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# Antiepileptic Medicinal Plants Used in Traditional Medicine to Treat Epilepsy

E. Ngo Bum et al.\*

<sup>1</sup>Department of Biological Sciences, Faculty of Science, University of Ngaoundéré,  
Ngaoundéré,  
Cameroon

## 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, Ngougou and collaborators estimated the prevalence in sub-Saharan Africa to be two or three time highest than the rate in developed world (Ngougou 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 sinensis* (Linn) Osbeck (Rutaceae), *Clerodendron thomsoniae* Balf (Verbenaceae), *Daniellia oliveri* (Rolfe) Hutch and Dalz (Caesalpiniaceae), *Datura stramonium* Linn (Solanaceae), *Detarium microcarpum* Guill et Perr (Caesalpiniaceae), *Euphorbia hirta* Linn (Euphorbiaceae), *Flacourtia indica* Willd (Flacourtiaceae), *Hymenocardia acida* Tul (Hymenocardiaceae), *Jatropha gossypifolia* 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)

\* G.S. Taiwe<sup>2</sup>, F.C.O. Moto<sup>1</sup>, G.T. Ngoupaye<sup>1</sup>, R.R.N. Vougat<sup>1</sup>, V.D. Sakoue<sup>1</sup>, C. Gwa<sup>1</sup>, E.R. Ayissi<sup>2</sup>, C. Dong<sup>2</sup>, A. Rakotonirina<sup>2</sup> and S.V. Rakotonirina<sup>2</sup>

<sup>1</sup> Department of Biological Sciences, Faculty of Science, University of Ngaoundéré, Ngaoundéré, Cameroon

<sup>2</sup> Department of Animal Biology and Physiology, Faculty of Sciences, University of Yaoundé 1, Yaoundé, Cameroon

(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	Pharmacological properties	Country
<i>Annona muricata</i>	Leaves	Infusion Decoction	Insomnia, diabetes Spasms, Fever	Steroid, cardiac glycosides	Antimicrobial	Cameroon, Forest areas
<i>Annona senegalensis</i>	Leaves Roots	Infusion	Convulsions, Epilepsy Sterility, diarrhoea, dysentery		anticonvulsant	Cameroon, Central Africa West Africa, South Africa
<i>Bidens pilosa</i>	Leaves	Decoction	Dizziness, migraines, headaches, rheumatism		Anti hypertensive	Cameroon, Central America
<i>Bryophyllum pinnatum</i>	Leaves	Application on head Decoction	Convulsions, rheumatism Arthritis	Flavonoids, antraquinones	Antinociceptive, anti-inflammatory antidiabetic	Central Africa
<i>Citrus sinensis</i>	Leaves + Flowers Barks Roots	Decoction Infusion	Epilepsy, convulsions, Insomnia, agitation Headaches, Malaria fever Anxiety, schizophrenia		Sedative	Humid tropical areas
<i>Clerodendron thomsoniae</i>	Leaves Roots	Decoction	Convulsions, head aches Parasitic diseases		effect on purinergic neurotransmission	Cameroon, India
<i>Daniellia oliveri</i>	Barks Roots		Epilepsy, Migraine, head aches Epilepsy, anxiety, schizophrenia			Angola, Cameroon Sudan, West Africa Central Africa
<i>Datura stramonium</i>	Fruits Leaves		Epilepsy Coughs, asthma, pains	Alkaloids, atropine		Africa, Asia, America, Europa
<i>Detarium microcarpum</i>	Leaves Barks Roots	Decoction	Dizziness, schizophrenia, paralysis malaria, diarrhoea Epilepsy, Pains Paralysis			West Africa Central Africa
<i>Euphorbia hirta</i>	Whole plant	Decoction	Convulsions, Insomnia Diarrhoea, amoeba, asthma, coughs, pains	Alkaloids, tannins	Anxiolytic	Africa continent
<i>Flacourtia indica</i>	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	Pharmacological properties	Country
<i>Hymenocardia acida</i>	Leaves Barks Roots	Infusion Powder	Headaches, fever, hypotension, diabetes, sickle cells Epilepsy, schizophrenia			Cameroon, Central Africa West Africa
<i>Jatropha gossypifolia</i>	Leaves + Roots Roots		Convulsions, fever, hypertension Convulsions,			Cameroon, Central Africa, West Africa
<i>Khaya senegalensis</i>	Leaves, Barks Roots	Decoction	Headaches, schizophrenia, malaria Fever	Saponins, tannins, triterpenes	Antiinflammatory	Cameroon
<i>Mentha cordifolia</i>	Leaves	Infusion	Insomnia, muscle relaxant,		Antioxydant	Cameroon
<i>Prosopis Africana</i>	Leaves Barks	Decoction	Epilepsy, insomnia, anxiety states, headaches, migraine, agitation, fever Vermifuge, fever		Antitrypanosomal	Cameroon West Africa
<i>Ricinus communis</i>	Leaves + flowers	Decoction	Epilepsy, convulsions, headaches, diarrhea, asthma	ricin	Neuroleptic like properties	Central Africa, West Africa
<i>Securidaca longepedunculata</i>	Barks Roots, Leaves		Epilepsy, schizophrenia Pains, Rheumatisms		Anxiolytic	Central Africa, West Africa
<i>Senna singueana</i>	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.
