 mg/kg	ACV	Awe te al., 1997
Kochia prostrate	Chenopodiaceae	-	-	-	-	SIS	Chauhan et al., 1988

Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
Lactuca sativa	Asteraceae	Seed	Egypt	po	2.5 ml/kg	PTZ	Said et al., 1996
Lantana camara	Verbenaceae	Root, Leaf	-	iv	-	LIS, SIS	Chauhan et al., 1988
Lantana microphylla	Verbenaceae	Leaf	Brazil	-	-	LIS, SIS	Adesina, 1982a
Laurus nobilis	Lauraceae	Leaf	Iran	ip	10 ml/kg	ACV	Sayyah et al., 2002
Lavandura stoechas	Lamiaceae	Flower	Africa	ip	600 mg/kg	PTZ	Gilani et al., 2000
Ledebouriella seseloides	Apiaceae	Root	China	-	-	ACV	Yen, 1977
Leea indica	Leeaceae	Leaf	India	ip	125 mg/kg	SIS	Dhar et al., 1968
Leonotis leonurus	Lamiaceae	Leaf	South Africa	ip	200 mg/kg	ACV	Beinvenu et al., 2002
Leonurus cardiaca	Lamiaceae	Aerial Parts	Bulgaria	ip	2-4 ml/kg	ACV, MES, SIS	Adesina, 1982a
Lettsomia setosa	Convolvulaceae	Aerial Parts	India	ip	500 mg/kg	MES	Bhakuni et al., 1971
Licaria puchury-major	Lauraceae	Dried Seed	Brazil	ip	200 mk/kg	MES	Carlini et al., 1983
Lippia alba	Verbenaceae	Leaf	Brazil	ip	200 mg/kg, 1g/kg	SIS, PIC	Barros Viana et al., 2000
Lobelia inflata	Campanulaceae	Leaf	Sclotand	po	10 ml	ACV	Bhakuni et al., 1971
Lobophytum species	Alcyoniidae	-	Australia	-	-	MIS	Baird-Lambert et al., 1980
Lonchocarpus sericeus	Leguminosae	Root	-	-	-	LIS, SIS	Chauhan et al., 1988
Luvunga scandens	Rutaceae	-	India	ip	100 mg/kg	ACV	Mishra et al., 1988
Lycium species	Solanaceae	Rootbark	South Korea	-	1 mg/kg	ACV	Hong et al., 1988
Magnolia grandiflora	Magnoliaceae	Seed	Mexico	ig	10 mg/kg	MES	Ramirez et al., 1998
Magnolia officinalis	Magnoliaceae	Bark	China,Japan	ip	-	ACV	Watanabe et al., 1983
Magnolia obovata	Magnoliaceae	-	-	-	-	SIS, PIC	Chauhan et al., 1988
Marsilea rajasthanesis	Marsileaceae	-	-	-	-	ACV	Chauhan et al., 1988
Marrubium peregrinum	Lamiaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MES, MIS	Athanassova et al., 1965
Marrubium vulgare	Lamiaceae	Leaf, Flower	Bulgaria	ip	2-4 ml/kg	ACV, CZIC, MES	Chauhan et al., 1988,
Maprounea africana	Euphorbiaceae	Leaf	Congo	ip	-	ACV, MES, PTZ, PIC	N'gouemo et al., 1994a
Matricaria chamomilla	Asteraceae	Flower	Bulgaria	ip	2-4 ml/kg	CZIC, MES, PIC	Athanassova et al., 1969
Matricaria recutita	Asteraceae	Flower	USA, Europe	iv	-	PTZ	Viola et al., 1995
Maytenus spp.	Celastraceae	Leaf	Brazil	ip, po	-	TCES, PTZ	Oliveira et al., 1991
Melia azedarach	Meliaceae	Root Bark	Nigeria	ip	-	MIS, SIS	Adesina, 1982a
Melothria maderaspatana	Cucurbitaceae	Aerial Parts	India	-	-	ACV	Sinha et al., 1997
Mentha piperita	Lamiaceae	Leaf	-	po	0.7, 10 ml/kg	ACV	Leslie, 1978
Mentha suaveolens	Lamiaceae	Leaf	Spain	ip	200 mg/kg	ACV	Moreno et al., 2002
