

## Plants with anticonvulsant properties - a review

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**RESUMO:** "Uma revisão de plantas com propriedades anticonvulsivantes". Cerca de um terço dos pacientes epiléticos 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 aspectos 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

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, sensorium, 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 give 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 performed 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 (Löscher & 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 pharmacoresistant patients (Nsour et al., 2000).

Many plants were known for their anticonvulsant activity. Reviews articles (Athanasova

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 *Xylopi* 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 spontaneously 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<sub>A</sub>-receptor antagonist PTZ. Soon thereafter, Lennox (1945) demonstrated that trimethadione was effective at attenuating petit mal (i.e., absence epilepsy) attacks but was ineffective in treating 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<sub>A</sub> 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
<i>Abelmoschus angulosus</i>	Malvaceae	Aerial Parts	India	ip	-	ACV	Bhakuni et al., 1988
<i>Abrus precatorius</i>	Leguminosae	Root	India	-	-	LIS, SIS	Adesina, 1982a
<i>Abrus precatorius</i>	Fabaceae	Root	Nigeria	ip	-	MIS	Adesina, 1982a
<i>Acanthus longifolius</i>	Acanthaceae	Entire Plant	Bulgaria	ip	2-4 mg/ml	MIS, MES	Rousinov et al., 1966
<i>Achillea millefolium</i>	Asteraceae	Aerial Parts	Bulgaria	ip	2-4 mg/ml	ACV, MES	Athanasova et al., 1965
<i>Aconitum species</i>	Ranunculaceae	-	China	iv	-	AVC	Ameri, 1997
<i>Acorus calamus</i>	Araceae	-	-	-	-	MIS	Chauthan et al., 1988
<i>Acosmium subelegans</i>	Leguminosae	Aerial Parts	Brazil	ig	100, 500, 1000 mg/kg	MES, PTZ	Vieira et al., 2002
<i>Adonis vernalis</i>	Ranunculaceae	-	-	-	-	AVC	Chauthan et al., 1988
<i>Afraegle paniculata</i>	Rutaceae	Root, Stem	Nigeria	ip	-	LIS, ACV	Ameri, 1997
<i>Albizia lebbek</i>	Leguminosae	Leaf, Root	India	ip	-	PIC, PTZ, MIS	Kasture et al., 1996
<i>Albizia zygia</i>	Leguminosae	Leaf	Africa	po	-	LIS, SIS	Adesina, 1982a
<i>Allium ascalonicum</i>	Liliaceae	Shallot	India	-	-	LIS	Adesina, 1982a
<i>Allium cepa</i>	Liliaceae	Bulb	India	-	-	LIS, SIS	Adesina, 1982a
<i>Allium sativum</i>	Liliaceae	Bulb	India	-	-	LIS	Adesina, 1982a
<i>Alstonia boonei</i>	Apocynaceae	Stem	India	-	-	LIS	Adesina, 1982a
<i>Alstonia schoarisi</i>	Apocynaceae	Stem	India	-	-	LIS	Adesina, 1982a
<i>Annona muricata</i>	Annonaceae	Flower	India	po	-	LIS, SIS	Adesina, 1982a
<i>Apium graveolens</i>	Umbelliferae	-	-	-	-	ACV	Chauthan et al., 1988
<i>Acorus calamus</i>	Araceae	Rhizome	Bulgaria	ip	2-4 mg/ml	ACV, MES, PTZ	Rousinov et al., 1966
<i>Acorus gramineus</i>	Araceae	Rhizome	Taiwan	ip	5 mg/kg	PTZ	Liao et al., 1998
<i>Afraegle paniculata</i>	Rutaceae	Rootbark	Nigeria	ip	150, 250 mg/kg	ACV, MIS	Adesina & Ete 1982
<i>Afromostia laxiflora</i>	Fabaceae	Root	Nigeria	ip	250 mg/kg	MES, PIC	Haruna, 2000
<i>Akebia speciosa</i>	Lardizabalaceae	Dried Stem	South Korea	ip	-	ACV	Hong et al., 1988
