Research Article

Medicinal Plants Used in the Treatment of Mental and Neurological Disorders in Ghana

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Ethnopharmacological Relevance. Mental and neurological disorders are a serious public health challenge globally, particularly in developing countries where cultural factors and limited access to standard healthcare have led to a reliance on traditional medicines. However, ethnopharmacological characterization of traditional medicines used to treat these diseases is lacking. In this study, an ethnobotanical description of plant species used in treating mental and neurological disorders in Ghana and an update of their experimentally validated pharmacological relevance are provided. Materials and Methods. Two hundred herbalists agreed to participate but sixty-six specialized in treating mental and neurological disorders were interviewed on their traditional medical practice. Literature review was conducted to verify the experimentally validated pharmacological importance of the reported plants. Results. Thirty-two plant species belonging to twenty-eight families were identified. Most plant species had either analgesic (50%), anxiolytic (18.8%), or anticonvulsant (15.6%) properties. Others had reported sedative, anti-Alzheimer's disease, motor coordination, antipsychotic, antidepressant, cognitive enhancement, and neuroprotective properties. While Ageratum conyzoides L. (Asteraceae) and Ocimum gratissimum L. (Lamiaceae) were the most commonly mentioned species with analgesic properties, Lantana camara L. (Verbenaceae) was the most-reported anxiolytic product, with Cymbopogon citratus DC. (Gramineae), Mangifera indica L., Tetrapleura tetraptera Schum Taub. (Fabaceae), and Persea Americana Mill (Lauraceae) being the most studied anticonvulsants. Conclusions. This study provides the first report specifically on medicinal plants used in treating mental and neurological disorders in Ghana. Most of the identified plants have been scientifically confirmed to possess neuro- and psychopharmacological properties and may serve as templates for drug development.

1. Introduction

The World Health Organization (WHO) estimates that more than one billion people suffer from central and peripheral

nervous system (CNS/PNS) disorders globally [1, 2]. These diseases include Parkinson's disease, epilepsy, schizophrenia, bipolar disorder, Alzheimer's disease and other dementias, neuroinfections, brain tumors, traumatic disorders, and

cerebrovascular diseases such as stroke and migraine. More than 6 million people reportedly die each year due to stroke, with over 80% of these deaths occurring in low- and middleincome countries [2]. Moreover, although little research attention has been paid to diseases such as schizophrenia, bipolar disorder, and other psychotic disorders in Africa, some studies have shown that schizophrenia is a major psychiatric diagnosis leading to in-patient admissions on these continents [3–6]. In addition, the CNS/PNS disease burden in Africa is exacerbated by the numerous but understudied neurological impairments associated with common tropical diseases such as the neglected tropical diseases [7].

Ghana is host to a wide array of medicinal flora and takes pride in the longstanding cultural use of traditional and alternative medicines (TAMs), as exhibited by the several published works on the ethnobotanical use of TAMs in the country [8-11]. Nonetheless, there are concerns about the safety and efficacy claims of some TAMs [12]. In order to address these concerns while enhancing the therapeutic potentials of TAMs and ensuring minimum adverse effects, the Ghanaian Government, academics, and TAM practitioners have institutionalized measures to regulate herbal medicine practice and also integrate TAMs into the mainstream healthcare system. For example, the Ghana Federation of Traditional Medical Practitioners Association (GHAFTRAM) was established in 1999 to help modernize, restructure, and regulate the traditional medical industry in the country [13]. GHAFTRAM has members from all parts of Ghana, working together towards advancing the development of TAMs. In addition, an undergraduate program in herbal medicine which complements university training with hands-on internships at a herbal medicine research centre as well as herbal and allopathic practitioners has been established [14]. On passing their professional qualifying examination, graduates are certified and regulated by Ghana's Traditional Medical Practice Council, and some are employed by the Government to practice as medical herbalists in herbal clinics established within public hospitals to work in partnership with medical and allied health staff to provide curative and preventive medical care [12, 14].

The foregoing measures emphasize that TAMs continue to play a significant role in the treatment of various disorders including those of CNS/PNS origin [15-17]. However, there have been no studies focusing primarily on the documentation of traditional methods of treating mental and neurological disorders in Ghana, and how these may inform healthcare practice, policy, and drug development. Consequently, comprehensive information on plant species, plant parts used, cultural practices, and methods of preparation and use of these TAMs are lacking. Moreover, the therapeutic potential, CNS properties, and the safety profile of most of these products are largely unknown. The present study sought to address this knowledge gap by using a guided survey to document TAMs used in the treatment of mental and neurological disorders in Ghana based on traditional knowledge. Moreover, we aimed to ascertain the scientifically confirmed pharmacological relevance of these medicinal products that may justify their clinical use and further research to isolate compounds of interest to drug discovery and development.

Specifically, the study was aimed at (a) identifying commonly used TAMs for CNS/PNS disorders and their modes of preparation and (b) documenting the therapeutic potentials of these products.

2. Materials and Methods

2.1. Selection of Participants, Obtaining prior Informed Consent, Ethical Approval, and Data Collection. An ethnobotanical approach was used to explore the knowledge and treatment practices of mental and nervous system disorders by traditional medical practitioners (TMPs) from various districts and subdistricts of the Greater Accra and Brong-Ahafo regions of Ghana. Study participants were TMPs who were all members of GHAFTRAM attending a meeting in Accra. The study objectives, method, and planned use of information were explained to the TMPs before the interviews. Among the 200 TMPs present at the GHAFTRAM meeting, 66 were included in this study. The excluded delegates were not specialized in the treatment of mental and neurological diseases, as they found such patients quite difficult to manage.

A guided questionnaire interview approach was used: during the interviews conducted in both English and Twi, a local Ghanaian dialect, information on the types and parts of plant materials used, the methods of preparation, the local names of plants, and the mode of administration of herbal products were obtained. To be included in the interview, one had to be a (a) TMP practicing in Ghana, potentially treating mental and neurological diseases directly or having some level of knowledge on products used in treating such patients or (b) registered member of GHAFTRAM willing to participate in the survey. Approval for this study was granted by the Scientific and Technical Committee of the Noguchi Memorial Institute for Medical Research, Accra, Ghana, reference number STC-4 (2) 2013-14. Prior to the study, permission was granted from the leadership of GHAFTRAM and all participants duly signed informed consents.

2.2. Data Management and Analysis. A list of the plants obtained from the survey was subjected to thorough review using Internet search engines (such as google scholar) and journal databases such as Medline, Embase, Scopus, and Pubmed to confirm their therapeutic potential. A search of Ghanaian and West African herbal pharmacopoeias was done using the following search terms: "neurological disorders", "psychiatric disorders", "schizophrenia", "Parkinson's disease", "Alzheimer's disease", and "mental disorders" in combination with either "Ghana", "West Africa", or "Africa".

Data obtained from the ethnobotanical study were analyzed using the Statistical Package for Social Sciences version 22.0 for Windows.

3. Results

3.1. Sociodemographic Characteristics of Respondents. In total, 66 TMPs were interviewed: 65 and 1 from the Greater Accra and Brong-Ahafo regions, respectively. About 56.1% were males and 43.9% were females. About 40.9% of the

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TABLE 1: Sociodemographic characteristics of traditional medical practitioners who treat mental and neurological disorders in Ghana.

