Journal of Medicinal Herbs

journal homepage:**www.jhd.iaushk.ac.ir**

Uses, phytochemistry and biological activity of Piper genus: a review

Clement Mbadiko[1,2], Gédéon Bongo[1,2*], Koto-te-Nyiwa Ngbolua[1], Nadege Ngombe[3], Paulin Kapepula[3], Marie Claire Yandju[1], Pius Mpiana[4], Theophile Mbemba[1,2]

[1] *Department of Biology, Faculty of Sciences, University of Kinshasa, P.O.Box 190, Kinshasa XI, Democratic Republic of the Congo;*

[2] *Laboratoire d'Analyse et de Recherche sur l'Alimentation et la Nutrition, Faculté des Sciences, Université de Kinshasa, République Démocratique du Congo (LARAN);*

[3] *Centre d'Etudes des Substances Naturelles d'Origine Végétale (CESNOV), Faculty of Pharmaceutical Sciences, University of Kinshasa, Kinshasa XI, Democratic Republic of Congo;*

[4] *Department of Chemistry, Faculty of Sciences, University of Kinshasa, P.O.Box 190, Kinshasa XI, Republic of the Congo;*

Email:** ***gedeonbongo@gmail.com

ARTICLE INFO

Type: *Review Research*
Topic: *Medicinal Plants*
Revised *April 23rd 2023*
Accepted *May 21st 2023*

Key words:
- ✓ *Piper*
- ✓ *Uses*
- ✓ *Biological activity*
- ✓ *Chemical compounds*

ABSTRACT

Background & Aim: *Piper* genus comprises more than 2000 species, mainly found in Asia and Africa. About 40 species are mentioned in the literature and only a small proportion of these species have been studied in depth. The aim of this review is to present data on the traditional uses, biological activities and the chemical composition of different *Piper* species.

Experimental: Several databases like PubMed, PubMed Central, Science Direct, DOAJ, etc.), were used for the search. The term Piper or the scientific names of different species or the combination of terms such as biological activity, phytochemistry and uses with the scientific names or the word "Piper" were used as keywords in the literature search.

Results: Species of the *Piper* genus are of great economic value as they can be used in various sectors such as food, traditional medicine, in the control of certain infectious diseases, crop pest control or in the pharmaceutical industry. Some species are considered a significant source of essential oils. About 400 chemical compounds have been isolated from *Piper* species, and the alkaloids are the most important group of secondary metabolites; and piperine is the main active alkaloid reported. Moreover, the literature indicates that these species present several biological properties like anti-inflammatory, antioxidant, antibacterial, antifungal, antiplasmodial, analgesic, immunomudatory, antitumour, insecticide, larvicide, amoebicide, antiviral, etc.

Recommended applications/industries: The species from *Piper* genus can be widely used both as a condiment and as medicines to relieve several health problems. However, further studies should be carried out to justify the uses of the less scientifically explored species of *Piper* genus, and to determine the mechanisms of action or the pharmacokinetics of the active principles already identified and probable synergies between the alkaloids and other chemical groups to evaluate the digestibility and toxicity of extracts from these species.

1. Introduction

Piper genus is the most important genus in the Piperaceae family and includes more than 2000

species, (Hashim, 2018; Xiang *et al.*, 2016; Torres *et al.*, 2016). The most known species are: *Piper nigrum*, *Piper longum et Piper bettle* (Srivastava *et al.*, 2017) although there are other species such as *Piper aduncum* L., *P. capens* L., *Piper aequale Vahl*, *Piper aereum Trel*., *Piper amalago* L., *Piper auritum Kunth*, *Piper berlandieri* C. DC., *Piper diandrum* C.DC., *Piper dilatatum Rich*, *Piper hispidum* Sw., *Piper lapathifolium* C.DC., *Piper obliquum* Ruiz & Pavon (synonyme : *Piper peltatum* et *Piper umbellatum* L. *Piper Peracuminatum* C. DC, *Piper pegamentifolium* Trel. & Standl, *Piper sanctum* (Miq.) Schltdl. ex C. DC., *Piper scabrum* Lam., *Piper Schiedeanum* Steud., *Piper yzabalanum* C. DC.; and *Piper berlandieri* C. CD., *Piper sanctum*, *Piperaduncum*, *Piper auritum*, *Piper amalago*, *Piper psilorhachis*, *Piper diandrum*, *Piper nudum*, *etc.* (Torres *et al.*, 2016). These species are most found in the tropical and subtropical regions, and they are mainly located in Asian and African countries.

Most of these species are used in food for seasoning or in traditional medicine (Stojanovi'c-Radi and Kumar, 2019; Araujo *et al.*, 2019). Several literature sources reported that extracts from different *Piper* species present a large spectrum of biological activities, which justify their use in traditional medicine (Lima *et al.*, 2020; Araujo *et al.*, 2018; Mgbeahuruike *et al.*, 2017). These activities would be related to the presence of alkaloids precisely the “piperine” which is often mentioned in the literature. However, other secondary metabolite groups (essential oils, flavonoids, lignins, etc.) of *Piper* species are also mentioned for their biological activities (Lima *et al.*, 2020; Stojanovi'c-Radi *et al.*, 2019; Srivastava, 2017; Weng *et al.*, 2014; Angone, 2014; Osorio *et al.*, 2013; Ahmad *et al.*, 2012). In the present work, we have briefly presented data on the biological uses, activities and the chemical composition of different *Piper* species.

2. Materials and methods

Several databases (PubMed, PubMed Central, Science Direct, Scielo, DOAJ, Science alert and Google scholar), were used to identify scientific works and publications related to the uses, chemical composition and biological activities of *Piper* species. The term *Piper* or the scientific names of different species or the combination of terms such as biological activity, phytochemistry and uses with the scientific names or the word "*Piper*" were used as keywords in the literature search.

