8

Antiepileptic Medicinal Plants Used in Traditional Medicine to Treat Epilepsy

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1. Introduction

Epilepsy is a disease that affects about 40 million people worldwide (Njamshi et al., 2010). In 1968, the prevalence of epilepsy in Africa was about 4.8 to 40 ‰. In 1996, Diop and collaborators reported in Senegal a prevalence of epilepsy of 21 ‰ (Diop et al., 1996). In 2006, Ngoungou and collaborators estimated the prevalence in sub-Saharan Africa to be two or three time highest than the rate in developed world (Ngoungou et al., 2007). In Cameroon, some epidemiological studies on epilepsy have shown that, the prevalence of epilepsy is estimated to vary from 5-136/1000. The highest ones are reported in some villages of the Cameroon Central Province located in the Sanaga and Mbam River Valley (Nchoji Nkwi & Tioko Ndonko, 1989; Dongmo et al., 2000; Preux et al., 2000; Boussinesq et al., 2002; Kamgno et al., 2003; Dongmo et al., 2004; Prischich et al., 2008). Cameroon is one of the countries most affected by epilepsy in Africa and in the world. Thus, epilepsy is among the major public health problems in Cameroon. In Africa and in Cameroon particularly, phytotherapy in traditional medicine still plays an important role in the management of diseases, mainly among populations with very low income (Geoffrey & Kirby, 1996). And phytotherapy relies on the use of a wide variety of plant species. *Annona muricata* Linn (Annonaceae), *Annona senegalensis* Pers (Annonaceae), *Bidens pilosa* Linn (Asteraceae), *Bryophyllum pinnatum* (Lam) Oken (Crassulaceae), *Citrus sinenis* (Linn) Osbeck (Rutaceae), *Clerodendron thomsoniae* Balf (Verbenaceae), *Daniellia oliveri* (Rolfe) Hutch and Dalz (Caesalpiniaceae), *Datura stramonium* Linn (Solanaceae), *Detarium microcarpum* Guil et Perr (Caesalpiniaceae), *Euphorbia hirta* Linn (Euphorbiaceae), *Flacourtia indica* Willd (Flacourtiaceae), *Hymenocardia acida* Tul (Hymenocardiaceae), *Jatropha gossypiifolia* Linn (Euphorbiaceae), *Khaya senegalensis* A Juss (Desrousseaux) (Meliaceae), *Mentha cordifolia* Auct (Lamiaceae), *Prosopis Africana* Guill and Perr (Taub) (Mimosaceae), *Ricinus communis* Linn (Euphorbiaceae), *Securidaca longepedunculata* Fres (Polygalaceae), *Senna singueana* (Delile) Lock 1988 (Caesalpiniaceae), *Terminalia glaucescens* Planch. ex Benth (Combretaceae), *Terminalia mollis* Laws (Combretaceae), *Tetrapleura tétraptera* Taub (Schum Thonn)

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(Mimosaceae), *Trichilia emetica* Vahl (Meliaceae) and *Vitellaria paradoxa* C F Gaertn (Sapotaceae) are plants that are being used empirically in traditional medicine in Cameroon to treat epilepsy and diseases related to the brain like agitations, anxiety, convulsions, dizziness, headaches, insomnia, migraines, pains and schizophrenia according to our traditional Healers and the literature (Abbiw, 1990; Adjanohoun et al., 1984, 1996; Arbonnier, 2000; Berhaut, 1975; Biholong, 1986; Bouquet, 1969; Brenan, 1959; Dalziel, 1937; Hutchinson & Dalziel, 1958; Iwu, 1993; Joyner, 2004; Malgras, 1992; Mutasa et al., 1990; Nwaiwu & Akah, 1986; Pousset, 1989; Raponda-Walker & Silans, 1961; Saulnier, 1998) (Table 1). Though the literature showed a lot of pharmacological studies done

Name of the plant	Part of the plant used	Form of the medicine	Diseases	Chemical characterization	Pharmaco-logical properties	Country
Annona muricata	Leaves	Infusion Decoction	Insomnia, diabetes Spasms, Fever	Steroid, cardiac glycosides	Antimicrobial	Cameroon, Forest areas
Annona senegalensis	Leaves Roots	Infusion	Convulsions, Epilepsy Sterility, diarrhoea, dysentery		anticonvulsant	Cameroon, Central Africa West Africa, South Africa
Bidens pilosa	Leaves	Decoction	Dizziness, migraines, headaches, rheumatism		Anti hypertensive	Cameroon, Central America
Bryophyllum pinnatum	Leaves	Applica-tion on head Decoction	Convulsions, rheumatism Arthritis	Flavonoids, antraquinones	Antinociceptive, anti-inflammatory antidiabetic	Central Africa
Citrus sinenis	Leaves + Flowers Barks Roots	Decoction Infusion	Epilepsy, convulsions, Insomnia, agitation Headaches, Malaria fever Anxiety, schizophrenia		Sedative	Humid tropical areas
Clerodendron thomsoniae	Leaves Roots	Decoction	Convulsions, head aches Parasitic diseases		effect on purinergic neurotransmission	Cameroon, India
Daniellia oliveri	Barks Roots		Epilepsy, Migraine, head aches Epilepsy, anxiety, schizophrenia			Angola, Cameroon Sudan, West Africa Central Africa
Datura stramonium	Fruits Leaves		Epilepsy Coughs, asthma, pains	Alkaloids, atropine		Africa, Asia, America, Europa
Detarium microcarpum	Leaves Barks Roots	Decoction	Dizziness, schizophrenia, paralysis malaria, diarrhoea Epilepsy, Pains Paralysis			West Africa Central Africa
Euphorbia hirta	Whole plant	Decoction	Convulsions, Insomnia Diarrhoea, amoeba, asthma, coughs, pains	Alkaloids, tannins	Anxiolytic	Africa continent
Flacourtia indica	Sterm barks Fruts Leaves		Epilepsy, headache, fever, stomach-ache, diarrhoea Sleep disorders	beta-sistosterol butyrolactone, steroids, flacourtine, flavonoids, coumarine, terpenoids, polyphenols	Antiplasmodial Protection against liver toxicity	