Variable	Frequency	Percentage (%)
Sex		
Male	37	56.1
Female	29	43.9
Age (years)		
20-29	1	1.5
30-39	8	12.1
40-49	12	18.2
50-59	27	40.9
60 and above	18	27.3
Marital status		
Single	15	22.7
Married	43	65.2
Divorced	1	1.5
Widowed	7	10.6
Highest educational level		
No Education	5	7.8
Primary	34	53.1
Secondary	18	28.1
Tertiary	7	10.9

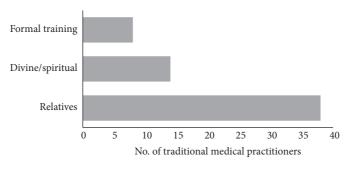


FIGURE 1: Source of traditional medical practitioners' knowledge for the treatment of mental and nervous system disorders in Ghana.

TMPs were either 50-59-year-old or 60 years and above (27.3%). In addition, while 65.2% were married, 22.7% were single, 10.6% were widowed, and 1.5% were divorced. Most TMPs had either primary school (53.1%) or secondary school (28.1%) education (Table 1); only 10.9% had some form of postsecondary education.

3.2. Source of the Knowledge of Herbal Medicine Practice and Duration of Practice. The TMPs' knowledge of traditional healing, including knowledge to treat mental and neurological disorders, was mainly acquired from relatives (Figure 1). About 36.5% had practiced for 16-20 years, while 27% had practiced for 1-5 years (Table 2).

3.3. Treatment of Mental and Neurological Diseases. Most of the TMPs (60.6%) had specific herbs for treating a variety of mental and neurological disorders. However, only 36.4% had actually treated such patients. Out of these, 19.7% had treated a maximum of 5 patients, with only 1.5% having treated more

than 20 patients. Overall, 31.8% of the treated patients had completely recovered (Table 3).

3.4. Species, Medicinal Uses, and Experimentally Validated Pharmacological Relevance of Plants. In all, 32 plant species were provided by the TMPs and these came from 28 different plant families (Table 4). The families Apocynaceae, Asteraceae, and Meliaceae were the most mentioned plant families, with Apocynaceae having the highest frequency of mentions and Asteraceae having the highest number of plant species (Figure 2). Rauwolfia vomitoria Afz. was the plant with the highest frequency of mention (mentioned 7 times; Figure 3). About 66% of the plants (21 species) used have been previously reported to have neuropharmacological activities. Half of the identified TAMs had analgesic (50%) properties, with the others having anxiolytic (18.8%), sedative (6.3%), anticonvulsant (15.6%), and antidepressant (9.4%) properties. R. vomitoria Afz., belonging to the family Apocynaceae, however, has been previously reported to have antipsychotic properties [16, 18] (Table 5).

Variable	Frequency	Percentage (%)
Source of the knowledge of herbal medical practice		
Inheritance (knowledge passed on from others)	38	63.3
Divine/spiritual	14	23.3
Formal training	8	13.3
Years of herbal medical practice		
1-5	17	27.0
6-10	10	15.9
11-15	13	20.6
16-20	23	36.5

TABLE 2: Sources of knowledge and duration of practice for traditional medicine practitioners who treat mental and neurological disorders in Ghana.

TABLE 3: Treatment of mental and neurological disorders by traditional medical practitioners in Ghana.

Variable	Frequency (n)	Percentage (%)
Knowledge of herbs for treating mental a	nd neurological disorders	
No	26	39.4
Yes	40	60.6
Total number of patients treated through	out herbal medical practice	
0	42	63.6
1-5	13	19.7
6-10	5	7.6
11-15	3	4.5
16-20	2	3.0
Above 20	1	1.5
Treatment options used		
Not applicable	42	63.6
Divine/spiritual only	1	1.5
Herbs only	16	24.3
Herbs and divine/spiritual	7	10.6
Recovery status of patients treated		
Not applicable/no recovery	42	63.6
Partial recovery	3	4.5
Total recovery	21	31.8

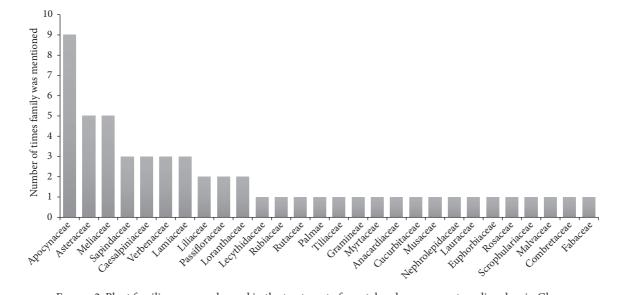


FIGURE 2: Plant families commonly used in the treatment of mental and nervous system disorders in Ghana.

Species	Family	Growth forms	Local names in different languages	Voucher specimen	Frequency of mention	Plant part used	Method of preparation
Ageratum conyzoides	Asteraceae	Herb	Ewe : mima, Nyigbe; Fante: Ahaban Kankan, Efumomoe; Twi: Gu-ekuro, Adwoa-kura, Guakuo, Gu-ekura; Nzema: Ebuakulo; Ga-Dangme: Ntumumu	PA01/UGSOP/GH17	ñ	Leaves	The fresh leaves are macerated and the liquid obtained is instilled into the nostrils; the fresh leaves can also be boiled, sieved and drank as required.
Allium sativum	Liliaceae	Herb	Twi : Gyene Kankan; Ga Adangme : Aya; Hausa : Tafarmuwa	PA02/UGSOP/GH17	2	Whole plant	, ,
Alstonia boonei	Apocynaceae	Tree	Twi: Nyame-dua, Nyamedua, Onyamedua, Osen Nuru; Ewe: Siaketreke Fante: Nyena,Sinuro,Nyamedua; Nzema: Bakunin	PA03/UGSOP/GH17	5	Bark	The leaves are boiled and drank as required
Azadiratcha indica	Meliaceae	Tree	Fante: Nim, Aboode, Abodua; Ewe: Liliti; Ga-Dangme: Kintso, Asante: Gyedua; Twi: Nimsi, Dua gyane	PA04/UGSOP/GH17	1	Leaves; Roots	The boiled leaves/roots are drank as required
Bertholletia excels	Lecythidaceae		Brazil nut	PA05/UGSOP/GH17	1	Nut; Leaves	The leaves/nuts are boiled and sieved extract is drank as required
Bidens pilosa.	Asteraceae	Herb	Twi: Dwirentwi,Gyinantwi; Ewe: Dzanikpikpi;	PA06/UGSOP/GH17	l	Leaves	The fresh leaves are macerated and the liquid obtained is instilled into the nose
Blighia unijucata	Sapindaceae	Tree	Asante : Akye, Akan, Akyibiri, Twi: Akyebiri, Fante : Etedua	PA07/UGSOP/GH17	3	Bark; Roots	The dried barks/roots are boiled and drank as required, the extract can also be smeared on the body
Cassia occidentalis.	Caesalpiniaceae		Nkwadowa bɔdeɛ	PA08/UGSOP/GH17	3	Leaves	The leaves are boiled and drank as required

TARE 4: Local names, plant parts, and methods of preparation of traditional African medicines used in treating nervous system and mental disorders in Ghana.