3. Results and discussion

3.1. Uses

Piper species are used in food as spices, but in traditional medicine to treat various ailments, such as fever, backache, diarrhea, rheumatism, boils, scabies and stomach ache, gastrointestinal problems, cancer, antihemorrhagic, antihelminthic, diuretic, pain and inflammation as well as high blood pressure. They are also used as an (Lima *et al.*, 2020; Stojanovi'c-Radi *et al.*, 2019; Araujo *et al.*, 2019; Mgbeahuruike *et al.*, 2017; Wang *et al.*, 2014 ; Sawadogo *et al.*, 2012). *Piper* species are cultivated primarily for their seeds and leaves which have flavouring properties while their leaves are used for the treatment of several diseases but also necessary for the cooking. However, these leaves are utilized for the production of essential oils (Araujo *et al.*, 2019; Mgbeahuruike *et al.*, 2017). Among this huge arsenal of *Piper* species, *P. nigrum* appears from the literature to be the most used worldwide and probably the most studied as well (Stojanovi'c-Radi *et al.*, 2019).

The Table 1 gives a brief overview of the different uses of the species of the genus Piper.

Table 1: Uses of different species of Piper genus.

Species	Part used	Uses	References
Piper aborescens Roxb.	Stems	This species is used as an anti-rheumatism	Tsai *et al.*, 2005
P. acutifolium Ruiz and Pav	Fresh leaves	The leaves of this plant are used as antiseptic, and treat wound healing, vaginal infections, skin ulcers and other ailments.	De Feo, 2003
P. aduncum L.	Inflorescence and leaves	The inflorescence and leaves of this species relieve cancer, ulcer, stomach ache, vaginitis, flu, rheumatism, cough, fever and general infections. Furthermore, they are also used as an insecticide, molluschicide, or as an antibacterial, diuretic,	Pereira *et al.*, 2016; Wang *et al.*, 2014; Chahal *et al.*, 2011

		astringent, etc.	
	Leaves and roots	The tea made from the leaves and roots is used to treat diarrhoea, dysentery, nausea, ulcers, genitourinary infections and to prevent bleeding during haemorrhage.	Pereira *et al.*, 2016; Chahal *et al.*, 2011
P. alatabaccum Trel. and Yunck	Leaves	The leaves of this plant are used to relieve stomach aches and diarrhea	Silva *et al.*, 2020; Salehi *et al.*, 2019
P. angustifolium Lam.	Leaves	They are used against skin lesions associated with leishmaniasis, stomatitis, vaginitis, liver disorders and as an antiseptic.	Salehi *et al.*, 2019; Bosquiroli *et al.*, 2015
P. amalago L.	Leaves	The leaves of this species are used as an antipyretic, vermifuge, diuretic or against renal stones, stomachache, headache, chest pain, menstrual pain, toothache, chest pain, skin diseases, skin inflammation and snake bites, They are also used traditionally in the prevention of miscarriage and relieve female disorders during pregnancy and postpartum	Araujo *et al.*, 2019; Pereira *et al.*, 2016
P. argyrites Ridl	Fruit, stem and leaves	This plant is used as a chewing-gum to sweeten the breath	Hashim, 2018
P. auritum Kunth	Fresh leaves	The leaves are used in food as a spices and also in traditional medicine against fever, respiratory problems, sore throat, backache, stomach ache, gonorrhoea, gout or as a diuretic, local anaesthetic or repellent, etc.	Torres *et al.*, 2016
P. baccatum (Blume) Miq	Leaves	The leaves of this plant are used to treat coughs and venereal diseases	Hashim, 2018
P. barbatum Kunth	Leaves	The leaves are used for headaches, stomach pains, dermatitis or as a disinfectant or for the treatment of wounds	Calderon *et al.*, 2010
P. betle L.	Leaves	The plant is used against cough, asthma but also stimulate the secretion of maternal milk. In addition, the leaves prevent oral malodor and vaginal odour. They are also used for cuts, boils, scabies, as a remedy for coughs, bronchitis and nosebleeds. They have a strong aromatic odour and flavour and are used as a wrapper for seasoning certain dishes.	Hashim 2018; Xiang *et al.*, 2016; Chahal *et al.*, 2011
P. boehmeriifolium (Wall Miq).C.D.C	The whole plant	This species despite the part used helps to relieve pain, rheumatism and arthritic conditions. Yet, roots are specifically used like a laxative, anthelminthic and carminative but contribute also to the treatment of bronchitis, spleen ailments and tumours.	Wang *et al.*, 2014; Tang *et al.*, 2011
P. canimum Blume	Leaves	This species is used to relieve hoarseness	Hashim, 2018
P. capens L.	Stem	This species is used in food to season dishes, but also in traditional medicine to treat stomach or abdominal pain, diarrhea and cough, diabetes, rheumatism, toothache, malaria, leishmaniasis, cancer, fever, indigestion, flatulence, heart and kidney problems, stomach ache, neoplasm, psychosis, and flu. Also, it is used as a diuretic, vermifuge and appetite stimulant.	Rusaati *et al.*, 2021; Wamba *et al.*, 2020; Saleh *et al.*, 2019; Bobasa *et al.*, 2018; Maryo *et al.*, 2015; Wang *et al.*, 2014; Njeri *et al.*, 2010
	Bark	This part of *P. capens* L. is utilized in the treatment of sterility, wounds, urinary disorders and venereal diseases. In addition, the macerated bark is drunk to relieve mouth and throat aches and chest problems while the infused bark is used against vaginal discharge.	Salehi *et al.*, 2019; Debebe *et al.*, 2018
	Leaves	The leaves are used in traditional medicine for fever, bilious fever, malnutrition, haematuria, skin infections, epilepsy, polio, malaria, urinary problems, diarrhea, coughs, stomach and other digestive problems, sore throat, infertility and to improve appetite.	Wamba *et al.*, 2021; Wansi *et al.*, 2019; Salehi *et al.*, 2019; Debebe *et al.*, 2018; Chahal *et al.*, 2011
	Fruit and seeds	Fruits or seeds are used against coughs, epilepsy, or as an antihelminthic or to protect the harvest against insects; is also used for sleep inducing	Wansi *et al.*, 2019; Salehi *et al.*, 2019; Bekele *et al.*, 2014; Sawadogo *et al.*, 2012