Name of the plant	Part of the plant used	Form of the medicine	Diseases	Chemical characterization	Pharmaco-logical properties	Country
Hymenocardia acida	Leaves Barks Roots	Infusion Powder	Headaches, fever, hypotension, diabetes, sickle cells Epilepsy, schizophrenia			Cameroon, Central Africa West Africa
Jatropha gossypiifolia	Leaves + Roots Roots		Convulsions, fever, hypertension Convulsions,			Cameroon, Central Africa, West Africa
Khaya senegalensis	Leaves, Barks Roots	Decoction	Headaches, schizophrenia, malaria Fever	Saponins, tannins, triterpenes	Antiinflamm-atory	Cameroon
Mentha cordifolia	Leaves	Infusion	Insomnia, muscle relaxant,		Antioxydant	Cameroon
Prosopis Africana	Leaves Barks	Decoction	Epilepsy, insomnia, anxiety states, headaches, migraine, agitation, fever Vermifuge, fever		Antitrypano-somal	Cameroon West Africa
Ricinus communis	Leaves + flowers	Decoction	Epilepsy, convulsions, headaches, diarrhea, asthma	ricin	Neuroleptic like properties	Central Africa, West Africa
Securidaca longepeduncul ata	Barks Roots, Leaves		Epilepsy, schizophrenia Pains, Rheumatisms		Anxiolytic	Central Africa, West Africa
Senna singueana	Leaves Leaves and flowers Barks and Roots,		Fever, Conjunctivitis, Convulsions, gonorrhoea, bilharzias, stomach-aches, constipation, Epilepsy, syphilis,	7-Methylphyscion Cassiamin A		Cameroon, Mali, Soudan, East and South Africa.
Terminalia glaucescens,	Leaves Barks Roots	Decoction Decoction Macera-tion	Malaria, stomach-aches, leucorrhoea, Hepatitis, leucorrhoea Epilepsy, diarrhoea, leucorrhoea	Terminalin A Glaucinoic Acid	antimicrobial	
Terminalia mollis	Roots		Epilepsy			Central Africa,
Tetrapleura tétraptera	Barks Fruits Roots	Decoction	Epilepsy Convulsions Fevers, malaria	Saponins, tannins	Anticonvulsant	Angola, Cameroon, Sudan, West Africa, Central Africa
Trichilia emetica	Roots Barks		Epilepsy, anti-parasitic diseases Head aches	Tannins, sterols		Savannah belt, open woodland in Africa
Vitelaria paradoxa	Leaves Leaves + Barks	Decoction	Convulsions, Epilepsy, headaches, stress Head aches	Saponins, alkaloids, tannins, cadiac glycosides	Antimicrobial	Cameroon, Brazil

Table 1. Parts of the plant, form of the medicine and diseases treated in traditional medicine. Adeyemi et al., 2010; Adjanohoum et al., 1984; Adjanouhoun et al., 1996; Adzu et al., 2003; Agassounon et al. 2008; Anete et al., 1998 ; Anuradha et al., 2008; Arbonnier, 2000; Berhaut, 1975; Brenan, 1959 ; Dimo et al., 2002; El-Mahmood et al., 2008; Ezugwu & Odoh, 2003; Gusman-Gutierez & Navarrete, 2009; Iwu, 1993; Joyner, 2004; Lompo et al., 1998; Malgras, 1992; Mutasa et al., 1990; Nazneen et al., 2009; Ogundiya, 2009; Ojewole, 2005; Palgrave, 2003; Pathak et al., 2010; Pousset, 1989; Satyarayana et al., 1996; Sunday et al., 2009; Saulnier, 1998; Seema Zareen, 2006; Worapan et al., 2009.

with these plants, very few were done to study their sedative and anticonvulsant properties. This study was undertaken to evaluate the anticonvulsant and sedative properties of these plants used in the treatment of insomnia and epilepsy in traditional medicine in Africa, particularly in Cameroon.

2. Materials and methods

2.1 Animals

Adult male mice (*Mus musculus* Swiss; 22 ± 2 g; 6 or 8 per group) were used for this study. The animals were housed in standard cages at 25°C, on a 12/12 h light-dark cycle. They were supplied with food and water *ad libitum*.

Drugs were administered in a volume of 10 ml/kg of mice body weight. The study was conducted in accordance with the nationally (N°.FWA-IRB00001954) and internationally accepted principles for laboratory animal use and care. In diazepam or sodium thiopental-induced sleep tests, mice were divided into negative control group that received distilled water and four test groups that received different doses of the plant extracts. In anticonvulsant tests, there was one more group that received a known anticonvulsant compound and served as a positive control.

2.2 Plant material

A voucher specimen of each plant was authenticated by a botanist, Professor Mapongmetsem Pierre Marie, Department of Biological Sciences, University of Ngaoundéré and deposited at the National Herbarium of Cameroon in Yaoundé.