<i>Albizia lebbek</i>	Fabaceae	Leaf	India	ip	10, 20, 40, 80 mg/kg	MES, PTZ, PIC	Kasture et al., 1996
<i>Allium ascalonicum</i>	Liliaceae	Flower	Nigeria	ip	-	MIS	Adesina, 1982a
<i>Allium cepa</i>	Liliaceae	Bulb	Nigeria	ip	-	MIS	Adesina, 1982a
<i>Allium sativum</i>	Liliaceae	Bulb	Nigeria	ip	-	ACV, MIS	Adesina, 1982a
<i>Alstonia boonei</i>	Apocynaceae	Stembark	Nigeria	ip	-	MIS	Adesina, 1982a
<i>Atingia excelsa</i>	Hamamelidaceae	Entire Plant	India	ip	-	ACV	Singh et al., 1985
<i>Anagallis arvensis</i>	Primulaceae	Entire Plant	Bulgaria	ip	2-4 ml/kg	MIS, SIS	Rousinov et al., 1966
<i>Angelica panicci</i>	Apiaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MIS	Rousinov et al., 1966
<i>Annona diversifolia</i>	Annonaceae	Leaf	Mexico	ip	200 mg/kg	ACV, PTZ	Gonzalez-Trujano, 1998
<i>Annona muricata</i>	Annonaceae	Leaf	Gabon	ip	100, 250 mg/kg	PTZ	N'gouemo et al., 1997
<i>Apium graveolens</i>	Apiaceae	Seed	India	sc, iv	0.73; 1 ml/kg-	PTZ, MES, MIS	Kulshrestha et al., 1970
<i>Areca catechu</i>	Palmae	-	-	-	-	ACV	Lodge et al., 1997
<i>Armilaria mellea</i>	Tricholomataceae	-	China	sc	10-20 ml/kg; 25 mg/kg	ACV	Junhua et al., 1990
<i>Artemisia absinthium</i>	Asteraceae	Aerial Parts	Bulgaria	ip	2-4 ml/kg	PTZ, MES, PILO	Athanasova et al., 1965
<i>Artemisia verlotorum</i>	Asteraceae	Whole Plant	Brazil	ip	-	MES, PILO, 3-MCAIC	Lima et al., 1993
<i>Artemisia vulgaris</i>	Asteraceae	Leaf, Stem	Israel	ip	-	PIC	Abdul-Ghani et al., 1987
<i>Asarum heterotropoides</i>	Anistolochiaceae	Whole Plant	China	-	-	ACV	Sun et al., 1991
<i>Asarum himalayicum</i>	Anistolochiaceae	Whole Plant	China	-	-	ACV	Sun et al., 1991
<i>Asarum ichangense</i>	Anistolochiaceae	Whole Plant	China	-	-	ACV	Sun et al., 1991
<i>Asparagus officinalis</i>	Liliaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	LIS, MIS	Chauthan et al., 1988
<i>Asparagus verticillatus</i>	Liliaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MIS, SIS	Athanasova et al., 1969
<i>Asperula odorata</i>	Rubiaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MIS, SIS	Athanasova et al., 1969
<i>Asplenium trichomanes</i>	Aspleniaceae	Entire Plant	Bulgaria	ip	2-4 ml/kg	MES, MIS, SIS	Athanasova et al., 1965

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

Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
<i>Cnestis ferruginea</i>	Verbenaceae	Root/bark	Ivory Coast	ip	0.7 mg/kg	SIS	Declume et al., 1984
<i>Cnestis glabra</i>	Comaraceae	-	-	-	-	ACV	Chauhan et al., 1988
<i>Cocculus hirsutus</i>	Menispermaceae	Root, Stem	India	ip	100 mg/kg	MES, MIS	Das et al., 1964
<i>Cola acuminata</i>	Sterculiaceae	-	-	-	-	LIS, SIS	Adesina, 1982a
<i>Conarus wightii</i>	Comaraceae	Aerial Part	India	ip	165 mg/kg	SIS	Dhar et al., 1973
<i>Consolida orientalis</i>	Ranunculaceae	Aerial Part	Bulgaria	ip	4 ml/kg	MES, MIS, SIS	Athanassova et al., 1969
<i>Convolvulus arvensis</i>	Convolvulaceae	Aerial Part	Bulgaria	ip	4, 44 ml/kg	ACV, MIS, SIS	Chauhan et al., 1988,
<i>Convolvulus hirsutus</i>	Convolvulaceae	Aerial Part	Bulgaria	ip	4 ml/kg	MIS, SIS	Athanassova et al., 1969
<i>Convolvulus pluricaulis</i>	Convolvulaceae	Entire Plant	India	ip	-	ACV, MES	Sharmaxvn et al., 1965
<i>Convolvulus sundermannii</i>	Convolvulaceae	Aerial Part	Bulgaria	ip	4 ml/kg	MIS, SIS	Athanassova et al., 1969