	Roots	The root extracts are used as an antiheminthic, aphrodisiac, or to treat coughs, paralysis, malaria, or as sleep inducing remedy	Wamba *et al.*, 2021; Pedersen *et al.*, 2009
P. carpunya Ruiz & Pav. (syn: *P. lenticellosum* C.D.C.),	Leaves	The leaves of this species are used as an anti-inflammatory, anti-ulcer, anti-diarrheal, anti-parasitic products and they are also reported to be efficient against skin diseases.	Chahal *et al.*, 2011
P. chaba Hunter	Leaves	This species is used to treat hemorrhoids, asthma, bronchitis, fever, hemorrhoids and stomach ache and contributes to the pain relief.	Hashim 2018; Chahal *et al.*, 2011
	Fruits	They are reported to be a stimulant and carminative, and are considered as antihelminthic, expectorant, appetite stimulant. They are also used in the treatment of haemorrhoidal infections, asthma, bronchitis, fever, inflammation, pain in the abdomen and anus.	Chahal *et al.*, 2011
	Roots	This part is used in the treatment of asthma, bronchitis and against the bites of poisonous animals	Chahal *et al.*, 2011
	Stem bark	It is known to be used against pain, rheumatism and diarrhea	Chaha *et al.*, 2011
P. consanguineum Kunth	Leaves	The leaves of this species are used against snake bites or to heal wounds	Pereira *et al.*, 2016
P. cubeba L.	Leaves	The plant is used as a flavouring agent or against kidney disorders, gonorrhoea, syphilis, abdominal pain, enteritis and asthma.	Chahal *et al.*, 2011
	Fruit and seeds	The plant is used against cancer or to treat gonorrhoea, syphilis, asthma, abdominal pain	Wang *et al.*, 2014
Piper cumanense Kunth	Fruits and leaves	The plant is used against malaria and fever	Garavito *et al.*, 2006
P. dennisii Trel.	Leaves	The plant is used to relieve rheumatic pain and arthritis.	Valadeau *et al.*, 2009
P. darienense C.D.C	Leaves	The plant is used during fishing to poison fish	Chahal *et al.*, 2011
P. febrifugum C.D.C	Leaves	The plant is used against fever	Hashim, 2018
P. gibbilimbum CDC.	Seeds	Traditional formulations used for the treatment of cancer or intestinal ailments	Wang *et al.*, 2014
P. glabratum Kunth	Leaves	The plant is used to treat skin diseases, skin ulcers, wounds and as an antiseptic.	Caldéron *et al.*, 2010
P. guineense Schum et Thonn	Fresh fruits and leaves	The plant is used against coughs, bronchitis, rheumatism, cancers, venereal diseases, female infertility, anaemia or as aphrodisiac an insecticide, carminative, stomachic or to relieve pain, etc.	Umoh *et al.*, 2013; Voukeng *et al.*, 2012; Diame 2010
	Leaves	They are used as an insecticide	Voukeng *et al.*, 2012
	Fruit and seeds	The plant is used against dysentery or as a stomachic or insecticide. The seeds are used to treat cancer. Seeds are mentioned in the management of sickle cell disease. The combination of *Piper guinensis* seeds, *Byrophyllum pinnatum* or *Xylopia aethiopica* leaves and *Aframomum melegueta* fruits are used as analgesics. The plant material is extracted in red wine or any other alcoholic beverage. One dose of the tincture is taken once a day. The combination of *Garcina kola* bark, *Securidaca longepedunculata*, root bark, *Olax subscorpioidea* root, *Piper guineense*, fruit and *Capsicum frutescens* fruit is used as anti-inflammatory. They are boiled for 15-20 minutes. The extract (100ml), is taken once daily.	Gbadamosi 2015; Wang *et al.*, 2014; Nkeoua and Boundzanga, 1999
P. hayneanum C.DC.	Stem and roots	The plant is used to treat wound and skin diseases	Bastos *et al.*, 2011
P. hispidum Sw	Leaves	The plant is used against pain, urinary infections, wounds and symptoms of cutaneous leishmaniasis, skin ailments, and stomach aches or to regulate menstruation	Chahal *et al.*, 2011
P. holtonii C.DC	Leaves	The treatment for leishmaniasis symptoms is assured by the leaves of this species.	Calderon *et al.*, 2010
P. jacquemontianum Kunth	Leaves	The plant is used against skin diseases, infections, anaemia and body pains.	Cruz *et al.*, 2011
P. lanceaefolium Kunth	Leaves	The plant is used against skin infection	Lopez *et al.*, 2002