2.3 Preparation of the extracts

2.3.1 Decoction

10 g of each plant material were macerated for 1 h in an amount of distilled water (25, 50, 75, 100 or 150 ml) according to the plant. The mixture was boiled for 20 min. After cooling, the supernatant (decoction) was collected and filtered. The decoction of each plant was diluted in distilled water to obtain less concentrated solutions. In another experiment, the decoction was dried and the w/w yield of the extract was calculated (table 2). The decoctions were prepared according to the methods close to the ones used in traditional medicine.

2.3.2 Maceration

10 g of dried fruits of *Datura stramonium* were macerated in 50 ml of distilled water. After 1 h the supernatant was collected, filtered and used in mice. The w/w yield of the extract was obtained (table 2).

2.4 Anticonvulsant tests

2.4.1 N-methyl-D-aspartate (NMDA) test

Six groups of 6 or 8 mice received different treatments. Group I (negative control) was treated with distilled water. Groups II to V (test groups) were treated with 4 doses of the plant extracts. Group VI (positive control) was treated with 3 mg/kg of CGP 37849 i.p. or 33 ηmol/kg of D-AP7 i.p. Mice were injected subcutaneously with NMDA, 75 mg/kg 1 h after administration of the different treatments. They were observed for 30 min. Animals

that did not exhibit turning behaviour within the 30 min of observation were declared protected. Turning behaviour was characterised by two consecutive 360° cycles fulfilled by the same animal (Croucher et al., 1982; Ngo Bum et al., 2001; 2009a; 2009b; Schmutz et al., 1990).

2.4.2 Strychnine (STR) test

Six groups of 6 or 8 mice received different treatments as above, except that group VI (positive control) was treated with clonazepam (3 mg/kg, i.p.). Convulsions followed by death were induced in mice by the i.p. injection of 2.5 mg/kg STR nitrate 1 h after administration of the different treatments. The animals which survived more than 10 min after strychnine injection were qualified protected (Ngo Bum et al., 2001, 2009a).

2.4.3 Picrotoxine (PIC) test

Six groups of 6 or 8 mice received different treatments as above, except that group VI (positive control) was treated with clonazepam (0.4 mg/kg, i.p.). Clonic seizures were induced in mice by the i.p. injection of 7.5 mg/kg PIC 1 h after administration of the different treatments. The animals which did not convulse within the 15 min of observation after PIC injection were qualified protected (Lehmann et al., 1988; Ngo Bum et al., 2001).

2.4.4 Pentylenetetrazol (PTZ) test

Six groups of 6 or 8 mice received different treatments as above, except that group VI (positive control) was treated with clonazepam (0.1 mg/kg, i.p.). Clonic seizures were induced in mice by the i.p. injection of 70 mg/kg PTZ 1 h after administration of the different treatments. The animals that did not convulse within the 10 min from the injection of PTZ were qualified protected (Ngo Bum et al., 2001, 2009a, 2009b).

2.4.5 Isonicotinic hydrazide acid (INH) test

Six groups of 6 or 8 mice received different treatments as above, except that group VI (positive control) was treated with diazepam, 10 mg/kg (per os). Animals were injected i.p. with INH 250 mg/kg 1 h after the administration of the different treatments. The time to the onset of clonic or tonic seizures was recorded. (Bernasconi et al., 1988; Ngo Bum et al., 2001).

2.5 Diazepam or sodium thiopental-induced sleep in mice

Five groups of 6 or 8 mice received different treatments. Group I (negative control) was treated with distilled water and groups II to V (test groups) were treated with 4 doses of the plant extracts.The methods described by Beretz et al., (1978) and modified by Rakotonirina et al., (2001) were used. Sleep potentiating effects of the plant were studied in mice that received sodium thiopental or diazepam at a dose of 50 mg/kg (i.p.) 1 hour after the administration of the different treatments. The time between the loss of the straightening reflex and the regain of this reflex measured the sleeping time. The loss or the regain of the straightening reflex was measured by stimulating the external ear. When the mouse anterior paw does not move after stimulation with horsehair, the animal is sleeping. When the mouse is awakened, it moves and shakes its paw.

Name of the plant	Part of the plant used	Quantity plant powder (g)	Quantity of water (ml)	Yield (%)	Root of administration
Annona muricata	Fresh leaves	10	50	6	i.p.
Annona senegalensis	Dried leaves	10	75	5	i.p.
Bidens pilosa	Fresh leaves	10	25	3.5	i.p.
Bryophyllum pinnatum	Fresh leaves	10	25	7	i.p.
Citrus sinenis	Fresh leaves	10	50	5	i.p.
Clerodendron thomsoniae	Dried leaves	10	50	6.7	i.p.
Daniellia oliveri	Dried barks	10	50	9.9	p.o.
Datura stramonium	Dried fruits	10 (macerate)	50	7	i.p.
Detarium microcarpum	Dried roots	10	50	7.43	p.o.
Euphorbia hirta	Fresh plant	10	50	7	i.p.
Flacourtia indica	Dried barks	10	100	10	p.o.
Hymenocardia acida	Fresh leaves	10	25	2.19	i.p.
Jatropha gossypiifolia	Dried leaves	10	50	7	i.p.
Khaya senegalensis	Dried leaves	10	75	5	i.p.
Mentha cordifolia	Fresh leaves	10	50	7	i.p.
Prosopis Africana	Dried leaves	10	50	5.6	i.p.
Ricinus communis	Fresh leaves	10	50	6	p.o.
Securidaca longepedunculata	Dried roots	10	150	10	i.p.
Senna singueana	Dried roots	10	50	8	p.o.
Terminalia glaucescens	Dried roots	10	100	7.6	p.o.
Terminalia mollis	Dried roots	10	50	7.1	p.o.
Tetrapleura tétraptera	Dried barks	10	50	4.2	i.p.
Trichilia emetic	Fresh roots	10	50	6.3	p.o.
Vitelaria paradoxa	Fresh leaves	10	150	12.6	i.p.

i.p. (intraperitoneal), p.o. (per os).