<i>Coptis chinensis</i>	Ranunculaceae	Rhizome	South Korea	-	1 mg/kg	ACV	Hong et al., 1988
<i>Corydalis cava</i>	Papaveraceae	Aerial Part	Bulgaria	ip	2-4 ml/kg, 4 mg/kg	MES	Athanassova et al., 1965
<i>Crassostrea gigas</i>	Ostreidae	-	Japan	po	10%	ACV	Bac et al., 1998
<i>Croton zehntneri</i>	Euphorbiaceae	Branches	Brazil	ip	20.80 mg/kg	ACV, PIC, SIS	Bernardi et al., 1991
<i>Coyledon orbiculata</i>	Crassulaceae	-	South Africa	ip	50-400 mg/kg	ACV, PIC, PTZ	Amabeoku et al., 2007
<i>Cryptotympana atrata</i>	Cicadidae	Skin	Taiwan	ig	0.5 mg/kg	PIC	Hsieh et al., 1991
<i>Cucurbita pepo</i>	Cucurbitaceae	-	Nigeria	-	-	LIS, SIS	Adesina, 1982a
<i>Cuminum cyminum</i>	Apiaceae	Fruit	Iran	ip	0.5 ml/mg	MES, PTZ	Sayyah et al., 2002
<i>Curcuma amada</i>	Zingiberaceae	Rhizome	India	ip	500 mg/kg	MES	Bhakumi et al., 1969
<i>Curcuma aromatica</i>	Zingiberaceae	Root	China	Ig, po	2.5 mg	ACV	Li, 1987
<i>Cuscuta chinensis</i>	Convolvulaceae	Entire Plant	China	ig	1 mg/kg	ACV	Akbar et al., 1985a
<i>Cyathea nilgirensis</i>	Cyatheaceae	Aerial Part	India	ip	0.25 mg/kg	MES	Dhawan et al., 1977
<i>Cylista scariosa</i>	Fabaceae	Root	India	ip	500 mg/kg	SIS	Dhar et al., 1968
<i>Cymbopogon citratus</i>	Gramineae	Leaf	Brazil	po, ip	-	ACV	Carlini et al., 1986
<i>Cynanchum otophyllum</i>	Asclepiadaceae	Rhizome	China	ip	12.5 mg/kg	ACV	Pei et al., 1981
<i>Cynodon dactylon</i>	Gramineae	Leaf	Nigeria	ip	600 mg/kg	MES, MIS, PTZ	Akah et al., 1997
<i>Cyperus articulatus</i>	Cyperaceae	Rhizome	L. America	po	50-2000 mg/kg	AVC	Ngo Bum et al., 1996
<i>Cyperus rotundus</i>	Cyperaceae	Root	Nigeria	ip	-	LIS, SIS	Adesina, 1982a
<i>Cystophora moniliformis</i>	Cystoscraceae	Thallus	Australia	-	-	ACV	Spence et al., 1979
<i>Cystoseira usneoides</i>	Cystoscraceae	Thallus	Spain	ip	6.25 mg/kg	ACV	Vazquez-Freire et al., 1995
<i>Delphinium consolida</i>	Ranunculaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	AVC, MIS, SIS	Nsour et al., 2000
<i>Delphinium denudatum</i>	Ranunculaceae	Root	Pakistan	ip	400, 600, 800 mg/kg	ACV, PIC, PTZ, SIS	Raza et al., 2001
<i>Desmodium adscendens</i>	Leguminosae	Leaf	Africa	ip	300 mg/kg	PTZ	N'gouemo et al., 1996
<i>Dictamnus albus</i>	Rutaceae	Entire Plant	Bulgaria	sc	2-4ml/kg	ACV	Athanassova et al., 1965
<i>Digitalis ferruginea</i>	Scrophulariaceae	Entire Plant	Bulgaria	sc	2-4 ml/kg	ACV, MES	Athanassova et al., 1965
<i>Digitalis lanata</i>	Scrophulariaceae	Entire Plant	Bulgaria	sc	2-4 ml/kg	ACV, MES	Athanassova et al., 1965
<i>Dillenia indica</i>	Dilleniaceae	Leaf	India	ip	400 mg/kg	MES	Bhakumi et al., 1969
<i>Diospyros kaki</i>	Ebenaceae	Calix	Japan	-	-	ACV	Fukuda & Shibata, 1994
<i>Diospyros peregrine</i>	Ebenaceae	Entire Plant	India	-	-	ACV	Singh et al., 1985
<i>Duboisia leichhardtii</i>	Solanaceae	-	-	-	-	AVC	Nsour et al., 2000
<i>Dunaliella tertilectia</i>	Dunaliellaceae	-	Spain	-	-	ACV	Laguna et al., 1990
<i>Echinacea purpurea</i>	Asteraceae	-	-	-	-	AVC	Nsour et al., 2000
<i>Echinium vulgare</i>	Boraginaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	ACV, MES, MIS, SIS	Nsour et al., 2000,
<i>Egletes viscosa</i>	Asteraceae	Flower	Brazil	ig	-	PTZ	Souza et al., 1998
<i>Elaeocarpus ganinus</i>	Elaeocarpaceae	Entire Plant/Fruit	India	ip	1.2, 100 mg/kg	MES, MIS	Bhattacharya et al., 1975
<i>Eleutheria cardamomum</i>	Zingiberaceae	Seed	India	ig	3, 10 mg/kg	ACV	Dasgupta et al., 1984