P. laetispicum C.D.C	Leaves	The plant is used to invigorate circulation and reduce stasis and as an analgesic.	Chahal *et al.*, 2011
P. longum L.	Roots and fruits	The species is used to treat tuberculosis, leprosy, coughs and colds, chronic bronchitis, heart and spleen problems, fever, gout, rheumatism, or as a rejuvenator and detoxifier, etc. They are as well used as an antidote to snake bites, scorpion stings.	Choudhary and Singh 2018; Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011
	Leaves	They are used to treat several diseases including brain cancer.	Wang *et al.*, 2014; Reshmi *et al.*, 2010
P. marginatum Jacq	Inflorescences and leaves	The plant is used against inflammation, snake bites, liver diseases and bile duct	Chahal *et al.*, 2011
	Fruit and leaves	The fruit is used as a flavouring agent and also as a substitute for *P. nigrum*. (black pepper). In addition, the fruit and leaf extracts are a source of essential oils	Mgbeahuruike *et al.*, 2017
P. methysticum G. Forst	Roots and rhizomes	Roots and rhizomes are used for pain and anxiety. Narcotic beverage made from roots is drunk to cure diseases.	Xiang *et al.*, 2016
P. multiplinervium C.DC.	Leaves	The plant is used for stomach aches	Mgbeahuruike *et al.*, 2017
P. nigrum L	Stem	It is used as a preservative or to season food and is also used in perfumery. This species is also used in traditional medicine for gastric problems, diarrhea, indigestion, fever, asthma, influenza, rheumatism, cough, obesity, colon toxins, colonic disorders, sinusitis, congestion, fever, paralysis, diarrhea and cholera, colds, cancer, backache, colic, kidney stones, etc.	Hashim 2018; Srivastava et al., 2017; Iwu 2014; Nkeoua and Boundzanga 1999
	Leaves	They are used to regulate menstruation or to treat female sterility, *Trichomonas vaginalis* infections, or as an antiplasmodial. The decoction of the leaves is used against coughs.	Bobasa *et al.*, 2018; Iwu 2014
	Fruit and seeds	They are used as a spice or in traditional medicine for the treatment of sickle cell disease, dysmenorrhoea or to relieve pain, rheumatism, flu, colds, fever, muscle aches, measles. They are also applied locally to relieve sore throats and skin disorders or to treat amoebiasis, dental decay, respiratory cancer and even respiratory pathologies such as bronchitis, asthma, etc. The fruits are also used as an aphrodisiac, The seeds are used for bronchial infections or as an insecticide. They are also used against paralysis, gout and lumbago	Stojanovi´c-Radi´ *et al.*, 2019; Ngbolua *et al.*, 2019; Xianga, *et al.*, 2016; Gbadamosi 2015; Wang *et al.*, 2014; Ganesh *et al.*, 2014; Iwu 2014; Reshmi *et al.*, 2010; Sonibare *et al.*, 2009; Traoré 2007
	Roots	Root extracts are used against cancer of the abdomen, colds, diseases of the respiratory tract (cough, bronchitis, asthma, etc.). Root extracts are also incorporated in medicinal preparations to treat infectious diseases such as gonorrhoea, syphilis, etc.	Wang *et al.*, 2014; Ganesh *et al.*, 2014; Iwu 2014
P. obliquum Ruiz & Pavon	Leaves	Leaves are used as an analgesic or anti-arthritic by applying it to the affected area	Chahal *et al.*, 2011
P. ovatum Vahl	Leaves	The plant is used as an analgesic and against inflammations	Chahal *et al.*, 2011
P. porphyrophyllum Lindl	Leaves	The plant is used for pain, especially bone pain	Hashim, 2018
P. pulchrum C.DC.	Leaves, branches and stems	The plant is used to treat the haemorrhagic effect of snakebite venom or as an antidote for snakebite.	Otero *et al.*, 2000
P. pyrifolium Vahl.	Fruits and stems	The plant is used against diarrhea or as a diuretic. Treatment of stomatitis in young children, blennorrhagia, asthma and neuralgia. This plant is also used as a depurative	Salehi *et al.*, 2019
P. regnelli (Miq.) C. DC.	Leaves and roots	These parts of the plant are used to treat wounds, skin irritations and swellings	Chahal *et al.*, 2011
P. retrofractum Vahl	Leaves	The plant is used for seasoning dishes or against intestinal problems and muscle pain and inflammation, or again as stimulant, carminative, and for postpartum treatment in women	Hashim, 2018
P. sarmentosum Roxb	Stems	The plant is used for toothache, headache, fungal dermatitis, cough, muscle weakness and bone pain.	Mgbeahuruike *et al.*, 2017

	Leaves	Leaves are used to treat high blood pressure, diabetes, muscle, joint and bone pain, rheumatism, toothache, backache, cough, asthma, paralysis, pleurisy, skin diseases and as an expectorant, The mixture of crushed leaves and water was used during the bath to treat kidney difficulties in urination and stones. The mixture of crushed leaves and water was used during bathing to treat kidney problems and stones, while the decoction of the leaves is recommended against bad breath.	Seyyedan *et al.*, 2013; Chahal *et al.*, 2011
	Fruit	Fruits are used for the treatment of various ailments such as: high blood pressure, diabetes, muscle, joint and bone pain, rheumatism, toothache, coughs, dysentery but also as an expectorant	Seyyedan *et al.*, 2013; Chahal *et al.*, 2011
	Roots	Like the leaves, the roots are used in traditional medicine to treat hypertension, diabetes, muscle, joint and bone pain, rheumatism, toothache, coughs and backache. They are also used to treat asthma, paralysis, pleurisy, skin diseases or as a stomachic, carminative, etc.	Seyyedan *et al.*, 2013; Chahal, *et al.*, 2011
P. strigosum Trel. & Yunck	Leaves	The plant is used for the treatment of symptoms associated with parasitosis and leishmaniasis or to treat plague, etc.	Estevez *et al.*, 2007
P. syhaticum Roxb	Roots	Roots are used as an antidote for snake bites	Chahal *et al.*, 2011
P. sylvaticum Roxb	Roots	They are used to treat cancer or as a laxative, antihelminthic, carminative or for the treatment of bronchitis, spleen ailments and tumours	Saheli *et al.*, 2019; Wang *et al.*, 2014
P. stylosum Miq.	Fresh leaves	The plant is used against fever and Pain.	Salleh *et al.*, 2014
P. truncatum Vell	Roots	Roots are used to reduce blood pressure	Chahal *et al.*, 2011
P. tuberculatum Jacq.	Roots	The plant is used for treatment of miscarriages, boils, dermatosis and leucorrhoea.	Bezerra *et al.*, 2006
P. umbellatum L.	Leaves	The plant is used in the treatment of wounds and skin diseases, rheumatism, malaria, miscarriages, boils, dermatitis and leucorrhoea. Moreover, leaves are used as well to calm epigastria and is also in the management of sickle cell anemia.	Hashim 2018; Pereira *et al.*, 2016; Amujoyegbe *et al.*, 2016; Nkeoua and Boundzanga 1999
P. xanthostachyum C. DC	Leaves	The plant is used for treatment of leishmaniasis symptoms	Mgbeahuruike *et al.*, 2017

3.2. Biological activity

The literature shows that different *Piper* species have these biological actions. interesting biological activities . The Table 2 shows

Table 2. Biological or pharmacological actions of species of the genus Piper.