Mikania cordata	Asteraceae	Aerial Parts	Spain	ip	400 mg/kg	MES	Moreno et al., 2002
Mitragyna africana	Rubiaceae	Stembark	Nigeria	ip	400 mg/kg	SIS	Aji et al., 2001
Momordica balsamina	Cucurbitaceae	Leaf	Nigeria	ip	-	LIS, SIS	Adesina, 1982a
Momordica charantia	Cucurbitaceae	Leaf, Flower	Nigeria	ip	-	LIS, SIS	Adesina, 1982a
Moringa oleifera	Moringaceae	Root	Nigeria	-	-	LIS, SIS	Adesina, 1982a
Moringa pterygosperma	Moringaceae	Root	Nigeria	ip	-	MIS, SIS	Adesina, 1982a
Nardostachys jatamansi	Valerianaceae	Rhizome	India	ip	-	ACV	Debelmas et al., 1976
Nepeta cataria	Lamiaceae	Leaf	Brazil	In ration	10 %	PTZ, SIS	Massoco et al., 1995
Nerium oleander	Apocynaceae	Leaf	Pakistan	ip	50 mg/kg	ACV	Zia et al., 1995
Newboldia leavis	Bignoniaceae	Leaf	Nigeria	ip	100, 145, 186 mg/kg	MES, PTZ	Olajide et al., 1997
Nicotiana tabacum	Solanaceae	Leaf	Nigeria	ip	-	LIS, MIS, SIS	Chauhan et al., 1988
Notopterygium incisum	Apiaceae	Root	China	ig	-	ACV	Yen, 1977
Ocimum americanum	Lamiaceae	Leaf	Nigeria	ip	-	LIS	Adesina, 1982a
Ocimum basilicum	Lamiaceae	Leaf	Nigeria	ip	-	LIS	Adesina, 1982a
Ocimum canun	Lamiaceae	Leaf	Thailand	ig	20-50 mg	SIS	Ketusingha et al., 1950
Ocimum gratissimum	Lamiaceae	Leaf	Nigeria	ip	-	LIS, SIS	Adesina, 1982a
Ocimum sanctum	Lamiaceae	Entire Plant	India	-	1mg	ACV	Sakina et al., 1990
Oplopanax elatus	Araliaceae	Root	China	-	-	ACV	Qu et al., 1984

Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
Ostrea species	Ostreidae	-	Japan	ig	1 mg/kg	PTZ	Tsuda et al., 1998
Pachyma species	Polyporaceae	Fruit	South Korea	-	1 mg/kg	ACV	Hong et al., 1988
Paconia radiz	Paconiaceae	Root	Japan	po	-	ACV	Tsuda et al., 1997
Paeonia alba	Paeoniaceae	Root	South Korea	ig	800 mg/kg	ACV	Hung et al., 1983
Paeonia albiflora	Paeoniaceae	Root	China	po	6 mg	ACV	Narita et al., 1982
Paeonia albiflora	Paeoniaceae	Root	Japan	ig	100 mg/kg	PTZ	Sugaya et al., 1991
Paeonia emodi	Paeoniaceae	Root	India	Ig	10 mg/kg	MIES, MIS	Ahmad et al., 1981
Paeonia japonica var. *pilosa*	Paeoniaceae	Root	South Korea	ip	2, 20 mg/kg	PIC, SIS	Hong et al., 1979
Paeonia rubra	Paeoniaceae	Root	South Korea	ip	1 mg/kg	ACV	Hong et al., 1988
Palisota ambigua	Commelinaceae	Leaf	Gabon	ip	50 mg/kg	PTZ	N'gouemo et al., 1994b
Panax ginseng	Araliaceae	Root, Leaf	China	ip	100, 200 mg/kg	MIS, PIC	Takagi, 1977; Mitra et al., 1996
Patrina intermedia	Valerianaceae	-	-	-	-	SIS	Chauhan et al., 1988
Passiflora alata	Passifloraceae	Dried Leaf	Brazil	ip	75, 150 mg/kg	MIS	Oga et al., 1984
Passiflora incarnata	Passifloraceae	Leaf	Italy	ip	160 mg/kg	PTZ	Speroni et al., 1988
Pausinystalia yohimbe	Rubiaceae	Bark	-	ip	-	ACV	Chermat et al., 1979
Persea indica	Lauraceae	Leaf	Canary Islands	-	2 mg/kg	PTZ	Mazzanti et al., 1993