Table 2. Quantities of plants powder and distilled water, and part of the plant used to prepare the decoctions.

2.6 Statistical analysis

Three parameters were measured: the protection against chemically-induced seizures, the latency to the onset of seizures (min) in INH test, the latency to the onset of sleep and the sleeping time (min) in the sleep potentiation test. Data of the control groups were compared to data of groups treated with the plants extracts and to data of the positive control groups. The statistical analysis were done using Fisher exact test and Anova followed by Dunnett (REGWQ). $P<0.05$ was considered significant.

2.7 Chemicals

D-2-amino-7-phosphonoheptanoate, Clonazepam, Isonicotinic hydrazide acid, N-methyl-D-aspartate, penthylenetetrazol, picrotoxine, sodium thiopental and strychnine are from Sigma Chemical, USA. Diazepam is from Roche, France.

3. Results

3.1 Sedative properties

The extracts of twenty one plants increased in a dose-dependent manner the sleeping time induced by sodium thiopental or diazepam. The most potent was *Datura stramonium*. it multiplied by a factor of 5 the sleeping time of the control group (from 16 ± 7 to 94 ± 25 min at a dose of 70 mg/kg), but this extract was very toxic for animals. The decoctions of eight plants multiplied by a factor of 4 the sleeping time of their control group: *Annona senegalensis* (from 19 ± 4 to 89 ± 29 min at a dose of 67 mg/kg), *Clerodendron thomsoniae* (from 19 ± 3 to 94 ± 30 min at a dose of 134 mg/kg), *Daniellia oliveri* (from 20 ± 8 to 81 ± 13 min at a dose of 198 mg/kg), *Hymenocardia acida* (from 20 ± 11 to 85 ± 21 min at a dose of 87.6 mg/kg), *Securidaca longepedunculata* (from 18 ± 3 to 78 ± 14 min at a dose of 66.7 mg/kg), *Terminalia mollis* (from 17 ± 1 to 84 ± 15 min at a dose of 70 mg/kg), *Tetrapleura tetraptera* (from 19 ± 3 to 91 ± 15 min at a dose of 84 mg/kg) and *Trichilia emetica* (from 17 ± 1 to 84 ± 10 min at a dose of 126 mg/kg). The sleeping time of the control groups were multiplied by a factor of 3 by six plants: *Flacourtia indica* (from 16 ± 12 to 49 ± 3 min at a dose of 100 mg/kg), *Jatropha gossypiifolia* (from 11 ± 5 to 43 ± 15 min at a dose of 140 mg/kg), *Prosopis Africana* (from 19 ± 3 to 61 ± 26 min at a dose of 112 mg/kg), *Senna singueana* (from 24 ± 2 to 86 ± 5 min at a dose of 20 mg/kg),*Terminalia glaucescens* (from 37 ± 13 to 120 ± 21 min at a dose of 76 mg/kg), and *Vitellaria paradoxa* (from 25 ± 4 to 84 ± 20 min at a dose of 84 mg/kg). The decoctions of five plants multiplied by a factor of 2 the sleeping time of their control group: *Annona muricata* (from 31 ± 11 to 71 ± 15 min at a dose of 120 mg/kg), *Bidens pilosa* (from 31 ± 2 to 80 ± 2 min at a dose of 140 mg/kg), *Detarium microcarpum* (from 20 ± 6 to 52 ± 12 min at a dose of 111.45 mg/kg), *Euphorbia hirta* (from 56 ± 16 to 145 ± 10 min at a dose of 140 mg/kg) and *Mentha cordifolia* (from 10 ± 2 to 24 ± 3 min at a dose of 140 mg/kg). *Bryophyllum pinnatum* induced a slight increase of the sleeping time. Only *Citrus sinenis* and *Kaya senegalensis* could not increase the total sleep time of mice (table 3). Some of those plants also reduced the onset time of sleep (Table 4).

3.2 Anticonvulsant properties

3.2.1 On PTZ- induced convulsions

78.3% of plants extract were effective against PTZ-induced convulsions. *Annona muricata, Annona senegalensis, Bidens pilosa, Clerodendron thomsoniae, Daniellia oliveri, Datura stramonium, Detarium microcarpum, Euphorbia hirta, Flacourtia indica, Hymenocardia acida, Mentha cordifolia, Ricinus communis, Securidaca longepedunculata, Senna singueana, Terminalia glaucescens, Terminalia mollis, Tetrapleura tétraptera, Trichilia emetica* and *Vitellaria paradoxa* protected mice against convulsions induced by PTZ (table 5).

3.2.2 On STR- induced convulsions

The percentage of plants extracts that protected mice against STR-induced convulsions was *77.8%. Annona muricata, Bidens pilosa, Daniellia oliveri, Detarium microcarpum, Flacourtia indica, Hymenocardia acida, Jatropha gossypiifolia, Khaya senegalensis, Mentha cordifolia, Prosopis Africana, Securidaca longepedunculata, Senna singueana, Terminalia mollis, Trichilia emetica* protected mice against STR- induced convulsions (table 5).

3.2.3 On PIC- induced convulsions

The percentage of plants extracts that protected mice against PIC-induced convulsions was *87.5%. Clerodendron thomsoniae, Flacourtia indica, Mentha cordifolia, Securidaca longepedunculata,*

Senna singueana, Terminalia glaucescens and *Vitellaria paradoxa* protected mice against convulsions induced by PIC (table 5).