<i>Eryngium foetidum</i>	Apiaceae	Leaf	Jamaica	ip	3 ml/kg	PIC	Shukia et al., 1987
<i>Erythroxylum</i> spp.	Erythroxylaceae	Leaf	-	-	-	MIS	Simon, 1986
							Adesina, 1982a



Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
<i>Erythraea centaureum</i>	Gentianaceae	Aerial Parts	Bulgaria	ip	2-4 ml/kg	CZIZ	Athamassova et al., 1965
<i>Erythrina velutina</i>	Fabaceae	Stem Bark	Brazil	ip	200-400 mg/kg	PTZ, SIS	Vasconcelos et al., 2007
<i>Erythrina mulungu</i>	Fabaceae	Stem Bark	Brazil	ip	200-400 mg/kg	PTZ, SIS	Vasconcelos et al., 2007
<i>Euphorbia antitiorum</i>	Euphorbiaceae	Whole Plant	India	ip	40 mg/kg	MIS	Dey et al., 1968
<i>Euphorbia dracunculoides</i>	Euphorbiaceae	Entire Plant	India	ip	500 mg/kg	ACV, MES	Bhakuni et al., 1969
<i>Euphorbia hirta</i>	Euphorbiaceae	Whole Plant	-	ip	-	ACV	Lanthers et al., 1996
<i>Euphorbia pilulifera</i>	Euphorbiaceae	Whole Plant	-	ip	-	ACV	Chauhan et al., 1988
<i>Euphorbia tinuicalli</i>	Euphorbiaceae	Aerial Part	India	ip	250 mg/kg	ACV, MIS	Dhar et al., 1968
<i>Evolvulus nummularius</i>	Convolvulaceae	Entire Plant	India	ip	40, 100 mg/kg	MES, MIS	Dey et al., 1968; Chatterjee 1964
<i>Ferula gummosa</i>	Apiaceae	Seed	Iran	ip	55, 198,3 mg/kg	MES, PTZ	Sayyah et al., 2002
<i>Galeopsis ladanum</i>	Lamiaceae	Aerial parts	poland	ip	200 mg/kg	PTZ	Czamecki et al., 1993
<i>Galia</i> spp.	Galiaceae	-	-	-	-	ACV	Chauhan et al., 1988
<i>Galium cruciata</i>	Rubiaceae	-	-	-	-	ACV	Chauhan et al., 1988
<i>Galium sylvaticum</i>	Rubiaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MIS, SIS	Chauhan et al., 1988,
<i>Galphimia glauca</i>	Malpighiaceae	Aerial Parts	Mexico	ip	500 mg/kg	ACV, LIS, SIS	Tortorello et al., 1992
<i>Galphimia glauca</i>	Malpighiaceae	Aerial Parts	Mexico	ip	-	ACV	Tortorello, 1993
<i>Ganoderma lucidum</i>	Ganodermataceae	Fruit	Japan	sc	300 mg/kg	PTZ, SIS	Kasahara et al., 1987
<i>Garcinia mangostana</i>	Clusiaceae	Fruit	-	-	-	ACV	Kurukawa et al., 1997
<i>Gastrodia elata</i>	Orchidaceae	-	China	-	5, 10, 20, 500 mg/kg	ACV, KAI	Chen, 1977; Chauhan et al., 1988, Hsieh et al., 2001
<i>Geranium rotundifolium</i>	Geraniaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MES, MIS, SIS	Athamassova et al., 1969
<i>Ginkgo biloba</i>	Ginkgoaceae	Rhizome	Africa	po	-	ACV	Rodriguez, 1993
<i>Gleditsia officinalis</i>	Fabaceae	Fruit	China	ig	-	ACV	Yen, 1977
<i>Glycyrrhiza glabra</i>	Fabaceae	Rhizome	Korea	-	1 mg/kg	ACV	Hong et al., 1988
<i>Grewia hirsuta</i>	Tiliaceae	Entire Plant	India	ip	500 mg/kg	SIS	Bhakuni et al., 1971
<i>Gymnosporia falconeri</i>	Celastraceae	Aerial Parts	India	ip	500 mg/kg	MIS	Bhakuni et al., 1971
<i>Haplophyllum perforatum</i>	Rutaceae	Seed	-	-	-	CZIC, LIS	Chauhan et al., 1988
<i>Haplophyllum locosum</i>	Rutaceae	Seed	-	-	-	CZIC, LIS	Chauhan et al., 1988
<i>Hedera rhombea</i>	Rutaceae	-	-	-	-	ACV	Chauhan et al., 1988
<i>Helianthus annuus</i>	Asteraceae	Leaf	South Korea	ip	0.1 mg/kg	SIS	Lee et al., 1992
<i>Heracleum sibiricum</i>	Asteraceae	Flower	Bulgaria	-	2-4 ml/kg	CZIZ, MES	Athamassova et al., 1965
<i>Heracleum verticillatum</i>	Umbelliferae	-	-	-	-	MES, PTZ, CZIC, SIS	Chauhan et al., 1988
<i>Herpestris monniera</i>	Umbelliferae	-	-	-	-	MES, PTZ, CZIC, SIS	Chauhan et al., 1988