Phaeodactylum tricoenutum	Fragilaricaceae	-	Spain	ip	150 mg/kg	PTZ	Laguna et al., 1990
Picnomon acarna	Asteraceae	-	-	-	-	ACV	Chauhan et al., 1988
Picrorhiza kurroa	Scrophulariaceae	Entire Plant	India	-	500 mg/kg	MIS	Debelmas et al., 1976
Pimpinella anisum	Apiaceae	Fruit	Bulgaria	ip	2-4 ml/kg	SZIC, MES	Athanassova et al., 1969
Pinellia ternata	Araceae	Tuber	China	po	5 mg	ACV	Narita et al., 1982
Piper guineense	Piperaceae	Flower	Nigeria	ip	-	MIS, NMDLAIC	Abila et al., 1993
Piper logum	Piperaceae	Fruit	China	ip	3.4, 263.4 mg/kg	ACV, MES, PIC, PTZ	Pei, 1983
Piper methysticum	Piperaceae	Flower	Fiji	ip	140 mg/kg	SIS	Klohs et al., 1959
Piper nigrum	Piperaceae	Flower	China	ip	2 mg/kg	ACV, NMDLAIC	Hu & Davies, 1997
Piscidia erythrina	Fabaceae	Bark	USA	ip	900 mg/kg	PTZ	Klohs et al., 1959
Pistacia integerrima	Anacardiaceae	-	India	ip	1 ml/kg	PTZ	Ansari et al., 1993
Pithecellobium samon	Leguminosae	-	-	-	-	PIC	Chauhan et al., 1988
Plectranthus amboinicus	Lamiaceae	Entire Plant	Cuba	ip	-	ACV	Buznego et al., 1999
Plumbago zeylanica	Plumbaginaceae	Root	Nigeria	ip	-	LIS	Adesina, 1982a
Polygala sabulosa	Polygalaceae	Whole Plant	Brazil	ip	250, 500, 1000 mg/kg	PTZ	Duarte et al., 2007
Polypodium vulgare	Polypodiaceae	Root	India	ip	100 mg/kg	MES, PTZ	Mannan et al., 1989
Portucala oleracea	Portulacaceae	Whole Plant	-	ip	-	LIS, SIS	Adesina, 1982a
Prunus spinosa	Rosaceae	Fruit	India	ig	1.5 mg/kg	PTZ	Mannan et al., 1989
Psidium guyanensis	Myrtaceae	Leaf	Brazil	po	-	PTZ, PIC, SIS	Santos et al., 1997
Psidium pohlianum	Myrtaceae	Leaf	Brazil	ig	400 mg/kg	PTZ	Santos et al., 1996
Pterocarpus santalinus	Fabaceae	Stem	India	-	-	MES	Mehta et al., 1979
Qingyangshen	Asclepiadaceae	Root	China	ip	-	KAI, ACV	Kuang et al., 1991; Guo & Kuang, 1993
Rauvolfia ligustrina	Apocynaceae	Root, Aerial	Brazil	ip, po	125, 250 mg/kg	PTZ, PIC, SIS	Quintans-Júnior et al.,2002;2007
Rauvolfia schueli	Apocynaceae	-	-	-	-	ACV	Adesina, 1982a
Rauvolfia serpentina	Apocynaceae	Root, Stem Bark	India	-	-	ACV	Adesina, 1982a
Rauvolfia tetraphylla	Apocynaceae	Entire Plant	India	ip	500 mg/kg	MES	Bhakuni et al., 1969
Rauvolfia vomitoria	Apocynaceae	Root	Nigeria	-	-	LIS, MIS, SIS	Sokomba et al., 1986
Rehmannia glutinosa	Scrophulariaceae	Root	South Korea	-	1 mg/kg	ACV	Hong et al., 1988
Rheum officinale	Polygonaceae	Rhizome	China	-	-	ACV	Yen, 1977
Rhodiola rosea	Crassulaceae	-	-	sc	-	SIS	Aksenova et al., 1966

Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
Ricinus communis	Euphorbiaceae	Root	Nigeria	ip	-	MIS, LIS	Adesina, 1982a
Rosmarinus officinalis	Lamiaceae	Entire Plant	Israel	ip	0.2 ml	PIC	Abdul-Ghani et al., 1987
Rubus brasiliensis	Rosaceae	Entire Plant	Brazil	Ip	300 mgkg	ACV	Nogueira et al., 2000