<i>Terminalia glaucescens,</i>	Leaves Barks Roots	Decoction Decoction Maceration	Malaria, stomach-aches, leucorrhoea, Hepatitis, leucorrhoea Epilepsy, diarrhoea, leucorrhoea	Terminalin A Glucinoic Acid	antimicrobial	
<i>Terminalia mollis</i>	Roots		Epilepsy			Central Africa,
<i>Tetrapleura tétaptera</i>	Barks Fruits Roots	Decoction	Epilepsy Convulsions Fever, malaria	Saponins, tannins	Anticonvulsant	Angola, Cameroon, Sudan, West Africa, Central Africa
<i>Trichilia emetica</i>	Roots Barks		Epilepsy, anti-parasitic diseases Head aches	Tannins, sterols		Savannah belt, open woodland in Africa
<i>Vitellaria paradoxa</i>	Leaves Leaves + Barks	Decoction	Convulsions, Epilepsy, headaches, stress Head aches	Saponins, alkaloids, tannins, cardiac 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-Gutierrez & 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;  $22 \pm 2$  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  $\mu$ mol/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
<i>Annona muricata</i>	Fresh leaves	10	50	6	i.p.
<i>Annona senegalensis</i>	Dried leaves	10	75	5	i.p.
<i>Bidens pilosa</i>	Fresh leaves	10	25	3.5	i.p.
<i>Bryophyllum pinnatum</i>	Fresh leaves	10	25	7	i.p.
<i>Citrus sinensis</i>	Fresh leaves	10	50	5	i.p.
<i>Clerodendron thomsoniae</i>	Dried leaves	10	50	6.7	i.p.
<i>Daniellia oliveri</i>	Dried barks	10	50	9.9	p.o.
<i>Datura stramonium</i>	Dried fruits	10 (macerate)	50	7	i.p.
<i>Detarium microcarpum</i>	Dried roots	10	50	7.43	p.o.
<i>Euphorbia hirta</i>	Fresh plant	10	50	7	i.p.
<i>Flacourtia indica</i>	Dried barks	10	100	10	p.o.
<i>Hymenocardia acida</i>	Fresh leaves	10	25	2.19	i.p.
<i>Jatropha gossypifolia</i>	Dried leaves	10	50	7	i.p.
<i>Khaya senegalensis</i>	Dried leaves	10	75	5	i.p.
<i>Mentha cordifolia</i>	Fresh leaves	10	50	7	i.p.
<i>Prosopis Africana</i>	Dried leaves	10	50	5.6	i.p.
<i>Ricinus communis</i>	Fresh leaves	10	50	6	p.o.
<i>Securidaca longepedunculata</i>	Dried roots	10	150	10	i.p.
<i>Senna singueana</i>	Dried roots	10	50	8	p.o.
<i>Terminalia glaucescens</i>	Dried roots	10	100	7.6	p.o.
<i>Terminalia mollis</i>	Dried roots	10	50	7.1	p.o.
<i>Tetrapleura tétraptera</i>	Dried barks	10	50	4.2	i.p.
<i>Trichilia emetic</i>	Fresh roots	10	50	6.3	p.o.