Species	Plant part or extracts analyzed	Biological action	References
Piper spp	Leaves and roots	The leaves and roots of this plant has shown anti-inflammatory, antioxidant, antibacterial, antifungal, antiplasmodial, analgesic, vasodilatory, immunomudatory, antitumour, insecticide, larvicide, amoebicide, antiviral, Anxiolytic, amoebicidal activities.	Lima *et al.*, 2020; Araujo *et al.*, 2018; Pereira *et al.*, 2016
P. aborescens Roxb.	Leaves	Cytotoxic activity and antiplatelet aggregation	Mgbeahuruike *et al.*, 2017
P. acutifolium Riuz & Pav	Benzoic acid derivatives	This fraction has shown action against *Plasmodium falciparum*, *Trypanosoma cruzi* and *Leishmania spp*.	Mgbeahuruike *et al.*, 2017
P. aduncum L.	Dichloromethane extracts of leaf	The dichloromethane extract is marginally cytotoxic to glioma (SF 268), human large cell lung carcinoma (H 460), and human breast carcinoma (MCF 7) cell lines with IC_{50} values of 23, 25, and 27 µg/ml, respectively	Wang *et al.*, 2014
	Piperaduncin A	This molecule inhibited the growth activity of human nasopharynx carcinoma (KB) cells (IC_{50} = 2.3 µg/ml)	Wang *et al.*, 2014
P. amalago L.	Essential oils from the	The essential oils from leaves displayed	Araujo *et al.*, 2019

	leaves	antibacterial activity against three strains of *Staphylococcus aureus*, *Enterococcus faecalis* and *Pseudomonas aeruginosa.* Besides the aforementioned activity, these essential oils showed the Anti-inflammatory, leishmanicidal, schistosomicidal, antioxidant, antilithiasic, anxiolytic, antihyperalgesic and antifungal activities.	
P. angustifolium Lam	Essential oils	The essential oils of this species showed an activity against *Leishmania infantum*	Mgbeahuruike *et al.*, 2017
P. auritum Kunth	Ethanol extract	The ethanol extract of this plant displayed an action against *P. falciparum*	Mgbeahuruike *et al.*, 2017
P. betle L.	Leaf extracts	The leaf extracts of this species showed an anti-itching activity, reduce the adherence of early dental plaque bacteria; antidiabetic, anti-pruritic effect. It may be useful in reducing allergic reactions by inhibiting rabbit platelet activating factor (PAF), it decreases histamine production, and may be useful in relieving histamine-induced allergic symptoms in Type I hypersensitive diseases. Furthermore, it improves the skin lesions of ringworm. Antioxidant, antibacterial and antifungal activities (*S. aureus*, group A β-hemolytic streptococcus, and dermatophytes responsible for skin infections).	Chahal *et al.*, 2011
P. boehmeriifolium (Wall Miq).C.D.C	Leaves	The leaves showed an anti-inflammatory and prostaglandin synthesis inhibitory activity.	Chahal *et al.*, 2011
P. borbonense (Miq) C.D.C	Essential oil of leaves	The essential oils of leaves showed an antioxidant, antibacterial (*B. subtilus*, *S. aureus*), antifungal (*Penicillium digitatum*, *Penicillium expensum.*, *Aspergillus niger*)	Soidrou *et al.*, 2019
P. capens L.	Methanol extract from fruit, essential oils, chloromethylenic extract	Different extracts showed anti-cancer (against leukaemia cell lines, human pancreatic cell lines, breast adenocarcinoma cell lines, malignant melanoma, and colon carcinoma cells, glioblastoma cell lines, etc.); and antibacterial, antiplasmodial (*Plasmodium falciparum*), antioxidant and hypoglycemic activities were reported.	Salehi *et al.*, 2019; Li *et al.*, 2016; Fankam *et al.*, 2011; Chahal *et al.*, 2011
	Root Extracts	The root extract showed hypoglycaemic, sedative and antiepileptic activities	Njeri *et al.*, 2017
	Bark extracts	The bark extract showed the antibacterial activity	Pedersen *et al.*, 2009
	Seed extracts	The seed extract showed an efficient action against several types of cancer, antihelminthic, or as sleep inducing.	Wang *et al.*, 2014; Sawadogo *et al.*, 2012
	Leaf extracts	The leaf extract showed an antiplasmodial activity.	Wamba *et al.*, 2020
P. cumanense Kunth	Ethanol extract	The ethanol extract showed an action against *Plasmodium falciparum* and *Plasmodium berghei*	Mgbeahuruike *et al.*, 2017
P. claussenianum m (Miq.) C. DC.	Nerolidol rich essential oil	This specific essential oil showed an activity against biofilms from *C. albicans*	Mgbeahuruike *et al.*, 2017
P. dennisi Trel	Ethanol extract	This extract showed an activity against *P. falciparum*	Mgbeahuruike *et al.*, 2017
P. fimbriulatum C.DC.	Ethanol extract	The ethanol extract showed an activity against *P. falciparum*, *T. cruzi*, *L. mexicana* and *Aedes aegypti*. It also showed an activity against pain.	Mgbeahuruike *et al.*, 2017
P. galeatum (Miq.) C.DC.	The crude extracts	These extracts displayed an activity to inhibit TNFa (tumour necrosis factor-a), they induced expression of cell adhesion molecule ICAM-1 (intercellular adhesion molecule-1) on the surface of human umbilical vein endothelial cells (HUVECs).	Chahal *et al.*, 2011
P. grande Vahl	Ethanol extract	The ethanol extract showed an action against *P. falciparum*, *T. cruzi*, *L. mexicana* and *Aedes aegypti* and against some lesions associated with leishmaniasis.	Mgbeahuruike *et al.*, 2017
P. guineense Schum et Thonn	Seed extracts	These extracts showed anti-cancer, antisickling (sickle-cell disorder), insecticidal and larvicidal activities.	Wang *et al.*, 2014; Siddiqui *et al.*, 2005
	Root extracts	Root extracts showed an efficient insect repellent.	Chahal *et al.*, 2011
P. hayneanum C.DC.	Methanol extracts	The methanol activity showed an activity against *S.*	Mgbeahuruike *et al.*,