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Species	Family	Growth forms	Local names in different languages	Voucher specimen	Frequency of mention	Plant part used	Method of preparation
Cinchona pubescens	Rubiaceae	Shrub		PA09/UGSOP/GH17	1		
citrus aurantifolia	Rutaceae		Twi: Ankaadwea, Akenkaa Ankaatwaree; Fante: Ankama, Ewe: Mumoe; Asante: Ankaatwaree; Dagbani: Nyamsa, Lim buri; Ga-Adangme: Abonua; Hausa: Olomankilisi; Nzema: Domunli; Mole: Leenu; Ga: Kpete	PA10/UGSOP/GH17	-1	Peel; Juice	The peels are squeezed directly on the forehead and into the nose
Cocos nucifera	Palmae	Tree	Twi: kube; Ewe: Agone	PA11/UGSOP/GH17	1	Juice	Drinking the fresh coconut juice at will
Corchorus olitorius	Tiliaceae	Herbaceous	Ewe: Ademe, Singui; Fante: Oturo; Twi: Otoro	PA12/UGSOP/GH17	1	Jute mallow, Leaves	Hot infusion is made from the leaves and drank as required
Cymbopogon citratus	Graminae	Herb	Ewe: Tigbe; Fante: Ti ahaban, Ga-Dangme:Ti-ba	PA13/UGSOP/GH17	1	Leaves; Oil	A decoction is made from the either the fresh/dried leaves and the oily content applied as a massage
Eucalyptus globulus	Myrtaceae		Eucalyptus	PA14/UGSOP/GH17	1	Oil	Cold infusion is made and the oily content obtained is rubbed on the body
Khaya senegalensis	Meliaceae	Tree	Hausa: Madwachi, Madachi, Ewe: Logo; Fante: Okum; GaAdangme: Kuga; Twi: Kuntunkuri; Mole: Kuka; Brong: Korobaa; Nzema: Anane	PA15/UGSOP/GH17	4	Bark	The leaves are boiled and drank as required
Lantana camara	Verbenaceae	Shrub	Akan ,Ananse dokono	PA16/UGSOP/GH17	ω	Leaves; Stem	The leaves/stem are boiled and the liquid obtained, drank as required
Mangifera indica	Anacardiaceae	Tree	Ewe/Asante/Twi/ Fante Mango, Amango,Ga: Mango	PA17/UGSOP/GH17	1	Bark	A decoction is made from the dried bark and drank as required
Momordica charantia	Cucurbitaceae	Herbaceous	Twi: Nyannya, Nyina, Nyinya; Ewe: Kakle; Dangme: Nyanyla, Nyanyra; Ga: Nyanyra; Nzema: Nyanya	PA18/UGSOP/GH17	1		

TABLE 4: Continued.

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			TABLE 4: Continued	ntinued.			
Species	Family	Growth forms	Local names in different languages	Voucher specimen	Frequency of mention	Plant part used	Method of preparation
Musa paradisiaca	Musaceae	Herbaceous	Twi : Brode; N zema : Banna Ga : Amadaa	PA19/UGSOP/GH17	1	Leaves	The leaves are boiled and drank as required The leaves are macerated and the
Nephrolepis cordifolia	Nephrolepidaceae		Twi: $Mm \varepsilon n$	PA20/UGSOP/GH17	1	Leaves	liquid instilled nasally or inhaled. The leaves can be boiled and the extracted liquid used as a bathing liquid.
Occimum gratissimum	Lamiaceae	Shrub	 Ewe: Babusui, Dzeveti; Ga: Sulu; Twi: Onunum, Nunum; Asante: Nunum; Ga-Dangme: Sulu; Hausa: Dardoyatagidi; Nzema: Amaloko; Wassa: Aprim; Fante: Onunum 	PA21/UGSOP/GH17	ω	Leaves	The leaves are boiled and drank as required
Passiflora edulis	Passifloraceae		Passion fruit tree	PA22/UGSOP/GH17	2	Leaves; Flowers; Fruit; Leaves	Boiling; grinding
Persea americana	Lauraceae	Tree	Dangme: Paya; Twi: Pee; Akan: Paya, Pae; Fante: Pae;	PA23/UGSOP/GH17	1	Fresh and dried leaves	A decoction is made from the either the fresh/dried leaves and
Phyllantus nuriri	Euphobiaceae	Herbaceous	Twi: Awommaguwakyi, Ewe: Lane; Krobo: Ofobiokpai, Ofobi; Ga: Omateoatsi:	PA24/UGSOP/GH17	1		drank as required
Rauwolfia vomitoria.	Apocynaceae	Shrub	Twi: Kakapenpen; Ewe: Dodemakpowoe; Fante: Kakapenpen; Ga-Dangme: Apototso; Hausa: Wada, Nzema: Bakapembene; Wassa: Aneene	PA25/UGSOP/GH17	М	Roots	The roots are boiled and the extract obtained are instilled into the nose
Rubus fruticosus	Rosaceae		Bramble	PA26/UGSOP/GH17	1	Berries, leaves and flowers	Blend dry leaves and mix with honey
Scoparia dulcis	Scrophulariaceae			PA27/UGSOP/GH17	1	ı	ı
Sida acuta	Malvaceae	Branchlets	Ewe: Afideme; Ga: Shwoboto; Twi: Obraneatuto	PA28/UGSOP/GH17	1	Leaves	The leaves are boiled and drank as required
Tapinanthus globiferrus	Loranthaceae	Parasitic Tree	Twi: nkranpan Mole: Welebe	PA29/UGSOP/GH17	2	Leaves; stem	The leaves/stem are boiled and the liquid obtained, drank as required
Terminalia catapa	Combretaceae		abrɔfo nkate $arepsilon$	PA30/UGSOP/GH17	1	Yellowed leaves	The leaves are boiled and the liquid drank as required
Tetrapleura tetraptera	Fabaceae	Tree	Twi: Prekese, Zate: Zamturi; Anyi: Aprekese, Kyeke, Fante: Esem, Ewe: Prekese	PA31/UGSOP/GH17	1	Seed	The seeds are ground and the liquid extract drank as required
Vernonia amygdalina	Asteraceae	Shrub	Ga:Tatso, Akpa, Dagbani: Biebingira, Ewe: Gbo, Gboti, Asante: Mbonasere, Mponasere; Nzema: Ayeanwole, Ga-Dangme: Tatsho	PA32/UGSOP/GH17	1	Leaves	A decoction is made from the either the fresh/dried leaves and drank as required

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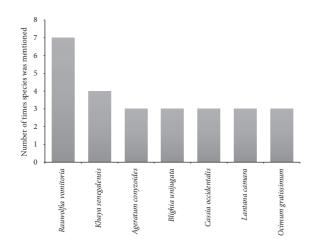


FIGURE 3: Most frequently used plant species in the treatment of mental and nervous system disorders in Ghana (only species with three or more mentions are shown).

3.5. Preparation and Administration of Herbal Products. The TAMs were prepared mostly as mixtures of two or more species. In some cases, however, the products were administered as monopreparations (prepared using a single plant species). The mode of preparation employed included decoction, infusion, and maceration, with decoction being the commonest (Table 4). While roots, fruits, flowers, stems, stem barks, whole plant of shrubs, etc. were all used in the preparation of these products (all together 42.4%), leaves (57.6%) were the commonest plant species are listed in Table 5.

Given that most TMPs do not preserve these TAMs, they generally prepared the products only when required. The products were administered orally, nasally, or applied on the forehead for periods ranging from one week to several years or until the patient recovers. The TMPs mostly used patient feedback and disappearance of symptoms to assess treatment outcomes. Where there is only a partial recovery or treatment failure, the patients are often referred to the nearest hospital.