			Doses of the plants in mg/kg			
Daniellia		**CON**	**49.5**	**99**	**148.5**	**198**
oliveri	DIAZ	9 ± 3	6 ± 1	6 ± 1	5 ± 2	3 ± 1**
Detarium		**CON**	**37.15**	**47.3**	**111.45**	**148.6**
microcarpum	DIAZ	9 ± 3	7 ± 2	6 ± 3	4 ± 2*	6 ± 3
Flacourtia		**CON**	**10**	**25**	**50**	**100**
indica	DIAZ	4 ± 2	8 ± 6	4 ± 4	11 ± 6	4 ± 4
Hymenocardia		**CON**	**8.7**	**21.9**	**43.8**	**87.6**
acida	DIAZ	9 ± 3	7 ± 3	6 ± 1*	5 ± 1**	3 ± 1***
Mentha		**CON**	**14**	**35**	**70**	**140**
cordifolia	DIAZ	3 ± 1	2 ± 1	2 ± 1	6 ± 3	4 ± 1
Securidaca		**CON**	**10**	**20**	**50**	**66.7**
longepedunculata	DIAZ	6 ± 1	5 ± 1	5 ± 1	4 ± 1*	4 ± 1*
Senna		**CON**	**20**	**40**	**80**	**160**
singueana	DIAZ	15 ± 3	6 ± 1***	6 ± 1***	7 ± 1***	8 ± 1***
Terminalia		**CON**	**9.5**	**19**	**38**	**76**
glaucescens	DIAZ	4 ± 2	7 ± 4	5 ± 1	6 ± 3	2 ± 2
Terminalia		**CON**	**14**	**35**	**70**	**140**
mollis	DIAZ	7 ± 2	5 ± 1	2 ± 1**	3 ± 1**	4 ± 1*
Trichilia		**CON**	**12.6**	**33**	**66**	**126**
emetica	DIAZ	6 ± 1	5 ± 1	4 ± 1***	2 ± 1***	2 ± 1***

Data represent the onset time of sleep time. Values are means ± ESM. N = 6 or 8 per dose, *<p 0.05, **<p 0.01, ***<p 0.001 vs control, Anova followed by Dunnett (REGWQ). CON = distilled water, DIAZ = diazepam 50 mg/kg.

Table 3. The effects of the different plants on the onset time of sleep induced in mice by sodium thiopental or diazepam.

3.2.4 On NMDA- induced turning behaviour

The percentage of plants extracts that protected mice against NMDA-induced turning behaviour was 100%. *Annona muricata*, *Bidens pilosa*, *Bryophyllum pinnatum*, *Citrus sinenis*, *Euphorbia hirta*, *Khaya senegalensis* protected mice against turning behaviour induced by NMDA (table 5).

3.2.5 On MES- induced convulsions

The percentage of plants extracts that protected mice against MES-induced convulsions was 25%. *Securidaca longepedunculata* protected mice against convulsions induced by MES (table 5).

3.2.6 On INH- induced convulsions

The percentage of plants extracts that were effective against INH-induced convulsions in mice was 60%. *Ricinus communis*, *Securidaca longepedunculata*, *Senna singueana* delayed the onset of seizures in INH test (table 5).

3.2.7 Plants efficacy

Flacourtia indica, *Ricinus communis*, *Securidaca longepedunculata*, *Senna singueana*, *Terminalia glaucescens* showed very good anticonvulsant activities (80 to 100% of protection against PTZ, PIC or INH induced seizures). The other eighteen plants tested protected 50 to 75% of