		aureus and *C. albicans*	2017
P. hispidum Sw	Leaves	The extract increases the expression of estrogen genes.	Chahal *et al.*, 2011
	Ethanol extracts	Action against *L. amazonensis*	Mgbeahuruike *et al.*, 2017
P. holtonii C.DC.	Ethanol extracts	This crude extract showed an activity against *P. falciparum, P. berghei, T. cruzi* et *L. spp*	Mgbeahuruike *et al.*, 2017
P. jericoense Trel. & Yunck	Ethanol extracts	This crude extract showed an activity against *P. falciparum*	Mgbeahuruike *et al.*, 2017
P. klotzschianum (Kunth) C.DC	1-butyl-3,4-methylenedioxy-phenyl (the major constituent of the oil extracted from the leaves, stems, fruits, and roots)	This fraction showed an activity against the larvae of *Aedes Aegypti*	Mgbeahuruike *et al.*, 2017
P. laetispicum C.DC	Ispicine (N-isobutyl -(3,4-ethylendioxyphenyl)-2E, 4E, 9E-undecatrienoamide)	This isolated molecule showed an antinociceptive and antidepressant activities in several animal models	Chahal *et al.*, 2011
P. lanceaefolium Kunth	Methanol extracts	The methanol extract showed an action against *K. pneumoniae, E. coli, S. faecalis, M. phlei, B. subtilis, S. aureus, P. aeruginosa* and *C. albicans*	Mgbeahuruike *et al.*, 2017
P. longum L. (syn. *P. latifolium* Forst)	Chloroform and methanolic extracts	The chloroform and methanolic extracts showed antioxidant, anti-inflammatory, hepatoprotective, immunomodulatory, antimicrobial, anti-hyperlipidemic, analgesic, anti-depressant, anti-obesity, cardioprotective, antifungal, anti-amoebic, radioprotective, anti-platelets activities. Clinical studies have shown that this plant is effective in treating asthma in children and have reported an action against vesicular stomatitis virus and human para influenza virus.	Choudhary and Singh 2018; Priya and Saravana, 2017
	Methanolic or ethanolic extract of Fruit or piperine	These two alcoholic extracts of the fruits have shown toxicity to Dalton's lymphoma ascites (DLA) cells, Ehrlich ascites carcinoma (EAC) cells. While Piperine has shown inhibition of the solid tumor development in mice induced with DLA cells and increases the life span of mice bearing Ehrlich ascites carcinoma tumor. It is also involved in memory repair and improving memory performance by using an *in vivo* model.	Choudhary and Singh 2018; Chahal *et al.*, 2011
	Crude extract and its hexane fraction	This mixture exhibited antifertility effect in female rats (experiment *in vivo*).	Chahal *et al.*, 2011
	The ethanolic, hexane and n- butanol fraction	These fractions exhibited an *in vitro* amoebicidal activity	Chahal *et al.*, 2011
	Root Extracts	The root extract showed an antidiabetic activity.	Choudhary and Singh, 2018
P. maingayi Hook F.	Stem oil and ethyl acetate crude extract	The essential oil form this species showed an action against tyrosinase.	Chahal *et al.*, 2011
P. marginatum Jacq	Inflorescences	The inflorescence of this plant exhibited an action against larvae of *Aedes aegyptii*	Chahal *et al.*, 2011
	Ethanol extracts	The ethanol extract of this plant exhibited an action against *P. falciparum*	Mgbeahuruike *et al.*, 2017
P. multiplinervium C. DC	Ethanol extracts	The extract showed an action against *P. falciparum, T. cruzi, L. mexicana* et Aedes aegypti	Chahal *et al.*, 2011
P. nigrum L.	Methanol or chloroform extracts	These extracts improve memory performance and has an antiviral action (vesicular stomatitis virus and human para-influenza virus on HeLa)	Srivastava *et al.*, 2017; Priya and Saravana, 2017
P. obrutum Trel &Yunck	Ethanol extracts	These extracts showed an antiplasmodial (Action against *P. falciparum*) and cytotoxic activities	Mgbeahuruike *et al.*, 2017
P. ovatum Vahl	Essential oils and hydroethanol extracts	The extracts showed an action against *Bacillus subtilis* and *Candida tropicalis*	Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011
P. peltatum Jacq.	Leaf extracts	The leaf extracts showed an action against liver inflammation and analgesic activity	Pereira *et al.*, 2016
P. pulchrum C. DC	Ethanol, n-hexanolic and aqueous extracts	These extracts showed an antibacterial activity against *S. aureus, Streptococcus β hemolytic, B. areus, P. aeruginosa, E. coli* and an antifungal activity against *C. albicans*	Mgbeahuruike *et al.*, 2017

P. pyrifolium Vahl.	Methanol extracts	These extracts showed an antiparasitic activity against *P. falciparum*	Mgbeahuruike *et al.*, 2017
P. sarmentosum Roxb	Leaf extracts	The leaf extracts showed antimicrobial, antitubercular, antioxidant, antifungal, antibacterial, antimalarial, adulticidal, antitermite, larvicide, hypoglycaemic, anti-inflammatory, antipyretic, anticancer, antiplasmoid, antinoceptive, antiangiogenesis, atherosclerotic, antifeedant and cytotoxic activities	Seyyedan *et al.*, 2013
	Methanol extracts	These extracts have an action against gram positive (*S. aureus* and methicillin-resistant Staphylococcus aureus) and gram-negative bacteria, precisely *P. aeruginosa*. In addition, they have exhibited antioxidant and anti-tubercular activities.	Seyyedan *et al.*, 2013
	Chloroform extract	This extract has shown an Anti-malarial activity.	Chahal *et al.*, 2011
	1-nitrosoimino-2,4,5-trimethoxybenzene isolated from the root	This isolated molecule has shown antinociceptive and antioxidant activities.	Seyyedan *et al.*, 2013; Chahal *et al.*, 2011
	Methanol extract of the root	The methanol extract showed an anti-amoebic effects against *Entamoeba histolytica* infection in the caecum of mice.	Seyyedan *et al.*, 2013; Chahal *et al.*, 2011
	Ethanol extract	The ethanol extract showed an effect against early 4th instar larvae of *Aedes aegypti* mosquitoes and an adulticidal activity against female mosquitoes *Stegomyia aegypti*, a main vector of dengue haemorrhagic fever.	Seyyedan *et al.*, 2013; Chahal *et al.*, 2011
P. strigosum Trel. & Yunck	Ethanol extracts	The ethanol extract showed an effect against *L. amazonensis*	Mgbeahuruike *et al.*, 2017
P. stylosum Miq.	Methanol extract	The methanol extract exhibited an antibacterial activity against *S. aureus*, *Bacillus subtilis* and *E. coli*.	Mgbeahuruike *et al.*, 2017
P. tuberculatum Jacq.	Ethanol extracts	The ethanol extract showed antioxidant, antiviral, antifungal, antibacterial, insecticide activities.	Osorio *et al.*, 2013
P. truncatum Vell	n-Hexane extract	The n-hexane extract exhibited cytotoxic, antibacterial, antifungal activities and inhibitory effects on tumor necrosis factor-alpha production. Moreover, relaxant effects on vascular and tracheal smooth muscles were also reported.	Chahal *et al.*, 2011
P. xanthostachyum C. DC	Methanol extract	The n-hexane extract exhibited an activity against some parasites precisely *P. falciparum*, *T. cruzi*, *L. mexicana*.	Mgbeahuruike *et al.*, 2017