4. Discussion

Mental and neurological disorders remain a major public health concern [2]. The disease burden is even more prominent in the developing world, including Ghana [3, 5, 6]. Recent discoveries and clinical usage of the anticancer agent taxol and the antimalarial artemisinin derived from plants have boosted interest in natural products as templates for the development of novel drug scaffolds [19, 20]. TAMs are widely accepted in African communities and there appears to be an increasing reliance on these products [13]. In Ghana, TAMs are used as the main treatment paradigm for a variety of diseases, but they are also used as complements to other medicines or as dietary supplements [21]. However, thorough examination and documentation of the medicinal properties of these products against mental and neurological disorders is lacking.

In the present study, several plant species (32 species) used by local TMPs to treat mental and neurological disorders

were reported, with most species belonging to the families Asteraceae, Apocynaceae, and Meliaceae. These are large and widespread plant families with several species. In particular, the Asteraceae family is of great importance due to its high numbers of medicinal species used in the treatment of a wide array of diseases including tuberculosis, malaria, and inflammatory disorders [11, 15, 22]. Members of the Asteraceae family are also known for their wide range of economically important products including cooking oils and phytochemicals such as sesquiterpene lactones, alkaloids, and tannins [23]. The family Apocynaceae also has a wide range of species that are of pharmacological importance, with some members synthesizing alkaloids useful against high blood pressure and inflammation and others synthesizing cardiac glycosides that affect heart function [24]. The family Meliaceae, on the other hand, is known for its species that are processed into important products including vegetable oil, as well as phytochemicals with anti-inflammatory, antioxidant, hepatoprotective, and cognitive-enhancing properties [25, 26].

While the plants used in treating CNS/PNS disorders in Ghana varied greatly, R. vomitoria Afz. was frequently mentioned (17.5%) by the TMPs who had knowledge of natural products for treating these disorders. Herbal preparations of this plant are also used by TMPs in other African countries for the treatment of mental disorders [27] and have been shown to be relatively safe with LD₅₀ of 17.5 g/kg [28]. Remarkably, R. vomitoria Afz. has been found to have activity on the nervous system, especially on locomotor behavior, anxiety, and psychosis [16, 18, 29]. Reserpine, which is one of the numerous alkaloids of this species, has been used in the management of schizophrenia, hypertension, and psychiatric disorders [30]. Beyond its CNS effect, extracts from the plant are reported to have anticancer (due to the alstonine and β carboline alkaloid) [31], antipyretic, anti-inflammatory [32], and antidiabetic activities [33].

The natural products used by the TMPs in treating mental and neurological disorders fall into the following broad categories: analgesics, anxiolytics, antidepressants,

Botanical name	Family	CNS uses
Ageratum conyzoides Linn.,	Asteraceae	Analgesia [15, 42, 43]
Allium sativum Linn.	Liliaceae	Motor coordination[44]; Analgesia [45]
Alstonia boonei De Wild	Apocynaceae	Analgesia [24]
Azadirachta indica A. Juss	Meliaceae	Analgesia [25, 46]; Anxiolytic [47]; Alzheimer's disease [26]
Bertholletia excelsa H&B	Lecythidaceae	None
Bidens pilosa Linn.	Asteraceae	Analgesia [48]
<i>Blighia unijugata</i> Bak	Sapindaceae	None
Cassia occidentalis Linn.	Caesalpiniaceae	None
Cinchona pubescens Vahl.	Rubiaceae	None
Citrus aurantifolia Swingle	Rutaceae	None
Cocos nucifera Linn.	Palmae	Analgesia [49–51]
Corchorus olitorius Linn.	Tiliaceae	Anticonvulsant [52]
Cymbopogon citratus DC.	Graminae	Anxiolytic [53–56]; Sedative [53]; Anticonvulsant [53, 54, 57]; Analgesia [58]
Eucalyptus globulus Labill.	Myrtaceae	None
Khaya senegalensis (Desr.) A. Juss.	Meliaceae	None
Lantana camara Linn.	Verbenaceae	Anxiolytic [59, 60]
		Analgesia [61, 62];
Mangifera indica Linn. F.T.A	Anacardiaceae	Cognitive performance [63]
		[64]; Neuroprotection, anticonvulsant [65]
Momordica charantia Linn.	Cucurbitaceae	Analgesia [66–68]; Antidepressant Anxiolytic [69]
Musa paradisiaca Walker et Sillans	Musaceae	None
Nephrolepis cordifolia Linn Presl	Nephrolepidaceae	None
Ocimum gratissimum Linn.	Lamiaceae	Analgesia, antidepressant [70–74]; and anxiolytic [75]
Passiflora edulis Sims	Passifloraceae	Anxiolytic [76-81] and sedative [78, 81, 82]
Persea Americana Mill F.W.T.A	Lauraceae	Analgesia and anticonvulsant [83, 84]
Phyllanthus niruri Schum.et Thnn.	Euphobiaceae	Analgesia [85, 86]
Rauwolfia vomitoria Afz.	Apocynaceae	Antipsychotic [16, 18, 29]
Rubus fruticosus Linn.	Rosaceae	None
Scoparia dulcis Linn.	Scrophulariaceae	Analgesia [87, 88]
<i>Sida acuta</i> Burn F.	Malvaceae	Analgesia and antidepressant [89, 90]
Tapinanthus globiferus A. Rich.	Loranthaceae	None
Terminalia catappa Linn.	Combretaceae	None
Tetrapleura tetraptera Schum Taub.	Fabaceae	Anticonvulsant [91, 92], Analgesia [92]
Vernonia amygdalina Del. Cent. Pl. Afr.	Asteraceae	Analgesia [22]

TABLE 5: Plant species used for the treatment of mental and nervous system disorders in Ghana and scientific validation of their ethnopharmacological activities.

antipsychotics, and anticonvulsants. Of these, those with analgesic (pain relieving), anxiolytic (anti-anxiety), and anticonvulsant (anti-epileptic) effects were the most commonly used, and this possibly reflects the common disorders treated by the TMPs. In particular, half of the identified TAMs were analgesics, possibly suggesting that the TMPs were most often presented with patients suffering from headache, migraine, or other associated conditions. Headache or cephalalgia is used to describe pain in the head and could be a symptom of a number of different conditions associated with the head and neck [1]. Although limited studies have been conducted to assess the epidemiology of headache and migraine in Ghana and Africa, headache is quite common among Africans and is often exacerbated by the hot climate in most African countries [34–36]. In assessing the profile of neurological disorders in an adult neurology clinic in Ghana, clinicians recorded a number of headache and migraine cases, although the frequency was found to be relatively low [37]. This low frequency was suggested to be due to the fact that primary headaches among Ghanaians are commonly reported to and managed by community pharmacists and primary healthcare physicians [37], although there are increasing reports indicating that several individuals with headache or migraine opt for traditional and herbal therapies [34, 35]. The analgesic species frequently used by the TMPs were *A. conyzoides L.* and *O. gratissimum L.* Also important are the anxiolytic (antianxiety) and anticonvulsant (antiepileptic) products that were often used by the TMPs, suggesting a potentially high prevalence of anxiety disorders and epilepsy and seizure disorders. Epilepsy, seizures, and anxiety disorders feature prominently among the mental and neurological conditions prevalent in Ghana [5, 37]. On the other hand, *L. camara L.* was the most frequently mentioned anxiolytic product, while *C. citratus* DC., *M. indica L., T. tetraptera* Schum Taub, and *Persea Americana* Mill were among the most frequently studied anticonvulsants used by the TMPs.