<i>Hippocastanum vittatum</i>	Scrophulariaceae	-	-	-	-	PTZ	Chauhan et al., 1988
<i>Holarrhena floribunda</i>	Amariyllidaceae	Bulbs	Brazil	ip	-	MES, PTZ	Silva et al., 2006
<i>Hosundia opposita</i>	Lamiaceae	Leaf	Nigeria	ip	-	MES, PTZ	Akah et al., 1997
<i>Humulus lupulus</i>	Cannabaceae	-	Switzerland	ip	50, 354, 398 mg/kg	MES, PTZ	Akah et al., 1993
<i>Hypericum perforatum</i>	Hypericaceae	Whole Plant	Greece	ip	250, 500 mg/kg	PTZ	Lee et al., 1993
<i>Icacina trichantha</i>	Iacinaceae	Tuber	Nigeria	ip	-	ACV, PTZ, SIS	Ozturk et al., 1996
<i>Ipomoea stans</i>	Convolvulaceae	Wood	Mexico	iv	80, 100, 400 mg/kg	MES, PTZ	Asuzu et al., 1990
<i>Iris kamaonensis</i>	Iridaceae	Entire Plant	India	ip	375 mg/kg	MES	Contreras et al., 1996
<i>Jatropha curcas</i>	Euphorbiaceae	Root	-	-	-	LIS, SIS	Dhawan et al., 1977
<i>Jatropha gossypifolia</i>	Euphorbiaceae	Root, Leaf	-	-	-	LIS, SIS	Adesina, 1982a
<i>Juniperus macrocarpa</i>	Cupressaceae	Fruit	India	ip	100 mg/kg	ACV	Mishra et al., 1989
<i>Kalanchoe crenata</i>	Crassalaceae	Leaf	Cameroon	ip	150, 300 mg/kg	PTZ, SIS	Ngelefac et al., 2006
<i>Khaya grandifoliola</i>	Meliaceae	Stembark	Nigeria	ip	50 mg/kg	ACV	Awe te al., 1997
<i>Kochia prostrata</i>	Chenopodiaceae	-	-	-	-	SIS	Chauhan et al., 1988

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

Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
<i>Ostrea species</i>	Ostreidae	-	Japan	ig	1 mg/kg	PTZ	Tsuda et al., 1998
<i>Pachyma species</i>	Polyporaceae	Fruit	South Korea	-	1 mg/kg	ACV	Hong et al., 1988
<i>Paconia radiz</i>	Paconiaceae	Root	Japan	po	-	ACV	Tsuda et al., 1997
<i>Paeonia alba</i>	Paeoniaceae	Root	South Korea	ig	800 mg/kg	ACV	Hung et al., 1983
<i>Paeonia albiflora</i>	Paeoniaceae	Root	China	po	6 mg	ACV	Narita et al., 1982
<i>Paeonia albiflora</i>	Paeoniaceae	Root	Japan	ig	100 mg/kg	PTZ	Sugaya et al., 1991
<i>Paeonia emodi</i>	Paeoniaceae	Root	India	lg	10 mg/kg	MES, MIS	Ahmad et al., 1981
<i>Paeonia japonica</i> var. <i>pilosa</i>	Paeoniaceae	Root	South Korea	ip	2, 20 mg/kg	PIC, SIS	Hong et al., 1979
<i>Paeonia rubra</i>	Paeoniaceae	Root	South Korea	ip	1 mg/kg	ACV	Hong et al., 1988
<i>Palisota ambigua</i>	Commelinaceae	Leaf	Gabon	ip	50 mg/kg	PTZ	N'gouemo et al., 1994b
<i>Panax ginseng</i>	Araliaceae	Root, Leaf	China	ip	100, 200 mg/kg	MIS, PIC	Takagi, 1977; Mitra et al., 1996
<i>Patrina intermedia</i>	Valerianaceae	-	-	-	-	SIS	Chaulhan et al., 1988
<i>Passiflora alata</i>	Passifloraceae	Dried Leaf	Brazil	ip	75, 150 mg/kg	MIS	Oga et al., 1984
<i>Passiflora incarnata</i>	Passifloraceae	Leaf	Italy	ip	160 mg/kg	PTZ	Speroni et al., 1988
<i>Pausinystalia yohimbe</i>	Rubiaceae	Bark	-	ip	-	ACV	Chermet et al., 1979
<i>Persea indica</i>	Lauraceae	Leaf	Canary Islands	-	2 mg/kg	PTZ	Mazzanti et al., 1993
<i>Phaeodactylum tricoenutum</i>	Fragilariaceae	-	Spain	ip	150 mg/kg	PTZ	Laguna et al., 1990
<i>Picramnia acarna</i>	Asteraceae	-	-	-	-	ACV	Chaulhan et al., 1988
<i>Picrohiza karroo</i>	Scrophulariaceae	Entire Plant	India	-	500 mg/kg	MIS	Debelmas et al., 1976
<i>Pimpinella anisum</i>	Apiaceae	Fruit	Bulgaria	ip	2-4 ml/kg	SZIC, MES	Athanassova et al., 1969
<i>Pinellia ternata</i>	Araceae	Tuber	China	po	5 mg	ACV	Narita et al., 1982
<i>Piper guineense</i>	Piperaceae	Flower	Nigeria	ip	-	MIS, NMDL/AIC	Abila et al., 1993
<i>Piper longum</i>	Piperaceae	Fruit	China	ip	3.4, 263.4 mg/kg	ACV, MES, PIC, PTZ	Pei, 1983