3.3. Bioactive compounds of Piper species

Amides, alkaloids, flavonoids, tannins, saponins, glycosides, terpenoids and phenolic compounds have been reported to be present in different organs (seeds, leaves and stem bark) of *Piper* species (Mgbeahuruike *et al.*, 2017). Although the literature indicates that the biological activities of *Piper* species are mainly related to alkaloids, particularly piperine. However, piperine is known to possess a variety of biological properties such as CNS stimulating, analgesic, antipyretic, antifeminant activities, etc. (Stojanovi'c-Radi *et al.*, 2019; Srivastava, 2017; Ahmad *et al.*, 2012). According to Chahal *et al.* (2011), piperine is cytotoxic to DLA and EAC cells and it showed cytotoxicity towards L929 cells. It also inhibits the development of solid tumours in mice induced with DLA cells and increases the life span of mice bearing an Ehrlich ascites carcinoma tumour (Chahal *et al.*, 2011)

Furthermore, it was reported that piperine can optimise the action or increase the bioavailability of many drugs (anti-epileptic drugs, sulphadiazine, tetracycline, amoxicillin, ampicillin, norfloxacin, ciprofloxcin, streptomicin, rifampicin, pyrazinamide, rosuvastatin, omeprazole, magnolol, theophylline, propanolol, carbamezepine, chlorzoxazone, fexofenadine, diclofenac, dexibuprofen, midazolam, resveratrol, nevirapine, vasicine, sparteine, tamoxifen, endoxifen, phenytoin, etc.), vaccines and nutrients (from vitamin B, β-carotene and micronutrients like selenium, etc.) (Stojanovi'c-Radi *et al.*, 2019; Srivastava, 2017; Ahmad *et al.*, 2012). The action of piperine on the bioavailability of certain enzymes or coenzymes (Coenzyme Q10), has also been reported in the literature. Piperine improves the bioavailability of curcumin, the main active ingredient of *Curcuma longa* (Stojanovi'c-Radi *et al.*, 2019). In addition, piperine is responsible for the flavour and aromatic power of *Piper*

species (Stojanovi'c-Radi *et al.*, 2019; Srivastava, 2017; Ahmad *et al.*, 2012).

Besides piperine, other alkaloids including piperlongumine, piplartine, guineensine, chabamide, pellitorine, have also been isolated from most *Piper* species and show biological actions (Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011). According to Mgbeahuruike *et al.* (2017), these bioactive compounds can improve the effectiveness of chemotherapeutic drugs with minimal systemic toxicity to normal cells in cancer therapy.

Several research studies listed alkaloids isolated from different *Piper* species with anti-cancer, anti-microbial, memory enhancer, anti-platelet activities, etc. These alkaloids are listed in the Table 3.

Table 3. Bioactive compounds and biological or pharmacological actions.

Bioactive compounds	Biological/pharmaological actions	References
Piperine; Piplartine (5,6-dihydro-1-[1-oxo-3-(3,4,5-trimethoxyphenyl)- 2-propenyl]-2(1H) pyridinone); 4, 5-dihydropiperine; Pipernonaline; (−)-Sesamin; Chabamide; (+)-Diayangambin; (+)-Arborone ; Piperlongumine; Piperarborenine C; Piperarborenine D; Dihydropiperlongumine; Dihydropiperlongumine; Aduncamide; Eupomatenoid-6 ; Conocarpan; Pellitorine; 1-[(4E, 9E)-10-(3,4-methylenedioxyphenyl)-4,9-nonadienoyl]pyrrolidine; 1-[(9E)-10-(3,4-methylenedioxyphenyl)-9-decenoyl]pyrrolidine; 1-[(2E, 4Z,9E)-10-(3,4methylenedioxyphenyl)-2,4,9-undecatrienoyl] pyrrolidine; 1-[(2E, 4Z,8E)-9-(3,4-mehtylenedioxyphenyl)-2,4,8-nonatrienoyl]pyrrolidine; R = H 3-(4-hydroxy-3, 5-dimethoxyphenyl) propanoylpyrrole; (2E, 4E)-N-[4-hydroxy-3-methoxyphenyl)ethyl]-2,4-decadienamide; (2E, 4E)-N-[2-(methylsufiny)ethyl)ethyl]-2,4-decadienamide	These molecules showed anticancer activities	Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011
Piperin; piperarborenine E; (−)-Sesamin; dihydropiperlongumine; 1-[(2E, 4Z,8E)-9-(3,4-mehtylenedioxyphenyl)-2,4,8-nonatrienoyl]pyrrolidine; dihydropiperlongumine; aduncamide	These molecules possess antimicrobial properties	Mgbeahuruike *et al.*, 2017
Piperine, Guineensine; (−) Sesamin ; Piperarborenine E; Piperlongumine have according Mgbeahuruike et al. (2017), anti-malarial properties while 4, 5-dihydropiperine has been reported as an antifungal agent. Cubebin; (−)-sesamin; Piperarborenine; E; 1-[(2E, 4Z,6E)-2,4,6-dodecatrienoyl] pyrrolidine	These molecules possess anti-tuberculosis properties	Mgbeahuruike *et al.*, 2017
Pipercide, Hinokinin, Cubebin and 1-[(2E, 4Z,6E)-2,4,6- dodecatrienoyl] pyrrolidine	These molecules showed an activity against leishmaniasis	Mgbeahuruike *et al.*, 2017
2E, 4E, 8Z-N-isobutyleicosatrienamide, pellitorin, trachyone, pergumidiene and isopiperolein B	These molecules showed an activity against *B. subtilis*, *B. sphaericus*, and *S.aureus* and *K. aerogenes* and *Chromobacterium violaceum*.	Chahal *et al.*, 2011
N-[7-(30,40-methylenedioxyphenyl)-2(Z),4(Z) heptadienoyl] pyrrolidine, (3Z,5Z)-N-isobutyl- 8-(30,40-methylenedioxyphenyl)- heptadienamide; 8(Z)-N- (12,13,14-trimethoxycinnamoyl)-3-pyridin-2-one; N-[10-(13,14-methylenedioxyphenyl)-7(E), 9(Z)- pentadienoyl]- pyrrolidine, arboreumine, N-[10- (13,14- methylenedioxyphenyl)- 7(E)-pentaenoyl]-pyrrolidine , its derivative N-[10-(13,14 methylenedioxyphenyl)-pentanoyl]- pyrrolidine and N-[10-(13,14 methylenedioxyphenyl)- 7(E), 9(E)-pentadienoyl]-pyrrolidine; pellitorine , _abdihydropiperine , piplartine, dihydropiplartine, cis-piplartine (or 8(Z)-N-(12,13, 14-trimethoxycinnamoyl)-_3-pyridin-2- one) and fagaramide; Prenyl methyl benzoate, chromenes and dihydrobenzopyran; (+)-conocarpan	These molecules showed an antifungal activity	Chahal *et al.*, 2011
Kaousine, apigenine dimethylether, and piperchabamide	These molecules showed an activity gainst *Plasmodium falciparum*.	Chahal *et al.*, 2011
piperovatine and piperlonguminine	These molecules showed an Anti-inflammatory	Chahal *et al.*, 2011
Chavicine, Pipperine	These molecules showed an antisickling activity	Gbadamosi, 2015
Chavibetol and allyl pyrocatechol	These molecules showed an antioxidant activity.	Chahal *et al.*, 2011
piperine, pipernonaline, piperoctadecalidine, piperlongumine, Chavicine and Chabamide	They have been reported to have memory enhancer and anti-platelet activities.	Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011
(+)-conocarpan; pyrrolidine, dihydropyridone and piperidine	These molecules showed an	Chahal *et al.*, 2011