<i>Vitellaria paradoxa</i>	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  $16 \pm 7$  to  $94 \pm 25$  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  $19 \pm 4$  to  $89 \pm 29$  min at a dose of 67 mg/kg), *Clerodendron thomsoniae* (from  $19 \pm 3$  to  $94 \pm 30$  min at a dose of 134 mg/kg), *Daniellia oliveri* (from  $20 \pm 8$  to  $81 \pm 13$  min at a dose of 198 mg/kg), *Hymenocardia acida* (from  $20 \pm 11$  to  $85 \pm 21$  min at a dose of 87.6 mg/kg), *Securidaca longepedunculata* (from  $18 \pm 3$  to  $78 \pm 14$  min at a dose of 66.7 mg/kg), *Terminalia mollis* (from  $17 \pm 1$  to  $84 \pm 15$  min at a dose of 70 mg/kg), *Tetrapleura tetraptera* (from  $19 \pm 3$  to  $91 \pm 15$  min at a dose of 84 mg/kg) and *Trichilia emetica* (from  $17 \pm 1$  to  $84 \pm 10$  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  $16 \pm 12$  to  $49 \pm 3$  min at a dose of 100 mg/kg), *Jatropha gossypifolia* (from  $11 \pm 5$  to  $43 \pm 15$  min at a dose of 140 mg/kg), *Prosopis Africana* (from  $19 \pm 3$  to  $61 \pm 26$  min at a dose of 112 mg/kg), *Senna singueana* (from  $24 \pm 2$  to  $86 \pm 5$  min at a dose of 20 mg/kg), *Terminalia glaucescens* (from  $37 \pm 13$  to  $120 \pm 21$  min at a dose of 76 mg/kg), and *Vitellaria paradoxa* (from  $25 \pm 4$  to  $84 \pm 20$  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  $31 \pm 11$  to  $71 \pm 15$  min at a dose of 120 mg/kg), *Bidens pilosa* (from  $31 \pm 2$  to  $80 \pm 2$  min at a dose of 140 mg/kg), *Detarium microcarpum* (from  $20 \pm 6$  to  $52 \pm 12$  min at a dose of 111.45 mg/kg), *Euphorbia hirta* (from  $56 \pm 16$  to  $145 \pm 10$  min at a dose of 140 mg/kg) and *Mentha cordifolia* (from  $10 \pm 2$  to  $24 \pm 3$  min at a dose of 140 mg/kg). *Bryophyllum pinnatum* induced a slight increase of the sleeping time. Only *Citrus sinensis* 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 gossypifolia*, *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				
<i>Daniellia</i>		CON	49.5	99	148.5	198
<i>oliveri</i>	DIAZ	9 ± 3	6 ± 1	6 ± 1	5 ± 2	3 ± 1**
<i>Detarium</i>		CON	37.15	47.3	111.45	148.6
<i>microcarpum</i>	DIAZ	9 ± 3	7 ± 2	6 ± 3	4 ± 2*	6 ± 3
<i>Flacourtia</i>		CON	10	25	50	100
<i>indica</i>	DIAZ	4 ± 2	8 ± 6	4 ± 4	11 ± 6	4 ± 4
<i>Hymenocardia</i>		CON	8.7	21.9	43.8	87.6
<i>acida</i>	DIAZ	9 ± 3	7 ± 3	6 ± 1*	5 ± 1**	3 ± 1***
<i>Mentha</i>		CON	14	35	70	140
<i>cordifolia</i>	DIAZ	3 ± 1	2 ± 1	2 ± 1	6 ± 3	4 ± 1
<i>Securidaca</i>		CON	10	20	50	66.7
<i>longepedunculata</i>	DIAZ	6 ± 1	5 ± 1	5 ± 1	4 ± 1*	4 ± 1*