Rubus ellipticus	Rosaceae	Leaf	India	-	-	MES	Rana et al., 1990
Ruta chalepensis	Rutaceae	Aerial Parts	Mexico	ip	450 mg/kg	PTZ	Aguilar-Santamaria et al., 1996
Roylea elegans	Lamiaceae	-	-	ip	-	ACV	Chauhan et al., 1988
Ruta chalepensis	Rutaceae	Leaf	Usa, Mexico	ip	-	MES, PTZ	Aguilar-Santamaria et al., 1996
Ruta graveolens	Rutaceae	Aerial Parts	Bulgaria	ip	2-4 ml/kg	CZIC, MES	Athanassova et al., 1969
Salvadora persica	Salvadoraceae	Stem	Italy	im	500 mg/kg	ACV	Monforte et al., 2002
Salvia guaranitica	Lamiaceae	Aerial Parts	Latin America	ip	-	ACV	Viola et al., 1997
Salvia haematodes	Lamiaceae	Root	India	ig	500 mg/kg	MES	Akbar et al., 1984a
Salvia nemorosa	Lamiaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MÊS, MIS, SIS	Athanassova et al., 1965
Salvia nemorsa	Lamiaceae	Leaf	Japan	po		ACV	Sugaya et al., 1988; 1997
Salvia guaranitica	Lamiaceae	Aerial Parts	Latin America	ip	-	ACV	Viola et al., 1997
Salvia sclarea	Lamiaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MIS, SIS	Athanassova et al., 1965
Salvia transsylvanica	Lamiaceae	Aerial Parts	Egypt	-	500, 1000 mg/kg	ACV, PTZ	Maklad et al., 1997
Sapindus trifoliatus	Sapindaceae	Seed	India	-	-	MES	Gupta et al., 1996
Satureja clinopodium	Lamiaceae	Aerial Parts	Bulgaria	Ip	4 ml/kg	MÊS, MIS, SIS	Athanassova et al., 1965
Schisandra chinensis	Schisandraceae	Fruit	South Korea	ip	-	ACV	Baek et al., 2000
Scolopendra subspinides	Scolopendridae	Entire Plant	South Korea	ip	1.7 mg/kg	PIC, SIS	Hong, 1976
Scutellaria baicalensis	Lamiaceae	Root	China	po	3 mg	ACV	Narita et al., 1982
Securidaca longepedunculata	Polygalaceae	Leaf	Nigeria	ip	50, 10 mg/kg	LIS	Ojewole, 2000
Senecio fuchsii	Asteraceae	Entire Plant	Bulgaria	-	-	MIS	Stoyanov et al., 1981
Senecio jacobaea	Asteraceae	Entire Plant	Bulgaria	sc	2-4 ml/kg	MES, MIS	Athanassova et al., 1969
Sepia officinalis	Seppidae	-	India	-	-	ACV	Reddy et al., 1994
Sesbania grandiflora	Fabaceae	Leaf	India	ig	25, 50, 100 mg/kg	MES	Kasture et al., 2002
Solanum americana	Solanaceae	Leaf, Flower	Nigeria	ip	-	ACV, LIS	Adesina, 1982a
Solanum gilo	Solanaceae	Flower	Nigeria	ip	-	LIS	Adesina, 1982a
Solanum indicum	Solanaceae	Entire Plant	Nigeria	ip	40 mg/kg	LIS, MIS, SIS	Dey et al., 1968; Adesina, 1982a
Solanum khasianum	Solanaceae	Entire Plant	India	ip	250 mg/kg	MES	Dhar et al., 1968
Solanum macrocarpon	Solanaceae	Leaf, Flower	Nigeria	ip	-	LIS, SIS	Adesina, 1982a
Solanum melongena	Solanaceae	Leaf, Flower	Nigeria	ip	-	LIS, SIS	Adesina, 1982a
Solanum nigrum	Solanaceae	Flower	Nigeria/Mexico	ip	255 mg/kg	PTZ, MIS, LIS, SIS	Adesina 1982a; Perez et al. 1998
Solanum torvum	Solanaceae	Flower	Nigeria	ip	-	LIS	Adesina, 1982a