<i>Piper methysticum</i>	Piperaceae	Flower	Fiji	ip	140 mg/kg	SIS	Klohs et al., 1959
<i>Piper nigrum</i>	Piperaceae	Flower	China	ip	2 mg/kg	ACV, NMDL/AIC	Hu & Davies, 1997
<i>Piscidia erythrina</i>	Fabaceae	Bark	USA	ip	900 mg/kg	PTZ	Klohs et al., 1959
<i>Pistacia integerrima</i>	Anacardiaceae	-	India	ip	1 ml/kg	PTZ	Ansari et al., 1993
<i>Pithecellobium samon</i>	Leguminosae	-	-	-	-	PIC	Chaulhan et al., 1988
<i>Plectranthusamboinicus</i>	Lamiaceae	Entire Plant	Cuba	ip	-	ACV	Buznego et al., 1999
<i>Plumbago zeylanica</i>	Plumbaginaceae	Root	Nigeria	ip	-	LIS	Adesina, 1982a
<i>Polygala sabulosa</i>	Polygalaceae	Whole Plant	Brazil	ip	250, 500, 1000 mg/kg	PTZ	Duarte et al., 2007
<i>Polypodium vulgare</i>	Polypodiaceae	Root	India	ip	100 mg/kg	MES, PTZ	Mannan et al., 1989
<i>Portulaca oleracea</i>	Portulacaceae	Whole Plant	-	ip	-	LIS, SIS	Adesina, 1982a
<i>Prunus spinosa</i>	Rosaceae	Fruit	India	ig	1.5 mg/kg	PTZ	Mannan et al., 1989
<i>Psidium guyanensis</i>	Myrtaceae	Leaf	Brazil	po	-	PTZ, PIC, SIS	Santos et al., 1997
<i>Psidium pohliatum</i>	Myrtaceae	Leaf	Brazil	ig	400 mg/kg	PTZ	Santos et al., 1996
<i>Pterocarpus santalinus</i>	Fabaceae	Stem	India	-	-	MES	Mehta et al., 1979
<i>Qingyangshen</i>	Asclepiadaceae	Root	China	ip	-	KAI, ACV	Kuang et al., 1991; Guo & Kuang, 1993
<i>Rauwolfia ligustrina</i>	Apocynaceae	Root, Aerial	Brazil	ip, po	12.5, 250 mg/kg	PTZ, PIC, SIS	Quintans-Júnior et al., 2002; 2007
<i>Rauwolfia schueli</i>	Apocynaceae	-	-	-	-	ACV	Adesina, 1982a
<i>Rauwolfia serpentina</i>	Apocynaceae	Root, Stem Bark	India	-	-	ACV	Adesina, 1982a
<i>Rauwolfia tetraphylla</i>	Apocynaceae	Entire Plant	India	ip	500 mg/kg	MES	Bhakuni et al., 1969
<i>Rauwolfia vomitoria</i>	Apocynaceae	Root	Nigeria	-	-	LIS, MIS, SIS	Sokomba et al., 1986
<i>Rehmannia glutinosa</i>	Scrophulariaceae	Root	South Korea	-	-	ACV	Hong et al., 1988
<i>Rheum officinale</i>	Polygonaceae	Rhizome	China	-	1 mg/kg	ACV	Yen, 1977
<i>Rhodiola rosea</i>	Crassulaceae	-	-	sc	-	SIS	Aksenova et al., 1966

Plant	Family	Part used	Place	Route Given	Dose	Method Used	References
<i>Ricinus communis</i>	Euphorbiaceae	Root	Nigeria	ip	-	MIS, LIS	Adesina, 1982a
<i>Rosmarinus officinalis</i>	Lamiaceae	Entire Plant	Israel	ip	0.2 ml	PIC	Abdul-Ghani et al., 1987
<i>Rubus brasiliensis</i>	Rosaceae	Entire Plant	Brazil	ip	300 mg/kg	ACV	Nogueira et al., 2000
<i>Rubus ellipticus</i>	Rosaceae	Leaf	India	-	-	MES	Rana et al., 1990
<i>Ruta chalepensis</i>	Rutaceae	Aerial Parts	Mexico	ip	450 mg/kg	PTZ	Aguilar-Santamaria et al., 1996
<i>Roylea elegans</i>	Lamiaceae	-	-	ip	-	ACV	Chauhan et al., 1988
<i>Ruta chalepensis</i>	Rutaceae	Leaf	Usa, Mexico	ip	-	MES, PTZ	Aguilar-Santamaria et al., 1996
<i>Ruta graveolens</i>	Rutaceae	Aerial Parts	Bulgaria	ip	2-4 ml/kg	CZIC, MES	Athanassova et al., 1969
<i>Salvadora persica</i>	Salvadoraceae	Stem	Italy	im	500 mg/kg	ACV	Monforte et al., 2002
<i>Salvia guaranitica</i>	Lamiaceae	Aerial Parts	Latin America	ip	-	ACV	Viola et al., 1997
<i>Salvia haematodes</i>	Lamiaceae	Root	India	ig	500 mg/kg	MES	Akbar et al., 1984a
<i>Salvia nemorosa</i>	Lamiaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MES, MIS, SIS	Athanassova et al., 1965
<i>Salvia nemorsa</i>	Lamiaceae	Leaf	Japan	po	-	ACV	Sugaya et al., 1988; 1997