<i>Senna</i>		CON	20	40	80	160
<i>singueana</i>	DIAZ	15 ± 3	6 ± 1***	6 ± 1***	7 ± 1***	8 ± 1***
<i>Terminalia</i>		CON	9.5	19	38	76
<i>glaucescens</i>	DIAZ	4 ± 2	7 ± 4	5 ± 1	6 ± 3	2 ± 2
<i>Terminalia</i>		CON	14	35	70	140
<i>mollis</i>	DIAZ	7 ± 2	5 ± 1	2 ± 1**	3 ± 1**	4 ± 1*
<i>Trichilia</i>		CON	12.6	33	66	126
<i>emetica</i>	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 sinensis*, *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				
<i>Annona muricata</i>	CON		<b>12</b>	<b>30</b>	<b>60</b>	<b>120</b>
	DIAZ	31 ± 11	51 ± 26*	67 ± 6***	68 ± 2***	71 ± 15***
<i>Annona senegalensis</i>	CON		<b>6.7</b>	<b>17</b>	<b>34</b>	<b>67</b>
	DIAZ	19 ± 4	52 ± 18***	72 ± 17***	79 ± 25***	89 ± 29***
<i>Bidens pilosa</i>	CON		<b>14</b>	<b>35</b>	<b>70</b>	<b>140</b>
	DIAZ	31 ± 2	70 ± 2***	66 ± 3***	79 ± 5***	80 ± 2***
<i>Bryophyllum pinnatum</i>	CON		<b>28</b>	<b>70</b>	<b>140</b>	<b>280</b>
	DIAZ	21 ± 2	32 ± 5**	26 ± 5	35 ± 1**	31 ± 6*
<i>Citrus sinensis</i>	CON		<b>10</b>	<b>25</b>	<b>50</b>	<b>100</b>
	DIAZ	56 ± 24	50 ± 20	40 ± 10	45 ± 12	57 ± 10
<i>Clerodendron thomsoniae</i>	CON		<b>13.4</b>	<b>33.5</b>	<b>67</b>	<b>134</b>
	DIAZ	19 ± 3	39 ± 9***	74 ± 22***	90 ± 16***	94 ± 30***
<i>Daniellia oliveri</i>	CON		<b>49.5</b>	<b>99</b>	<b>148.5</b>	<b>198</b>
	DIAZ	20 ± 8	50 ± 3***	74 ± 8***	74 ± 7***	81 ± 13***
<i>Datura stramonium</i>	CON		<b>3.5</b>	<b>7</b>	<b>35</b>	<b>70</b>
	THIO	16 ± 7	55 ± 15***	63 ± 21***	85 ± 23***	94 ± 25***
<i>Detarium microcarpum</i>	CON		<b>37.15</b>	<b>47.3</b>	<b>111.45</b>	<b>148.6</b>
	DIAZ	20 ± 6	38 ± 10**	46 ± 13**	52 ± 12***	45 ± 9***
<i>Euphorbia hirta</i>	CON		<b>14</b>	<b>35</b>	<b>70</b>	<b>140</b>
	DIAZ	56 ± 16	99 ± 24**	97 ± 21**	117 ± 26***	145 ± 10***
<i>Flacourtia indica</i>	CON		<b>10</b>	<b>25</b>	<b>50</b>	<b>100</b>
	DIAZ	16 ± 12	15 ± 11	38 ± 25*	44 ± 4***	49 ± 3***
<i>Hymenocardia acida</i>	CON		<b>8.7</b>	<b>21.9</b>	<b>43.8</b>	<b>87.6</b>
	DIAZ	20 ± 11	51 ± 12***	70 ± 15***	77 ± 23***	85 ± 21***
<i>Jatropha gossypifolia</i>	CON		<b>14</b>	<b>35</b>	<b>70</b>	<b>140</b>
	DIAZ	11 ± 5	29 ± 14*	27 ± 13*	32 ± 10***	43 ± 15***
<i>Kaya senegalensis</i>	CON		<b>6.7</b>	<b>17</b>	<b>34</b>	<b>67</b>
	DIAZ	63 ± 15	52 ± 21	58 ± 25	58 ± 23	61 ± 23
<i>Mentha cordifolia</i>	CON		<b>14</b>	<b>35</b>	<b>70</b>	<b>140</b>
	DIAZ	10 ± 2	16 ± 5*	21 ± 5**	21 ± 4**	24 ± 3**
<i>Prosopis africana</i>	CON		<b>11.2</b>	<b>28</b>	<b>56</b>	<b>112</b>
	DIAZ	19 ± 3	52 ± 26*	57 ± 17**	31 ± 17	61 ± 26***
<i>Securidaca longepedunculata</i>	CON		<b>10</b>	<b>20</b>	<b>50</b>	<b>66.7</b>
	DIAZ	18 ± 3	60 ± 27**	65 ± 14***	67 ± 27**	78 ± 14***