Sphencostylis stenocarpa	Fabaceae	Seed	Nigeria	ip	60 mg/kg	LIS	Asuzu, 1986
Spondias monbin	Anacardiaceae	Flower	Nigeria	ip	-	LIS, SIS	Adesina, 1982a
Stenochilaena palustris	Blechnaceae	Entire Plant	India	ip	375 mg/kg	SIS	Dhar et al., 1973
Swertia purpurascens	Gentianaceae	Entire Plant	India	ip	100 mg/kg	MES, MIS	Dhar et al., 1973
Symphytum officinale	Boraginaceae	Root	Bulgaria	ip	2-4 ml/kg	CZIC, MES	Athanassova et al., 1969
Syzygium cumini	Myrtaceae	Seed	Brazil	ig	-	PTZ	De Lima et al., 1998
Tabernaemontana pandacaqui	Apocynaceae	Stem	Thailand	ip	50 mg/kg	PTZ	Taesotikul et al., 1998
Talinum triangulare	Portulacaceae	Flower	-	-	-	LIS, SIS	Adesina, 1982a
Taraxacum spp	Asteraceae	-	-	-	-	ACV	Chauhan et al., 1988
Teclea simplifolia	Rutaceae	-	-	-	-	ACV	Chauhan et al., 1988
Ternstroemia pinglei	Theaceae	Flower	Mexico	ip	450, 850 mg/kg	PTZ, SIS	Aguilar-Santamaria et al., 1996

Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
Tetrapleura tetraptera	Fabaceae	Arillus, Fruit	Nigeria	ip	-	LIS, MIS, PTZ	Nwaiwu & Akah, 1986, Adesina & Sofowora, 1979
Tetraselmis suecica	Chlamydomonadaceae	-	-	ip	400 mg/kg	PTZ	Laguna et al., 1993
Thalictrum thumbergii	Ranunculaceae	-	-	-	-	ACV	Chauhan et al., 1988
Thalictrum hernandezii	Ranunculaceae	-	-	-	-	ACV	Chauhan et al., 1988
Theobroma cacao	Sterculiaceae	Seed	Usa	po	-	ACV	Marcus et al., 1997
Tilia species	Tiliaceae	Aerial Parts	Bulgaria	ip	2-4 ml/kg	MES	Athanassova et al., 1969
Trema guineensis	Ulmaceae	Leaf	Gabon	ip	0.3, 1 mg/kg	PTZ, MÊS, PIC, KAI	N'gouemo et al., 1994a
Trema orientalis	Ulmaceae	-	-	-	-	MIS	Chauhan et al., 1988
Triticum aestivum	Poaceae	Seed	Japan	-	-	ACV	Tsuda et al., 1986
Uncaria rhynchophylla	Rubiaceae	-	China,	-, ip	1, 70 mg/kg	KAI, PTZ	Hsieh et al., 1999
Uncaria sinensis	Rubiaceae	-	-	-	-	ACV	Chauhan et al., 1988
Valeriana angustifolia	Valerianaceae	Leaf	Austria	ip	2.05, 2.20, 2.50 mg/kg	MIS	Pfeifer et al., 1953
Valeriana fauriei	Valerianaceae	Root	Japan	ig	17.2	ACV	Yoshitomi et al., 2000
Valeriana jatamansi	Valerianaceae	Root	Nepal	-	500 mg/kg	SIS	Debelmas et al., 1976
Valeriana latifolia	Valerianaceae	Leaf	Austria	ip	2.10 mg/kg	MIS	Pfeifer et al., 1953
Valeriana officinalis	Valerianaceae	Rhizome	France	-	50 mg/kg	ACV	Fehri et al., 1991
Valeriana sambucifolia	Valerianaceae	Root	Austria	ip	2.35 mg/kg	MIS	Pfeifer et al., 1953
Vanda roxburghii	Orchidaceae	Entire Plant	India	ip	500 mg/kg	MES	Bhakuni et al., 1969
Veratrum viride	Liliaceae	-	-	-	-	ACV	Chauhan et al., 1988
Vernonia gratiosa	Asteraceae	Aerial Parts	Taiwan	ip	3 mg/kg	PIC, PTZ, SIS	Hyou et al., 2001
Vinca erecta	Apocynaceae	-	-	-	-	ACV	Chauhan et al., 1988
Vitex negundo	Verbenaceae	Leaf	India	ip	0.15 mg/kg	LIS, SIS	Gupta et al., 1990