			Doses of the plants in mg/kg			
Annona muricata	DIAZ	**CON** 31 ± 11	**12** 51 ± 26*	**30** 67 ± 6***	**60** 68 ± 2***	**120** 71 ± 15***
Annona senegalensis	DIAZ	**CON** 19 ± 4	**6.7** 52 ± 18***	**17** 72 ± 17***	**34** 79 ± 25***	**67** 89 ± 29***
Bidens pilosa	DIAZ	**CON** 31 ± 2	**14** 70 ± 2***	**35** 66 ± 3***	**70** 79 ± 5***	**140** 80 ± 2***
Bryophyllum pinnatum	DIAZ	**CON** 21 ± 2	**28** 32 ± 5**	**70** 26 ± 5	**140** 35 ± 1**	**280** 31 ± 6*
Citrus sinenis	DIAZ	**CON** 56 ± 24	**10** 50 ± 20	**25** 40 ± 10	**50** 45 ± 12	**100** 57 ± 10
Clerodendron thomsoniae	DIAZ	**CON** 19 ± 3	**13.4** 39 ± 9***	**33.5** 74 ± 22***	**67** 90 ± 16***	**134** 94 ± 30***
Daniellia oliveri	DIAZ	**CON** 20 ± 8	**49.5** 50 ± 3***	**99** 74 ± 8***	**148.5** 74 ± 7***	**198** 81 ± 13***
Datura stramonium	THIO	**CON** 16 ± 7	**3.5** 55 ± 15***	**7** 63 ± 21***	**35** 85 ± 23***	**70** 94 ± 25***
Detarium microcarpum	DIAZ	**CON** 20 ± 6	**37.15** 38 ± 10**	**47.3** 46 ± 13**	**111.45** 52 ± 12***	**148.6** 45 ± 9***
Euphorbia hirta	DIAZ	**CON** 56 ± 16	**14** 99 ± 24**	**35** 97 ± 21**	**70** 117 ± 26***	**140** 145 ± 10***
Flacourtia indica	DIAZ	**CON** 16 ± 12	**10** 15 ± 11	**25** 38 ± 25*	**50** 44 ± 4***	**100** 49 ± 3***
Hymenocardia acida	DIAZ	**CON** 20 ± 11	**8.7** 51 ± 12***	**21.9** 70 ± 15***	**43.8** 77 ± 23***	**87.6** 85 ± 21***
Jatropha gossypiifolia	DIAZ	**CON** 11 ± 5	**14** 29 ± 14*	**35** 27 ± 13*	**70** 32 ± 10***	**140** 43 ± 15***
Kaya senegalensis	DIAZ	**CON** 63 ± 15	**6.7** 52 ± 21	**17** 58 ± 25	**34** 58 ± 23	**67** 61 ± 23
Mentha cordifolia	DIAZ	**CON** 10 ± 2	**14** 16 ± 5*	**35** 21 ± 5**	**70** 21 ± 4**	**140** 24 ± 3**
Prosopis africana	DIAZ	**CON** 19 ± 3	**11.2** 52 ± 26*	**28** 57 ± 17**	**56** 31 ± 17	**112** 61 ± 26***
Securidaca longepedunculata	DIAZ	**CON** 18 ± 3	**10** 60 ± 27**	**20** 65 ± 14***	**50** 67 ± 27**	**66.7** 78 ± 14***
Senna singueana	DIAZ	**CON** 24 ± 2	**20** 86 ± 5**	**40** 77 ± 3***	**80** 44 ± 7**	**160** 29 ± 9***
Terminalia glaucescens	DIAZ	**CON** 37 ± 13	**9.5** 31 ± 15	**19** 79 ± 40*	**38** 86 ± 17***	**76** 120 ± 21***
Terminalia mollis	DIAZ	**CON** 17 ± 1	**14** 44 ± 7***	**35** 64 ± 11***	**70** 84 ± 15***	**140** 73 ± 8***
Tetrapleura tétraptera	DIAZ	**CON** 19 ± 3	**8.4** 39 ± 10**	**21** 67 ± 18***	**42** 82 ± 14***	**84** 91 ± 15***
Trichilia emetica	DIAZ	**CON** 17 ± 1	**12.6** 22 ± 2*	**33** 29 ± 4**	**66** 71 ± 7***	**126** 84 ± 10***
Vitelaria paradoxa	DIAZ	**CON** 25 ± 4	**12** 40 ± 13***	**21** 57 ± 6***	**42** 59 ± 8***	**84** 84 ± 20***

Data represent the total sleep time. Values are means ± ESM. N = 6 or 8 per dose, *p< 0.05, **p<0.01, ***p< 0.001 vs control, Anova followed by Dunnett (REGWQ). CON = distilled water, DIAZ = diazepam 50 mg/kg, THIO = sodium thiopental 50 mg/kg.

Table 4. The effects of the different plants on the total sleep time induced in mice by sodium thiopental or diazepam.

			Doses of the plants in mg/kg				
Annona		**CON**	**12**	**30**	**60**	**120**	**CP**
Muricata	PTZ	0	16	50*	33	50*	100***
	STR	0	12	0	12	50*	100***
	NMDA	0	16	16	33	50*	100***
Annona		**CON**	**6.7**	**17**	**34**	**67**	**CP**
Senegalensis	PTZ	0	12	37	50*	25	100***
Bidens		**CON**	**14**	**35**	**70**	**140**	**CP**
pilosa	PTZ	0	16	50*	33	50*	100***
	STR	0	16	50*	40	50*	100***
	NMDA	0	33	33	66**	50*	100***
Bryophyllum		**CON**	**28**	**70**	**140**	**280**	**CP**
pinnatum	PTZ	0	16	33	16	33	100***
	STR	0	0	10	0	16	100***
	NMDA	0	33	50*	50*	50*	100***
Citrus		**CON**	**10**	**25**	**50**	**100**	**CP**
sinenis	PTZ	0	25	25	12	0	100***
	STR	0	0	0	12	12	100***
	NMDA	0	50*	50*	75**	75**	100***
Clerodendron		**CON**	**13.4**	**33.5**	**67**	**134**	**CP**
Thomsoniae	PTZ	0	12	37	37	62*	100***
	PIC	0	0	25	50*	50*	100***
Daniellia		**CON**	**49.5**	**99**	**148.5**	**198**	**CP**
oliveri	PTZ	0	25	37	37	50*	100***
	STR	0	16	66**	50*	50*	100***
Detarium		**CON**	**37**	**47**	**111**	**148**	CP
microcarpum	PTZ	0	50*	37	0	0	100***
	STR	0	50*	33	33	16	100***
Euphorbia		**CON**	**14**	**35**	**70**	**140**	**CP**
hirta	PTZ	0	0	25	0	50*	100***
	STR	0	12	37	25	37	100***
	NMDA	0	33	33	50*	50*	100***
Flacourtia		**CON**	**10**	**25**	**50**	**100**	**CP**
indica	PTZ	0	80**	60*	40	40	100***
	STR	0	20	40	40	60*	100***
	PIC	0	40	60*	60*	80**	100***
	MES	0	40	0	0	40	100
	INH	36 ± 7	48 ± 5	36 ± 10	50 ± 12	49 ± 6	73 ± 11***
Hymenocardia		**CON**	**8.76**	**21.9**	**43.8**	**87.6**	**CP**
acida	PTZ	0	0	25	37	62*	100***
	STR	0	16	33	33	50*	100***
Jatropha		**CON**	**14**	**35**	**70**	**140**	**CP**
gossypiifolia	PTZ	0	0	25	37	0	100***
	STR	0	50*	50*	62*	25	100***
	PIC	0	0	0	0	0	100***
Khaya		**CON**	**6.7**	**17**	**34**	**67**	**CP**
senegalensis	PTZ	0	12	12	0	25	100***
	STR	0	25	50*	25	50*	100***
	NMDA	0	62*	33	33	50*	100***
Mentha		**CON**	**14**	**35**	**70**	**140**	**CP**
cordifolia	PTZ	0	16	33	66**	50*	100***
	STR	0	33	33	33	66**	100***
	PIC	0	16	50*	33	50*	100***
Prosopis		**CON**	**11.2**	**28**	**56**	**112**	**CP**
africana	PTZ	0	0	0	25	37	100***
	STR	0	62*	25	50*	50*	100***
Ricinus		**CON**	**12**	**30**	**60**	**120**	**CP**
communis	PTZ	0	37	50*	62*	87***	100***