<i>Senna singueana</i>	CON		<b>20</b>	<b>40</b>	<b>80</b>	<b>160</b>
	DIAZ	24 ± 2	86 ± 5**	77 ± 3***	44 ± 7**	29 ± 9***
<i>Terminalia glaucescens</i>	CON		<b>9.5</b>	<b>19</b>	<b>38</b>	<b>76</b>
	DIAZ	37 ± 13	31 ± 15	79 ± 40*	86 ± 17***	120 ± 21***
<i>Terminalia mollis</i>	CON		<b>14</b>	<b>35</b>	<b>70</b>	<b>140</b>
	DIAZ	17 ± 1	44 ± 7***	64 ± 11***	84 ± 15***	73 ± 8***
<i>Tetrapleura tétaptera</i>	CON		<b>8.4</b>	<b>21</b>	<b>42</b>	<b>84</b>
	DIAZ	19 ± 3	39 ± 10**	67 ± 18***	82 ± 14***	91 ± 15***
<i>Trichilia emetica</i>	CON		<b>12.6</b>	<b>33</b>	<b>66</b>	<b>126</b>
	DIAZ	17 ± 1	22 ± 2*	29 ± 4**	71 ± 7***	84 ± 10***
<i>Vitellaria paradoxa</i>	CON		<b>12</b>	<b>21</b>	<b>42</b>	<b>84</b>
	DIAZ	25 ± 4	40 ± 13***	57 ± 6***	59 ± 8***	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						
<i>Annona</i>		<b>CON</b>	<b>12</b>	<b>30</b>	<b>60</b>	<b>120</b>	<b>CP</b>	
<i>Muricata</i>	PTZ	0	16	50*	33	50*	100***	
	STR	0	12	0	12	50*	100***	
	NMDA	0	16	16	33	50*	100***	
<i>Annona</i>		<b>CON</b>	<b>6.7</b>	<b>17</b>	<b>34</b>	<b>67</b>	<b>CP</b>	
<i>Senegalensis</i>	PTZ	0	12	37	50*	25	100***	
<i>Bidens</i>		<b>CON</b>	<b>14</b>	<b>35</b>	<b>70</b>	<b>140</b>	<b>CP</b>	
<i>pilosa</i>	PTZ	0	16	50*	33	50*	100***	
	STR	0	16	50*	40	50*	100***	
	NMDA	0	33	33	66**	50*	100***	
<i>Bryophyllum</i>		<b>CON</b>	<b>28</b>	<b>70</b>	<b>140</b>	<b>280</b>	<b>CP</b>	
<i>pinnatum</i>	PTZ	0	16	33	16	33	100***	
	STR	0	0	10	0	16	100***	
	NMDA	0	33	50*	50*	50*	100***	
<i>Citrus</i>		<b>CON</b>	<b>10</b>	<b>25</b>	<b>50</b>	<b>100</b>	<b>CP</b>	
<i>sinensis</i>	PTZ	0	25	25	12	0	100***	
	STR	0	0	0	12	12	100***	
	NMDA	0	50*	50*	75**	75**	100***	
<i>Clerodendron</i>		<b>CON</b>	<b>13.4</b>	<b>33.5</b>	<b>67</b>	<b>134</b>	<b>CP</b>	
<i>Thomsoniae</i>	PTZ	0	12	37	37	62*	100***	
	PIC	0	0	25	50*	50*	100***	
<i>Daniellia</i>		<b>CON</b>	<b>49.5</b>	<b>99</b>	<b>148.5</b>	<b>198</b>	<b>CP</b>	
<i>oliveri</i>	PTZ	0	25	37	37	50*	100***	
	STR	0	16	66**	50*	50*	100***	
<i>Detarium</i>		<b>CON</b>	<b>37</b>	<b>47</b>	<b>111</b>	<b>148</b>	<b>CP</b>	
<i>microcarpum</i>	PTZ	0	50*	37	0	0	100***	
	STR	0	50*	33	33	16	100***	
<i>Euphorbia</i>		<b>CON</b>	<b>14</b>	<b>35</b>	<b>70</b>	<b>140</b>	<b>CP</b>	
<i>hirta</i>	PTZ	0	0	25	0	50*	100***	
	STR	0	12	37	25	37	100***	
	NMDA	0	33	33	50*	50*	100***	
<i>Flacourtia</i>		<b>CON</b>	<b>10</b>	<b>25</b>	<b>50</b>	<b>100</b>	<b>CP</b>	
<i>indica</i>	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***	
<i>Hymenocardia</i>		<b>CON</b>	<b>8.76</b>	<b>21.9</b>	<b>43.8</b>	<b>87.6</b>	<b>CP</b>	
<i>acida</i>	PTZ	0	0	25	37	62*	100***	