Viscum capense	Loranthaceae	Stem	South Africa	ip	50, 400 mg/kg	NMDLAIC, PTZ	Amabeoku et al., 1998
Vithania ashvagandha	Solanaceae	Root	India	ip	-	ACV	Prasad et al., 1968
Withania somnifera	Solanaceae	Entire Plant	India	-	-	ACV	Singh et al., 1985
Xylopia spp	Annonaceae	-	Brazil	ip	-	LIS, SIS	Adesina, 1982a
Xylopia aethiopica	Annonaceae	-	Brazil	ip	-	LIS, SIS	Adesina, 1982a
Xylopia carminative	Annonaceae	-	Brazil	ip	-	LIS, SIS	Adesina, 1982a
Xylopia frutescens	Annonaceae	-	Brazil	ip	-	LIS, SIS	Adesina, 1982a
Xylopia grandiflora	Annonaceae	-	Brazil	ip	-	LIS, SIS	Adesina, 1982a
Xylopia sericea	Annonaceae	-	Brazil	ip	-	LIS, SIS	Adesina, 1982a
Ximenia americana	Olacaceae	Whole Plant	Brazil	ip	150 mg/kg	PTZ	Quintans-Júnior et al., 2002
Zea mays	Gramineae	-	-	-	-	LIS, SIS	Adesina, 1982a
Zingiber officinale	Zingiberaceae	Rhizome	Japan	-	-	ACV	Sugaya et al., 1978
Ziziphus jujuba	Rhamnaceae	Fruit	Japan	ip	2-4 mg/kg	PTZ	Tsuda et al., 1986

Table 2. Common methods used to induce convulsion in animal models*.

- (I) Models for acute simple partial seizures:
    - (1) Topical convulsants
        - (a) penicillin
        - (b) bicuculline
        - (c) picrotoxin
        - (d) strychnine
        - (e) cholinergics
        - (f) anticholinergics
    - (2) Acute electrical stimulation of cortical tissue
    - (3) GABA withdrawal
- (II) Models for chronic simple partial seizures:
    - (1) Cortically implanted metal
    - (2) Crytogenic injury
    - (3) Ganglioside antibody injection
- (III) Models for complex partial seizure:
    - (1) Kainate
    - (2) Tetanus toxin
    - (3) Injections into area tempesta
    - (4) Kindling model
    - (5) Pilocarpine
- (IV) Models for generalized tonic-clonic seizures:
    - (1) Genetic
        - (a) Photosensitive baboons
        - (b) Audigenic seizure mice
        - (c) Totterer mice and other seizure-prone mouse strains
        - (d) Genetically epilepsy-prone rats
    - (2) Maximal electroshock
    - (3) Systemic convulsants
        - (a) Pentylenetetrazole
        - (b) Penicillin
        - (c) Other: picrotoxin, bicuculline, methionine, sulfoximine, strychnine
    - (4) Metabolic derangements
- (V) Models for absence seizures:
    - (1) Thalamic stimulation
    - (2) Bilateral cortical foci
    - (3) Systemic penicillin
    - (4) Gamma-hydroxybutyrate
    - (5) Intraventricular opiates
    - (6) THIP (4,5,6,7-tetrahydroxyisoxazolo-4,5-pyridine-3-ol)
    - (7) Genetic rodent models of absence
- (VI) Status epilepticus
    - Large amounts of NMDA, kainate, pilocarpine, bicuculline, pentylenetetrazole.

* Adapted from Nsour et al., 2000.

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