Given that drugs for managing mental disorders are often in shortage in Ghanaian psychiatric hospitals [6, 38], it may be important that TAMs whose therapeutic relevance has been confirmed experimentally are considered for clinical usage. The long history of TAMs usage in African societies with seemingly minimal adverse effects [21, 39] support this perspective. While clinical integration of TAMs may be beneficial, at present, this should be approached with caution due to the inadequacy of studies exploring their efficacy and safety. Therefore, increasing TAMs-based research in Ghana would be a crucial step towards rigorous establishment of their safety, therapeutic, and adverse reaction profiles.

The natural products identified in this study are a valuable collection of resources that may provide leads for drug discovery and development. However, a potential criticism of the traditional approach being employed by the TMPs in relation to the pharmaceutical industry approach to drug discovery is that whole plant extracts may contain several bioactive components, making it difficult to attribute therapeutic benefits and mechanism(s) of action to particular compounds (Rasoanaivo et al., 2011). Moreover, some plant extract components may be negative modulators of active drug ingredients, with adverse implications for drug potential. A feasible means to refine, extend, and enhance the beneficial effects of the plant products identified in this study is to isolate, screen, and characterize bioactive compounds responsible for the positive disease-modifying effects reported. On the other hand, it is possible that components of the different plant extracts used in combination may produce positive interactions leading to complementarity in observed therapeutic effects that are more effective than single components administered at equal doses. In such a case, plant extracts whose benefits are observed when used as combinations by the traditional healers should be explored further to identify their possible synergistic activities. For example, the antimalarial drugs Quinimax® (a combination of quinone, cinchonine, and quinidine) and Malarone[®] (proguanil and avoquone) are produced and marketed as synergistic complementary drugs (Bunnag et al., 1989; Fivelman et al., 2004). Further drug discovery and development research should be conducted on the reported plant products to identify lead compounds whose in vivo therapeutic capacities would be revealed in preclinical and clinical studies. This would enable the industrialscale production and marketing of successful drug candidates

following drug authority approval. The high cost of the drug discovery and development process would, however, require strengthening academia-industry collaborative research and better provision of research funding and infrastructure [5, 40, 41].

5. Conclusion

The identified natural products used in Ghanaian communities are a potential source of a novel class of drugs for the management of mental and neurological disorders. Many of the plant species used have been investigated for their CNS-specific pharmacologic effects, with the majority having analgesic, anxiolytic, or anticonvulsant properties. However, the most prominent and often used plant, *R. vomitoria* Afz., has potent antipsychotic properties. The increased reliance and the claimed therapeutic value of the identified TAMs indicate that there is an urgent need for the preservation and extensive investigation of these products to establish their clinical effectiveness. Such studies may help in the isolation and purification of the bioactive compounds, confirm the safety and tolerability of these products, and enable the clinical integration of TAMs.

Abbreviations

CNS:	Central nervous system
GHAFTRAM:	Ghana Federation of Traditional Medical
	Practitioners' Association
GPs:	General practitioners
TAMs:	Traditional African medicines
TMPs:	Traditional medicine practitioners.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there are no conflicts of interest in the publication of this manuscript.

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References

- M. I. Calvo and R. Y. Cavero, "Medicinal plants used for neurological and mental disorders in Navarra and their validation from official sources," *Journal of Ethnopharmacology*, vol. 169, pp. 263–268, 2015.
- [2] WHO, What Are Neurological Disorders, World Health Organization, 2016, http://www.who.int/features/qa/55/en/.
- [3] A. Fekadu, C. Hanlon, E. Gebre-Eyesus et al., "Burden of mental disorders and unmet needs among street homeless people in Addis Ababa, Ethiopia," *BMC Medicine*, vol. 12, no. 1, 2014.
- [4] D. Mamah, A. Owoso, A. W. Mbwayo et al., "Classes of psychotic experiences in kenyan children and adolescents," *Child Psychiatry & Human Development*, vol. 44, no. 3, pp. 452–459, 2013.
- [5] E. Quansah and T. K. Karikari, "Neuroscience-related research in ghana: A systematic evaluation of direction and capacity," *Metabolic Brain Disease*, vol. 31, no. 1, pp. 11–24, 2016.
- [6] M. Roberts, C. Mogan, and J. B. Asare, "An overview of Ghana's mental health system: results from an assessment using the World Health Organization's Assessment Instrument for Mental Health Systems (WHO-AIMS)," *International Journal of Mental Health Systems*, vol. 8, no. 1, p. 16, 2014.
- [7] E. Quansah, E. Sarpong, and T. K. Karikari, "Disregard of neurological impairments associated with neglected tropical diseases in Africa," *eNeurologicalSci*, vol. 3, pp. 11–14, 2016.
- [8] F. Duah, P. Owusu, J. Knapp, D. Slatkin, and P. Schiff, "Constituents of West African Medicinal Plants," *Planta Medica*, vol. 42, pp. 275–278, 1981.
- [9] D. Dwuma-Badu, J. S. K. Ayim, T. T. Dabra et al., "Constituents of West African medicinal plants. XIV. Constituents of Piper guineense Schum. and Thonn," *Lloydia*, vol. 39, no. 1, pp. 60– 64, 1976.
- [10] K. D. Kwofie, N. H. Tung, M. Suzuki-Ohashi et al., "Antitrypanosomal activities and mechanisms of action of novel tetracyclic iridoids from Morinda lucida Benth," *Antimicrobial Agents and Chemotherapy*, vol. 60, no. 6, pp. 3283–3290, 2016.
- [11] J. M. Nguta, R. Appiah-Opong, A. K. Nyarko et al., "In vitro antimycobacterial and cytotoxic data on medicinal plants used to treat tuberculosis," *Data in Brief*, vol. 7, pp. 1124–1130, 2016.
- [12] M. A. Boateng, A. Danso-Appiah, B. K. Turkson, and B. P. Tersbøl, "Integrating biomedical and herbal medicine in Ghana - experiences from the Kumasi South Hospital: A qualitative study," *BMC Complementary and Alternative Medicine*, vol. 16, no. 1, 2016.
- [13] WHO, WHO Global Atlas of Traditional, Complementary and Alternative Medicine, World Health Organization, 2005.
- [14] Y. Adusi-Poku, L. K.-N. Okine, F. K. Hlortsi-Akakpo et al., "Assessing herbal medical practitioners in professional qualifying examination in Ghana, a model," *African Journal of Traditional, Complementary and Alternative Medicines*, vol. 7, no. 1, pp. 85–87, 2010.
- [15] A. A. Abena, G. S. Kintsangoula-Mbaya, J. Diantama, and D. Bioka, "Analgesic effects of Ageratum conyzoides extract in the rat," *L'Encéphale*, vol. 19, no. 4, pp. 329–332, 1993.
- [16] S. A. Bisong, R. Brown, and E. E. Osim, "Comparative effects of *Rauwolfia vomitoria* and chlorpromazine on locomotor behaviour and anxiety in mice," *Journal of Ethnopharmacology*, vol. 132, no. 1, pp. 334–339, 2010.
- [17] J. R. S. Tabuti, C. B. Kukunda, and P. J. Waako, "Medicinal plants used by traditional medicine practitioners in the treatment

of tuberculosis and related ailments in Uganda," *Journal of Ethnopharmacology*, vol. 127, no. 1, pp. 130–136, 2010.