<i>Salvia guaranitica</i>	Lamiaceae	Aerial Parts	Latin America	ip	-	ACV	Viola et al., 1997
<i>Salvia sclarea</i>	Lamiaceae	Aerial Parts	Bulgaria	ip	4 ml/kg	MIS, SIS	Athanassova et al., 1965
<i>Salvia transsylvanica</i>	Lamiaceae	Aerial Parts	Bulgaria	ip	500, 1000 mg/kg	ACV, PTZ	Maklad et al., 1997
<i>Sapindus trifoliatus</i>	Sapindaceae	Seed	Egypt	-	-	MES	Gupta et al., 1996
<i>Satureja chinopodium</i>	Lamiaceae	Aerial Parts	India	ip	4 ml/kg	MES, MIS, SIS	Athanassova et al., 1965
<i>Satureja chinopodium</i>	Lamiaceae	Fruit	South Korea	ip	-	ACV	Baek et al., 2000
<i>Schisandra chinensis</i>	Schisandraceae	Fruit	South Korea	ip	1.7 mg/kg	PIC, SIS	Hong, 1976
<i>Scolopendra subspinipes</i>	Scolopendridae	Entire Plant	South Korea	ip	3 mg	ACV	Narita et al., 1982
<i>Scutellaria baicalensis</i>	Lamiaceae	Root	China	po	50, 10 mg/kg	LIS	Ojewole, 2000
<i>Securidaca longepedunculata</i>	Polygalaceae	Leaf	Nigeria	ip	-	MIS	Stoyanov et al., 1981
<i>Senecio jacobaea</i>	Asteraceae	Entire Plant	Bulgaria	-	-	MES, MIS	Athanassova et al., 1969
<i>Senecio jacobaea</i>	Asteraceae	Entire Plant	Bulgaria	sc	2-4 ml/kg	ACV	Reddy et al., 1994
<i>Seppia officinalis</i>	Seppidae	-	India	-	-	MES	Kasture et al., 2002
<i>Sesbania grandiflora</i>	Fabaceae	Leaf	India	ig	25, 50, 100 mg/kg	MES	Adesina, 1982a
<i>Solanum americanum</i>	Solanaceae	Leaf, Flower	Nigeria	ip	-	ACV, LIS	Adesina, 1982a
<i>Solanum gilo</i>	Solanaceae	Flower	Nigeria	ip	-	LIS	Adesina, 1982a
<i>Solanum indicum</i>	Solanaceae	Entire Plant	Nigeria	ip	40 mg/kg	LIS, MIS, SIS	Dey et al., 1968; Adesina, 1982a
<i>Solanum khasianum</i>	Solanaceae	Entire Plant	India	ip	250 mg/kg	MES	Dhar et al., 1968
<i>Solanum macrocarpon</i>	Solanaceae	Leaf, Flower	Nigeria	ip	-	LIS, SIS	Adesina, 1982a
<i>Solanum melongena</i>	Solanaceae	Leaf, Flower	Nigeria	ip	-	LIS, SIS	Adesina, 1982a
<i>Solanum nigrum</i>	Solanaceae	Flower	Nigeria/Mexico	ip	255 mg/kg	PTZ, MIS, LIS, SIS	Adesina 1982a; Perez et al., 1998
<i>Solanum torum</i>	Solanaceae	Flower	Nigeria	ip	-	LIS	Adesina, 1982a
<i>Sphencosyllis sienocarpa</i>	Fabaceae	Seed	Nigeria	ip	60 mg/kg	LIS	Asuzu, 1986
<i>Spondias mombin</i>	Anacardiaceae	Flower	Nigeria	ip	-	LIS, SIS	Adesina, 1982a
<i>Stenochlaena palustris</i>	Blechnaceae	Entire Plant	India	ip	375 mg/kg	SIS	Dhar et al., 1973
<i>Swericia purpurascens</i>	Gentianaceae	Entire Plant	India	ip	100 mg/kg	MES, MIS	Dhar et al., 1973
<i>Symphytum officinale</i>	Boraginaceae	Root	Bulgaria	ip	2-4 ml/kg	CZIC, MES	Athanassova et al., 1969
<i>Syzgium cumini</i>	Myrtaceae	Seed	Brazil	ig	-	PTZ	De Lima et al., 1998
<i>Tabernaemontana pandacaqui</i>	Poecynaceae	Stem	Thailand	ip	50 mg/kg	PTZ	Taesotikul et al., 1998
<i>Talinum triangulare</i>	Portulacaceae	Flower	-	-	-	LIS, SIS	Adesina, 1982a
<i>Taraxacum spp</i>	Asteraceae	-	-	-	-	ACV	Chauhan et al., 1988
<i>Teclea simplicifolia</i>	Rutaceae	-	-	-	-	ACV	Chauhan et al., 1988
<i>Ternstroemia pinglei</i>	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
<i>Tetrapleura tetraptera</i>	Fabaceae	Arillus, Fruit	Nigeria	ip	-	LIS, MIS, PTZ	Nwaiwu & Akah, 1986,
<i>Tetraselmis suecica</i>	Chlamydomonadaceae	-	-	ip	400 mg/kg	PTZ	Adesina & Sofowora, 1979
<i>Thalictrum thubergii</i>	Ranunculaceae	-	-	-	-	ACV	Laguna et al., 1993