	INH	31 ± 9	33 ± 6	36 ± 8	40 ± 7	56 ± 16*	77 ± 11**
Securidaca		**CON**	**10**	**20**	**50**	**66.7**	**CP**
longepedunculata	PTZ	0	67**	67**	83***	100***	100***
	STR	0	50*	67**	67**	67**	100***
	PIC	0	67**	100***	83**	83**	100***
	INH	46 ± 3	51 ± 5*	62 ± 12**	67 ± 20**	78 ± 21**	97 ± 20***
Senna		**CON**	**20**	**40**	**80**	**160**	**CP**
singueana	PTZ	0	80**	80**	40	40	100***
	STR	0	80**	80**	40	40	100***
	PIC	0	20	60*	0	20	100***
	MES	0	40	40	20	20	80**
	INH	21 ± 1	30 ± 1**	29 ± 6	32 ± 9**	37 ± 1**	42 ± 6**
Terminalia		**CON**	**9.5**	**19**	**38**	**76**	**CP**
glaucescens	PTZ	0	40	60*	40	100***	100***
	STR	0	40	20	0	0	100***
	PIC	0	20	60*	40	20	100***
	MES	0	20	40	0	40	80**
	INH	36 ± 7	41 ± 13	18 ± 5	42 ± 9	47 ± 13	85 ± 26***
Terminalia		**CON**	**14**	**35**	**70**	**140**	**CP**
mollis	PTZ	0	50*	37	25	37	100***
	STR	0	66**	33	33	50*	100***
Tetrapleura		**CON**	**8.4**	**21**	**42**	**84**	**CP**
tetraptera	PTZ	0	25	50*	50*	50*	100***
Trichilia		**CON**	**12.6**	**33**	**66**	**126**	**CP**
emetica	PTZ	0	25	50*	50*	50*	100***
	STR	0	12	25	50*	50*	100***
Vitelaria		**CON**	**12**	**21**	**42**	**84**	**CP**
paradoxa	PTZ	0	12	50*	62*	50*	100***
	PIC	0	0	12	50*	37	100***

Data represent the percentage of protected mice in different tests. N = 6 or 8 per dose, *p< 0.05, **p<0.01, ***p< 0.001 vs control, Anova followed by Dunnett (REGWQ). CON (negative control) = distilled water, CP (positive control) = clonazepam 0.1 mg/kg for PTZ test, clonazepam 0.4 mg/kg for PIC test, clonazepam 3 mg/kg for STR test, diazepam 10 mg/kg for INH test and D-AP7 33 ηmol/kg or CGP 37849 3 mg/kg for NMDA test.

Table 5. The effects of the different plants on the convulsions and turning behaviour induced in mice by INH, NMDA, PIC, PTZ and STR.

mice against the induced convulsions. 78% of plants protected both PTZ and STR-induced convulsions. 80.6% of plants protected both PTZ and PIC-induced convulsions. 80.8% of plants protected both STR and PIC-induced convulsions. Finally, 66.7% of plants at the same time protected PTZ, STR and PIC-induced convulsions.

3.2.8 Plants toxicity

Datura stramonium, *Ricinus communis and Securidaca longepedunculata* were also showed to be toxic. Their extract killed animal in 24h after their administration to mice.

4. Discussion and conclusions

The extracts of twenty one plants (91.3% of plants) increased the sleeping time induced by sodium thiopental or diazepam. The potentiation of the sleep time suggests the presence of sedative properties in the extracts of these plants (Rakotonirina et al., 2001; Ngo Bum et al., 2009a; 2009b). These sedative properties could be related to the presence of some components in the extracts activating the benzodiazepine, barbiturate and/or GABA

receptors in the $GABA_A$ receptor complex (Rang et al., 1999; Bonin & Orser, 2008; Olkkola & Ahonen, 2008). Diazepam (benzodiazepine) and sodium thiopental (barbiturate) all bind to the $GABA_A$ receptor complex. Diazepam potentiates GABA-mediated inhibition via the increase in the affinity of this inhibitory neurotransmitter to its recognition sites within the $GABA_A$ receptor complex, by increasing the opening frequency of the chloride ion channel which leads to the enhancement of influx of chloride anions into the neuron and subsequent hyperpolarisation (Czapinsky et al., 2005). While sodium thiopental that act on the barbiturate binding site directly gate the chloride ion channel of the $GABA_A$ receptor complex. The sedative properties found here could explain the use of the twenty one plants in traditional medicine in Africa, particularly in Cameroon in the treatment of insomnia. The first eight more potent plants to induced sedation were: *Datura stramonium* > *Clerodendron thomsoniae* > *Terminalia mollis* > *Trichilia emetica* > *Tetrapleura tétraptera* > *Annona senegalensis* > *Securidaca longepedunculata* > *Hymenocardia acida* > *Daniellia oliveri*. Two plants, *Citrus sinenis* and *Kaya senegalensis* did not show sedative properties. The results also showed that 95.6% of the tested plants possess anticonvulsant properties by inhibiting convulsions induced chemically or electrically. Five plants (*Flacourtia indica*, *Ricinus communis*, *Securidaca longepedunculata*, *Senna singueana*, *Terminalia glaucescens*) showed very good anticonvulsant activities against PTZ, PIC or INH induced seizures.