- [18] S. Bisong, R. Brown, and E. Osim, "Comparative effects of Rauwolfia vomitoria and chlorpromazine on social behaviour and pain," *North American Journal of Medical Sciences*, vol. 3, no. 1, pp. 48–54, 2011.
- [19] C. Khanna, M. Rosenberg, and D. M. Vail, "A review of paclitaxel and novel formulations including those suitable for use in dogs," *Journal of Veterinary Internal Medicine*, vol. 29, no. 4, pp. 1006–1012, 2015.
- [20] L. H. Miller and X. Su, "Artemisinin: discovery from the Chinese herbal garden," *Cell*, vol. 146, no. 6, pp. 855–858, 2011.
- [21] J. M. Nguta, R. Appiah-Opong, A. K. Nyarko, D. Yeboah-Manu, and P. G. A. Addo, "Medicinal plants used to treat TB in Ghana," *International Journal of Mycobacteriology*, vol. 4, no. 2, pp. 116– 123, 2015.
- [22] A. A. Adedapo, O. J. Aremu, and A. A. Oyagbemi, "Anti-Oxidant, anti-inflammatory and antinociceptive properties of the acetone leaf extract of Vernonia Amygdalina in some laboratory animals," *Advanced Pharmaceutical Bulletin*, vol. 4, pp. 591–598, 2014.
- [23] S. Guenne, N. Ouattara, A. Hilou, J. F. Millogo, and O. G. Nacoulma, "Antioxidant, enzyme inhibition activities and polyphenol contents of three Asteraceae species used in Burkina Faso traditionally medicine," *International Journal of Pharmacy and Pharmaceutical Sciences*, vol. 3, no. 5, pp. 524–528, 2011.
- [24] O. A. Olajide, S. O. Awe, J. M. Makinde et al., "Studies on the anti-inflammatory, antipyretic and analgesic properties of Alstonia boonei stem bark," *Journal of Ethnopharmacology*, vol. 71, no. 1-2, pp. 179–186, 2000.
- [25] K. Ilango, G. Maharajan, and S. Narasimhan, "Anti-nociceptive and anti-inflammatory activities of *Azadirachta indica* fruit skin extract and its isolated constituent azadiradione," *Natural Product Research*, vol. 27, no. 16, pp. 1463–1467, 2013.
- [26] R. Maiti, S. Kumar, S. Acharya, and M. Raghavendra, "Role of aqueous extract of Azadirachta indica leaves in an experimental model of Alzheimer's disease in rats," *International Journal of Applied and Basic Medical Research*, vol. 3, no. 1, p. 37, 2013.
- [27] M. I. Akpanabiatu, I. B. Umoh, E. U. Eyong, E. E. Edet, and F. E. Uboh, "Influence of Rauwolfia vomitoria root bark on cardiac enzymes o normal Wistar albino rats," *Biopharmaceuticals*, vol. 14, pp. 273–278, 2006.
- [28] A. O. Olatokunboh, Y. O. Kayode, and O. K. Adeola, "Anticonvulsant activity of Rauvolfia Vomitoria (Afzel)," *African Journal* of *Pharmacy and Pharmacology*, vol. 3, no. 6, pp. 319–322, 2009.
- [29] S. A. Bisong, R. E. Brown, and E. E. Osim, "Comparative extrapyramidal effects of Rauwolfia vomitoria, chlorpromazine and reserpine in mice," *Journal of Natural Medicines*, vol. 67, no. 1, pp. 107–112, 2013.
- [30] F. López-Muñoz, V. S. Bhatara, C. Álamo, and E. Cuenca, "Historical approach to reserpine discovery and its introduction in psychiatry," *Actas Españolas de Psiquiatría*, vol. 32, no. 6, pp. 387–395, 2004.
- [31] D. L. Bemis, J. L. Capodice, P. Gorroochurn, A. E. Katz, and R. Buttyan, "Anti-prostate cancer activity of a β-carboline alkaloid enriched extract from Rauwolfia vomitoria," *International Journal of Oncology*, vol. 29, no. 5, pp. 1065–1073, 2006.
- [32] G. Kweifio-Okai, D. Bird, B. Field et al., "Antiinflammatory activity of a Ghanaian antiarthritic herbal preparation: III," *Journal of Ethnopharmacology*, vol. 46, no. 1, pp. 7–15, 1995.

- [33] J. I. A. Campbell, A. Mortensen, and P. Mølgaard, "Tissue lipid lowering-effect of a traditional Nigerian anti-diabetic infusion of Rauwolfia vomitoria foilage and Citrus aurantium fruit," *Journal of Ethnopharmacology*, vol. 104, no. 3, pp. 379–386, 2006.
- [34] R. T. Haimanot, "Headache in the Tropics: Sub-Saharan Africa," in *Handbook of Headache*, P. Martelletti and T. J. Steiner, Eds., pp. 533–540, Springer, Milan, 2011.
- [35] T. Haimanot, B. Seraw, L. Forsgren, J. Ekstedt, and K. Ekbom, "Migraine, chronic tension-type headache, and cluster headache in an ethiopian rural community," *Cephalalgia*, vol. 15, no. 6, pp. 482–488, 1995.
- [36] B. O. Osuntokun, B. S. Schoenberg, V. Nottidge et al., "Migraine headache in a rural community in nigeria: Results of a pilot study," *Neuroepidemiology*, vol. 1, no. 1, pp. 31–39, 1982.
- [37] F. S. Sarfo, J. Akassi, E. Badu, A. Okorozo, B. Ovbiagele, and A. Akpalu, "Profile of neurological disorders in an adult neurology clinic in Kumasi, Ghana," *eNeurologicalSci*, vol. 3, pp. 69–74, 2016.
- [38] D. Silberberg and E. Katabira, "Neurological Disorders," in Disease and Mortality in Sub-Saharan Africa, D. T. Jamison, R. G. Feachem, M. W. Makgoba, E. R. Bos, F. K. Baingana, K. J. Hofman et al., Eds., World Bank, Washington, DC, USA, 2nd edition, 2006, http://www.ncbi.nlm.nih.gov/books/NBK2295/.
- [39] L. J. McGaw, N. Lall, J. J. M. Meyer, and J. N. Eloff, "The potential of South African plants against *Mycobacterium* infections," *Journal of Ethnopharmacology*, vol. 119, no. 3, pp. 482–500, 2008.
- [40] T. K. Karikari, A. E. Cobham, and I. S. Ndams, "Building sustainable neuroscience capacity in Africa: the role of nonprofit organisations," *Metabolic Brain Disease*, 2015.
- [41] E. Quansah and T. K. Karikari, "Motor neuron diseases in subsaharan africa: the need for more population-based studies," *BioMed Research International*, vol. 2015, Article ID 298409, 9 pages, 2015.
- [42] H. Hossain, U. K. Karmakar, S. K. Biswas et al., "Antinociceptive and antioxidant potential of the crude ethanol extract of the leaves of *Ageratum conyzoides* grown in Bangladesh," *Pharmaceutical Biology*, vol. 51, no. 7, pp. 893–898, 2013.
- [43] L. A. Yamamoto, J. C. Soldera, J. A. Emim, R. O. Godinho, C. Souccar, and A. J. Lapa, "Pharmacological screening of Ageratum conyzoides L. (mentrasto)," *Memórias do Instituto Oswaldo Cruz*, vol. 86, no. 2, pp. 145–147, 1991.
- [44] M. Aminuddin, G. Partadiredja, and D. C. R. Sari, "The effects of black garlic (Allium sativum L.) ethanol extract on the estimated total number of Purkinje cells and motor coordination of male adolescent Wistar rats treated with monosodium glutamate," *Anatomical Science International*, vol. 90, no. 2, pp. 75–81, 2014.
- [45] G. R. Kumar and K. P. Reddy, "Reduced nociceptive responses in mice with alloxan induced hyperglycemia after garlic (Allium sativum Linn.) treatment," *Indian Journal of Experimental Biology (IJEB)*, vol. 37, no. 7, pp. 662–666, 1999.
- [46] N. Khanna, M. Goswami, P. Sen, and A. Ray, "Antinociceptive action of Azadirachta indica (Neem) in mice: Possible mechanisms involved," *Indian Journal of Experimental Biology (IJEB)*, vol. 33, no. 11, pp. 848–850, 1995.
- [47] A. K. Jaiswal, S. K. Bhattacharya, and S. B. Acharya, "Anxiolytic activity of *Azadirachta indica* leaf extract in rats," *Indian Journal* of *Experimental Biology*, vol. 32, no. 7, pp. 489–491, 1994.
- [48] A. F. Fotso, F. Longo, P. D. D. Djomeni et al., "Analgesic and antiinflammatory activities of the ethyl acetate fraction of

Bidens pilosa (Asteraceae)," *Inflammopharmacology*, vol. 22, no. 2, pp. 105–114, 2014.