<i>Thalicttrum hermandezii</i>	Ranunculaceae	-	-	-	-	ACV	Chauhan et al., 1988
<i>Theobroma cacao</i>	Sterculiaceae	Seed	Usa	po	-	ACV	Chauhan et al., 1988
<i>Tilia species</i>	Tiliaceae	Aerial Parts	Bulgaria	ip	2-4 ml/kg	MES	Marcus et al., 1997
<i>Trema guineensis</i>	Ulmaceae	Leaf	Gabon	ip	0.3, 1 mg/kg	PTZ, MES, PIC, KAI	Athanasova et al., 1969
<i>Trema orientalis</i>	Ulmaceae	Seed	-	-	-	MIS	N' goumo et al., 1994a
<i>Triticum aestivum</i>	Poaceae	Seed	Japan	-	-	ACV	Chauhan et al., 1988
<i>Uncaria rhynchophylla</i>	Rubiaceae	-	China,	, ip	1, 70 mg/kg	KAI, PTZ	Hsieh et al., 1999
<i>Uncaria sinensis</i>	Rubiaceae	-	-	-	-	ACV	Chauhan et al., 1988
<i>Valeriana angustifolia</i>	Valerianaceae	Leaf	Austria	ip	2.05, 2.20, 2.50 mg/kg	MIS	Pfeifer et al., 1953
<i>Valeriana fauriei</i>	Valerianaceae	Root	Japan	ig	17.2	ACV	Yoshitomi et al., 2000
<i>Valeriana jatamansi</i>	Valerianaceae	Root	Nepal	-	500 mg/kg	SIS	Debelmas et al., 1976
<i>Valeriana latifolia</i>	Valerianaceae	Leaf	Austria	ip	2.10 mg/kg	MIS	Pfeifer et al., 1953
<i>Valeriana officinalis</i>	Valerianaceae	Rhizome	France	-	50 mg/kg	ACV	Fehri et al., 1991
<i>Valeriana sambucifolia</i>	Valerianaceae	Root	Austria	ip	2.35 mg/kg	MIS	Pfeifer et al., 1953
<i>Vanda roxburghii</i>	Orchidaceae	Entire Plant	India	ip	500 mg/kg	MES	Bhakuni et al., 1969
<i>Veratrum viride</i>	Liliaceae	-	-	-	-	ACV	Chauhan et al., 1988
<i>Vernonia gratio</i>	Asteraceae	Aerial Parts	Taiwan	ip	3 mg/kg	PIC, PTZ, SIS	Hyou et al., 2001
<i>Vinca erecta</i>	Apocynaceae	-	-	-	-	ACV	Chauhan et al., 1988
<i>Vitex negundo</i>	Verbenaceae	Leaf	India	ip	0.15 mg/kg	LIS, SIS	Gupta et al., 1990
<i>Viscum capense</i>	Loranthaceae	Stem	South Africa	ip	50, 400 mg/kg	NMDL, AIC, PTZ	Amabeoku et al., 1998
<i>Vithania ashvagandha</i>	Solanaceae	Root	India	ip	-	ACV	Prasad et al., 1968
<i>Withania somnifera</i>	Solanaceae	Entire Plant	India	-	-	ACV	Singh et al., 1985
<i>Xylopiia spp</i>	Annonaceae	-	Brazil	ip	-	LIS, SIS	Adesina, 1982a
<i>Xylopiia aethiopia</i>	Annonaceae	-	Brazil	ip	-	LIS, SIS	Adesina, 1982a
<i>Xylopiia carminative</i>	Annonaceae	-	Brazil	ip	-	LIS, SIS	Adesina, 1982a
<i>Xylopiia frutescens</i>	Annonaceae	-	Brazil	ip	-	LIS, SIS	Adesina, 1982a
<i>Xylopiia grandiflora</i>	Annonaceae	-	Brazil	ip	-	LIS, SIS	Adesina, 1982a
<i>Xylopiia sericea</i>	Oliaceae	Whole Plant	Brazil	ip	150 mg/kg	PTZ	Adesina, 1982a
<i>Ximentia americana</i>	Gramineae	-	-	-	-	LIS, SIS	Quintans-Júnior et al., 2002
<i>Zea mays</i>	Gramineae	-	Japan	-	-	ACV	Adesina, 1982a
<i>Zingiber officinale</i>	Zingiberaceae	Rhizome	Japan	-	-	ACV	Sugaya et al., 1978
<i>Ziziphus jujuba</i>	Rhamnaceae	Fruit	Japan	ip	2-4 mg/kg	PTZ	Tsuda et al., 1986

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

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- (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) Cryptogenic 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) Pentylentetrazole
    - (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-tetrahydroisoxazolo-4,5-pyridine-3-ol)
  - (7) Genetic rodent models of absence
- (VI) Status epilepticus
- Large amounts of NMDA, kainate, pilocarpine, bicuculline, pentylentetrazole.
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\* Adapted from Nsour et al., 2000.

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