The effect was moderate for the rest of plants. *Tetrapleura tetraptera* one of the plants studied showed also anticonvulsant properties in fruits (Nwaiwu, 1986; Ojewole, 2005). The antagonism of INH, PTZ- and PIC-induced seizures suggests the interaction of these plants with the GABA-ergic neurotransmission (De Deyn et al., 1992; Doctor et al., 1982; Löscher & Schmidt, 1988; Salih & Mustafa, 2008; Perez-Saad & Buznego, 2008). GABA is the main inhibitory neurotransmitter substance in the brain and is widely implicated in epilepsy. Inhibition of GABA-ergic neurotransmission or activity has been shown to promote and facilitate seizures, while enhancement of GABA-ergic neurotransmission is known to inhibit or attenuate seizures (Gale, 1992; Li-Ping et al., 2008). Moreover, some studies indicated that PTZ diminishes the GABAergic tone (Mcdonald & Baker. 1977; Ahmadiani, 2003), probably by a competitive antagonist action on the BZD receptors (Rehavi et al., 1982). Correspondingly, drugs that enhance $GABA_A$-receptor neurotransmission, such as BZDs (White, 1997; Ahmadiani et al., 2003) can block seizures induced by PTZ. PIC is known to be a non competitive GABA antagonist exerting his effect by blocking the chloride channel in the $GABA_A$ receptor complex. Isoniazide can precipitate convulsions in patients with seizure disorders, and it is regarded as a GABA-synthesis inhibitor (Kale Shubhangi et al., 2010**)**. The antagonism of STR -induced convulsions suggests the presence of anticonvulsant effect through glycine-STR-sensitive receptors (Findlay et al., 2002). Few plants extract antatagonized MES induced convulsions, by probably prolonging neurons sodium channels inactivation (Holmes, 2007). The results show no difference in plants inhibiting convulsions induced by PTZ, PIC and STR. GABA and glycine-STR-sensitive neurotransmission are equally involved. But very few plants produced their anticonvulsant activities by prolonging neurons sodium channels inactivation. *Datura stramonium*, *Ricinus communis* and *Securidaca longepedunculata* were found toxic and therefore they are not suitable to be used to treat people. The toxicity of *Ricinus communis* could be related to the presence of a very toxic component named ricin (Iwu, 1993). The toxicity of *Datura stramonium* could be related to its delirants or anticholinergics compounds.

5. Conclusion

The purported anticonvulsant and sedative properties of the medicinal plants are scientifically shown. The ethnopharmacological study on Cameroon anticonvulsant and sedative medicinal plants is accurate in 90% of cases. A great amount of plants extract interacted through GABA and glycine-STR-sensitive neurotransmissions to inhibit convulsions. Many anticonvulsant plants also possess sedative properties. Twenty one plants possess sedative properties, but only eighteen plants could be used in traditional medicine in Africa in the treatment of insomnia. Eighteen plants possess at least moderate anticonvulsant effects, while five plants possess very good anticonvulsant properties. However only twenty medicinal plants could be used in the treatment of epilepsy. Three plants were found very toxic.

6. Acknowledgment

We would like to thank Professor AMVAM ZOLLO Paul Henri, Professor Ngounouno Ismaila, and Dr Megueni Clautilde for their support.

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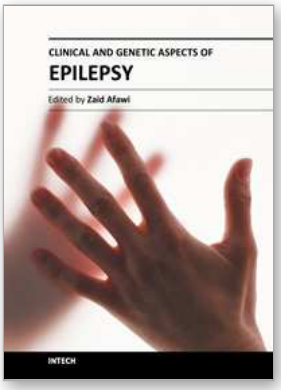

Clinical and Genetic Aspects of Epilepsy

Edited by Dr. Zaid Afawi

ISBN 978-953-307-700-0
Hard cover, 204 pages
Publisher Intech
Published online 15, September, 2011
Published in print edition September, 2011

This book on Epilepsy was conceived and produced as a source of information on wide range of issues in epilepsy. We hope that it will help health care providers in daily practices and increase their understanding on diagnosis and treatment of epilepsies. The book was designed as an update for neuroscientists who are interested in epilepsy, primary care physicians and students in health care professions.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

E. Ngo Bum, G.S. Taiwe, F.C.O. Moto, G.T. Ngoupaye, R.R.N. Vougat, V.D. Sakoue, C. Gwa, E.R. Ayissi, C. Dong, A. Rakotonirina and S.V. Rakotonirina (2011). Antiepileptic Medicinal Plants used in Traditional Medicine to Treat Epilepsy, Clinical and Genetic Aspects of Epilepsy, Dr. Zaid Afawi (Ed.), ISBN: 978-953-307-700-0, InTech, Available from: http://www.intechopen.com/books/clinical-and-genetic-aspects-of-epilepsy/antiepileptic-medicinal-plants-used-in-traditional-medicine-to-treat-epilepsy

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