- [49] D. S. Alviano, K. F. Rodrigues, S. G. Leitão et al., "Antinociceptive and free radical scavenging activities of Cocos nucifera L. (Palmae) husk fiber aqueous extract," *Journal of Ethnopharmacology*, vol. 92, no. 2-3, pp. 269–273, 2004.
- [50] S. Naskar, U. K. Mazumder, G. Pramanik, P. Saha, P. K. Haldar, and M. Gupta, "Evaluation of antinociceptive and antiinflammatory activity of hydromethanol extract of cocos nucifera l.," *Inflammopharmacology*, vol. 21, no. 1, pp. 31–35, 2013.
- [51] S. Rinaldi, D. O. Silva, F. Bello et al., "Characterization of the antinociceptive and anti-inflammatory activities from Cocos nucifera L. (Palmae)," *Journal of Ethnopharmacology*, vol. 122, no. 3, pp. 541–546, 2009.
- [52] M. Gupta, U. K. Mazumder, D. Pal, S. Bhattacharya, and S. Chakrabarty, "Studies on brain biogenic amines in methanolic extract of Cuscuta reflexa Roxb. and Corchorus olitorius linn. sees treated mice," *Acta Poloniae Pharmaceutica. Drug Research*, vol. 60, no. 3, pp. 207–210, 2003.
- [53] M. M. Blanco, C. A. R. A. Costa, A. O. Freire, J. G. Santos Jr., and M. Costa, "Neurobehavioral effect of essential oil of Cymbopogon citratus in mice," *Phytomedicine*, vol. 16, no. 2-3, pp. 265–270, 2009.
- [54] E. A. Carlini, J. De D.P. Contar, A. R. Silva-Filho, N. G. Da Silveira-Filho, M. L. Frochtengarten, and O. F. A. Bueno, "Pharmacology of lemongrass (Cymbopogon citratus Stapf). I. Effects of teas prepared from the leaves on laboratory animals," *Journal of Ethnopharmacology*, vol. 17, no. 1, pp. 37–64, 1986.
- [55] C. A. R. D. A. Costa, D. O. Kohn, V. M. De Lima, A. C. Gargano, J. C. Flório, and M. Costa, "The GABAergic system contributes to the anxiolytic-like effect of essential oil from Cymbopogon citratus (lemongrass)," *Journal of Ethnopharmacology*, vol. 137, no. 1, pp. 828–836, 2011.
- [56] J. Leite, M. De Lourdes V. Seabra, E. Maluf et al., "Pharmacology of lemongrass (Cymbopogon citratus Stapf). III. Assessment of eventual toxic, hypnotic and anxiolytic effects on humans," *Journal of Ethnopharmacology*, vol. 17, no. 1, pp. 75–83, 1986.
- [57] M. R. Silva, R. M. Ximenes, J. G. M. da Costa, L. K. A. M. Leal, A. A. de Lopes, and G. S. de Barros Viana, "Comparative anticonvulsant activities of the essential oils (EOs) from *Cymbopogon winterianus* Jowitt and *Cymbopogon citratus* (DC) Stapf. in mice," *Naunyn-Schmiedeberg's Archives of Pharmacology*, vol. 381, no. 5, pp. 415–426, 2010.
- [58] G. S. B. Viana, T. G. Vale, R. S. N. Pinho, and F. J. A. Matos, "Antinociceptive effect of the essential oil from *Cymbopogon citratus* in mice," *Journal of Ethnopharmacology*, vol. 70, no. 3, pp. 323–327, 2000.
- [59] I. Kazmi, M. Afzal, B. Ali, Z. A. Damanhouri, A. Ahmaol, and F. Anwar, "Anxiolytic potential of ursolic acid derivative-a stearoyl glucoside isolated from Lantana camara L. (verbanaceae)," *Asian Pacific Journal of Tropical Medicine*, vol. 6, no. 6, pp. 433– 437, 2013.
- [60] I. Kazmi, G. Gupta, M. Afzal, M. Rahman, and F. Anwar, "Pharmacological evaluation of anxiolytic activity of ursolic acid stearoyl glucoside isolated from lantana camara," CNS Neuroscience & Therapeutics, vol. 18, no. 8, pp. 707-708, 2012.
- [61] G. Garrido, D. Gonzalez, C. Delporte et al., "Analgesic and antiinflammatory effects of Mangifera indica L. extract (Vimang)," *Phytotherapy Research*, vol. 15, no. 1, pp. 18–21, 2001.
- [62] M. A. A. Khan and M. T. Islam, "Analgesic and cytotoxic activity of Acorus calamus L., Kigelia pinnata L., Mangifera indica L.

and Tabernaemontana divaricata L.," *Journal of Pharmacy and Bioallied Sciences*, vol. 4, no. 2, pp. 149–154, 2012.