	STR	0	16	33	33	50*	100***	
<i>Jatropha</i>		<b>CON</b>	<b>14</b>	<b>35</b>	<b>70</b>	<b>140</b>	<b>CP</b>	
<i>gossypifolia</i>	PTZ	0	0	25	37	0	100***	
	STR	0	50*	50*	62*	25	100***	
	PIC	0	0	0	0	0	100***	
<i>Khaya</i>		<b>CON</b>	<b>6.7</b>	<b>17</b>	<b>34</b>	<b>67</b>	<b>CP</b>	
<i>senegalensis</i>	PTZ	0	12	12	0	25	100***	
	STR	0	25	50*	25	50*	100***	
	NMDA	0	62*	33	33	50*	100***	
<i>Mentha</i>		<b>CON</b>	<b>14</b>	<b>35</b>	<b>70</b>	<b>140</b>	<b>CP</b>	
<i>cordifolia</i>	PTZ	0	16	33	66**	50*	100***	
	STR	0	33	33	33	66**	100***	
	PIC	0	16	50*	33	50*	100***	
<i>Prosopis</i>		<b>CON</b>	<b>11.2</b>	<b>28</b>	<b>56</b>	<b>112</b>	<b>CP</b>	
<i>africana</i>	PTZ	0	0	0	25	37	100***	
	STR	0	62*	25	50*	50*	100***	
<i>Ricinus</i>		<b>CON</b>	<b>12</b>	<b>30</b>	<b>60</b>	<b>120</b>	<b>CP</b>	
<i>communis</i>	PTZ	0	37	50*	62*	87***	100***	

	INH	31 ± 9	33 ± 6	36 ± 8	40 ± 7	56 ± 16*	77 ± 11**
<i>Securidaca longepedunculata</i>	CON	10	20	50	66.7	CP	
	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***
<i>Senna singueana</i>	CON	20	40	80	160	CP	
	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**
<i>Terminalia glaucescens</i>	CON	9.5	19	38	76	CP	
	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***
<i>Terminalia mollis</i>	CON	14	35	70	140	CP	
	PTZ	0	50*	37	25	37	100***
	STR	0	66**	33	33	50*	100***
<i>Tetrapleura tetraptera</i>	CON	8.4	21	42	84	CP	
	PTZ	0	25	50*	50*	50*	100***
<i>Trichilia emetica</i>	CON	12.6	33	66	126	CP	
	PTZ	0	25	50*	50*	50*	100***
	STR	0	12	25	50*	50*	100***
<i>Vitellaria paradoxa</i>	CON	12	21	42	84	CP	
	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 nmol/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<sub>A</sub> receptor complex (Rang et al., 1999; Bonin & Orser, 2008; Olkkola & Ahonen, 2008). Diazepam (benzodiazepine) and sodium thiopental (barbiturate) all bind to the GABA<sub>A</sub> receptor complex. Diazepam potentiates GABA-mediated inhibition via the increase in the affinity of this inhibitory neurotransmitter to its recognition sites within the GABA<sub>A</sub> 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<sub>A</sub> 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 sinensis* 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<sub>A</sub>-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<sub>A</sub> 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 antagonized 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.

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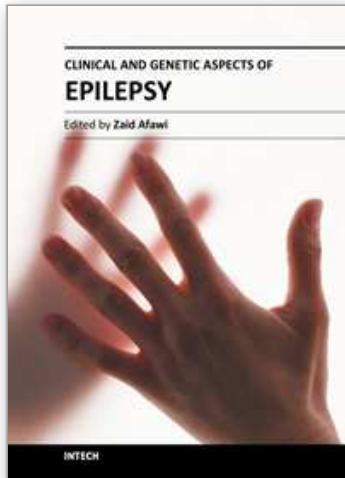
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