- [63] S. Kumar, K. K. Maheshwari, and V. Singh, "Effects of Mangifera indica fruit extract on cognitive deficits in mice," *Journal of Environmental Biology*, vol. 30, pp. 563–566, 2009.
- [64] Y. Lemus-Molina, M. V. Sánchez-Gómez, R. Delgado-Hernández, and C. Matute, "Mangifera indica L. extract attenuates glutamate-induced neurotoxicity on rat cortical neurons," *NeuroToxicology*, vol. 30, no. 6, pp. 1053–1058, 2009.
- [65] G. L. Viswanatha, C. G. Mohan, H. Shylaja, H. C. Yuvaraj, and V. Sunil, "Anticonvulsant activity of 1,2,3,4,6-penta-O-galloylβ-d-glucopyranose isolated from leaves of Mangifera indica," *Naunyn-Schmiedeberg's Archives of Pharmacology*, vol. 386, no. 7, pp. 599–604, 2013.
- [66] A. R. Biswas, S. Ramaswamy, and J. S. Bapna, "Analgesic effect of Momordica charantia seed extract in mice and rats," *Journal* of *Ethnopharmacology*, vol. 31, no. 1, pp. 115–118, 1991.
- [67] V. Jain, A. Pareek, N. Paliwal, Y. Ratan, A. S. Jaggi, and N. Singh, "Antinociceptive and antiallodynic effects of momordica charantia L. in tibial and sural nerve transection-induced neuropathic pain in rats," *Nutritional Neuroscience*, vol. 17, no. 2, pp. 88–96, 2014.
- [68] R. Patel, N. Mahobia, N. Upwar, N. Waseem, H. Talaviya, and Z. Patel, "Analgesic and antipyretic activities of Momordica charantia linn. fruits," *Journal of Advanced Pharmaceutical Technology & Research*, vol. 1, no. 4, pp. 415–418, 2010.
- [69] I. O. Ishola, A. A. Akinyede, and A. M. Sholarin, "Antidepressant and anxiolytic properties of the methanolic extract of Momordica charantia Linn (Cucurbitaceae) and its mechanism of action," *Drug Research*, vol. 64, no. 7, pp. 368–376, 2014.
- [70] P. I. Aziba, D. Bass, and Y. Elegbe, "Pharmacological investigation of Ocimum gratissimum in rodents," *Phytotherapy Research*, vol. 13, no. 5, pp. 427–429, 1999.
- [71] L. I. G. Paula-Freire, M. L. Andersen, G. R. Molska, D. O. Köhn, and E. L. A. Carlini, "Evaluation of the antinociceptive activity of ocimum gratissimum L. (Lamiaceae) essential oil and its isolated active principles in mice," *Phytotherapy Research*, vol. 27, no. 8, pp. 1220–1224, 2013.
- [72] M. Rabelo, E. P. Souza, P. M. G. Soares, A. V. Miranda, F. J. A. Matos, and D. N. Criddle, "Antinociceptive properties of the essential oil of Ocimum gratissimum L. (Labiatae) in mice," *Brazilian Journal of Medical and Biological Research*, vol. 36, no. 4, pp. 521–524, 2003.
- [73] Y. Tanko, G. M. Magaji, M. Yerima, R. A. Magaji, and A. Mohammed, "Anti-nociceptive and anti-inflammatory activities of aqueous leaves extract of Ocimum Gratissimum (Labiate) in Rodents," *African Journal of Traditional, Complementary and Alternative Medicines*, vol. 5, no. 2, pp. 141–146, 2008.
- [74] M. Zamin, "An analgesic and hepatoprotective plant: Ocimum gratissimum," *Pakistan Journal of Biological Sciences*, vol. 14, no. 20, pp. 954-955, 2011.
- [75] C. O. Okoli, A. C. Ezike, O. C. Agwagah, and P. A. Akah, "Anticonvulsant and anxiolytic evaluation of leaf extracts of *Ocimum* gratissimum, a culinary herb," *Pharmacognosy Research*, vol. 2, no. 1, pp. 36–40, 2010.
- [76] P. R. Barbosa, S. S. Valvassori, C. L. Bordignon Jr. et al., "The aqueous extracts of *Passiflora alata* and *Passiflora edulis* reduce anxiety-related behaviors without affecting memory process in rats," *Journal of Medicinal Food*, vol. 11, no. 2, pp. 282–288, 2008.
- [77] M. Coleta, M. T. Batista, M. G. Campos et al., "Neuropharmacological evaluation of the putative anxiolytic effects of Passiflora

edulis Sims, its sub-fractions and flavonoid constituents," *Phy-totherapy Research*, vol. 20, no. 12, pp. 1067–1073, 2006.

- [78] J. Deng, Y. Zhou, M. Bai, H. Li, and L. Li, "Anxiolytic and sedative activities of *Passiflora edulis* f. flavicarpa," *Journal of Ethnopharmacology*, vol. 128, no. 1, pp. 148–153, 2010.
- [79] A. Otify, C. George, A. Elsayed, and M. A. Farag, "Mechanistic evidence of Passiflora edulis (Passifloraceae) anxiolytic activity in relation to its metabolite fingerprint as revealed via LC-MS and chemometrics," *Food & Function*, vol. 6, no. 12, pp. 3807– 3817, 2015.
- [80] R. D. Petry, F. Reginatto, and F. de-Paris, "Comparative pharmacological study of hydroethanol extracts of *Passiflora alata* and *Passiflora edulis* leaves," *Phytotherapy Research*, vol. 15, no. 2, pp. 162–164, 2001.
- [81] L. M. Sena, S. M. Zucolotto, F. H. Reginatto, E. P. Schenkel, and T. C. M. De Lima, "Neuropharmacological activity of the pericarp of Passiflora edulis flavicarpa Degener: Putative involvement of C-glycosylflavonoids," *Experimental Biology and Medicine*, vol. 234, no. 8, pp. 967–975, 2009.
- [82] N. Klein, A. C. Gazola, T. C. M. De Lima, E. Schenkel, K. Nieber, and V. Butterweck, "Assessment of sedative effects of passiflora edulis f. flavicarpa and passiflora alata extracts in mice, measured by telemetry," *Phytotherapy Research*, vol. 28, no. 5, pp. 706–713, 2014.
- [83] O. O. Adeyemi, S. O. Okpo, and O. O. Ogunti, "Analgesic and anti-inflammatory effects of the aqueous extract of leaves of *Persea americana* Mill (Lauraceae)," *Fitoterapia*, vol. 73, no. 5, pp. 375–380, 2002.
- [84] J. A. O. Ojewole and G. J. Amabeoku, "Anticonvulsant effect of Persea americana mill (Lauraceae) (avocado) leaf aqueous extract in mice," *Phytotherapy Research*, vol. 20, no. 8, pp. 696– 700, 2006.
- [85] J. Moreira, L. C. Klein-Júnior, V. Cechinel Filho, and F. de Campos Buzzi, "Anti-hyperalgesic activity of corilagin, a tannin isolated from *Phyllanthus niruri* L. (Euphorbiaceae)," *Journal of Ethnopharmacology*, vol. 146, no. 1, pp. 318–323, 2013.
- [86] I. C. Obidike, O. A. Salawu, M. Ndukuba, C. O. Okoli, and U. A. Osunkwo, "The anti-inflammatory and antinociceptive properties of the chloroform fraction from Phyllanthus niruri plant is mediated via the peripheral nervous system," *Journal of Dietary Supplements*, vol. 7, no. 4, pp. 341–350, 2010.
- [87] M. Ahmed, H. A. Shikha, S. K. Sadhu, M. T. Rahman, and B. K. Datta, "Analgesic, diuretic, and anti-inflammatory principle from Scoparia dulcis," *Die Pharmazie*, vol. 56, pp. 657–660, 2001.
- [88] S. M. Freire, L. M. Torres, N. F. Roque, C. Souccar, and A. J. Lapa, "Analgesic activity of a triterpene isolated from Scoparia dulcis L. (vassourinha)," *Memórias do Instituto Oswaldo Cruz*, vol. 86, no. 2, pp. 149–151, 1991.
- [89] G. F. Ibironke, A. S. Umukoro, and D. C. Ajonijebu, "Central nervous system activity of the ethanol leaf extract of Sida acuta in rats," *African Journal of Medicine and Medical Sciences*, vol. 43, pp. 11–16, 2014.
- [90] K. Konaté, I. H. N. Bassolé, A. Hilou et al., "Toxicity assessment and analgesic activity investigation of aqueous acetone extracts of Sida acuta Burn f . and Sida cordifolia L. (Malvaceae), medicinal plants of Burkina Faso," *BMC Complementary and Alternative Medicine*, vol. 12, Article ID 120, 2012.
- [91] J. I. Nwaiwu and P. A. Akah, "Anticonvulsant activity of the volatile oil from the fruit of tetrapleura tetraptera," *Journal of Ethnopharmacology*, vol. 18, no. 2, pp. 103–107, 1986.

[92] J. A. O. Ojewole, "Analgesic and anticonvulsant properties of Tetrapleura tetraptera (Taub) (Fabaceae) fruit aqueous extract in mice," *Phytotherapy Research*, vol. 19, no. 12, pp. 1023–1029, 2005.