	insecticidal activity	
sitosterol	This molecule inhibits TNFa (tumour necrosis factor-a)-induced expression of cell adhesion molecule ICAM-1 (intercellular adhesion molecule-1) on the surface of human umbilical vein endothelial cells (HUVECs).	Chahal *et al.*, 2011

Some compounds have broad biological or pharmacological potential like piperine. For instance, Piplartine (5,6-dihydro-1-[1-oxo-3-(3,4,5-trimethoxyphenyl)-2-propenyl]-2(1H) pyridinone), an amide alkaloid component of *Piper* species, has significant cytotoxic activity against tumour cell lines, in particular human leukaemia cell lines, such as HL-60, K562, Jurkat and Molt-4, as well as antifungal, anti-platelet aggregation, anxiolytic and antidepressant properties. Piplartine has also been studied for its genotoxicity and the induction of apoptosis by V79 cells and its mutagenic along with its recombinogenic potential in *Saccharomyces cerevisiae* and its treatment can also induce DNA strand breaks in V79 cells. In cell cycle analysis, Moreover, piplartine has also shown apoptosis in a dose-dependent manner, as observed by a decrease in mitochondrial membrane potential and an increase in internucleosomal DNA fragmentation as well as it has been proven to be cytotoxic to DLA and EAC cells or to L929 cells (Chahal *et al.*, 2011). Conocarpan as major compound of *Piper regnellii* displayed a variety of biological activities including anti-PAF, antifungal and insecticidal activity (Chahal *et al.*, 2011). Amides and alkaloids, often called piperazides, are present in large quantities in their fruits (Mgbeahuruike *et al.*, 2017). Table 4 shows origins of some alkaloids with biological activities.

Table 4. Origin biologically active alkaloids from Piper species.

Species	Alkaloids	References
Piper spp	N-[10-(13,14-methylenedioxyphenyl)-7(E),9(Z)- pentadienoyl]- pyrrolidine, arboreumine; N-[10- (13,14- methylenedioxyphenyl)- 7(E)-pentaenoyl]-pyrrolidine , its derivative N-[10-(13,14 methylenedioxyphenyl)-pentanoyl]-pyrrolidine and N-[10-(13,14 methylenedioxyphenyl)- 7(E),9(E)-pentadienoyl]-pyrrolidine; pellitorine , _abdihydropiperine , piplartine, dihydropiplartine, cis-piplartine (or 8(Z)-N-(12,13, 14- trimethoxycinnamoyl)-_3-pyridin-2- one) ; piperine, piperlongumine, guineensine, chabamide, pellitorine, pinoresinol, guineensine, fagaramide, etc.	Araujo *et al.*, 2018; Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011
P. aduncum L.	Dihydro piperlongumine	Mgbeahuruike *et al.*, 2017
P. arborescens Roxb	(+)-Arborone; Chabamide, (+)-Diayangambin; Piperarborenine C; Piperarborenine D; Piperarborenine E ;	Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011
P. betle L.	1-[(2E, 4Z,8E)-9-(3,4-mehtylenedioxyphenyl)-2,4,8-nonatrienoyl]pyrrolidine; chavibetol and allyl pyrocatechol	Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011
P. boehmeriaefolium, (Miq.) C.DC	Conocarpan; Pipernonaline; pellitorine; 1-[(4E, 9E)-10-(3,4-methylenedioxyphenyl)-4,9-nonadienoyl]pyrrolidine; 1-[(9E)-10-(3,4-methylenedioxyphenyl)-9-decenoyl]pyrrolidine; 1-[(9E)-10-(3,4-methylenedioxyphenyl)-9-decenoyl]pyrrolidine; 1-[(2E, 4Z,9E)-10-(3,4methylenedioxyphenyl)-2,4,9-undecatrienoyl] pyrrolidine; 1-[(2E, 4Z,9E)-10-(3,4methylenedioxyphenyl)-2,4,9-undecatrienoyl] pyrrolidine; R = H 3-(4-hydroxy-3, 5-dimethoxyphenyl) propanoylpyrrole; (2E, 4E)-N-[4-hydroxy-3-methoxyphenyl) ethyl]-2,4-decadienamide; (2E, 4E)-N-[2-(methylsufiny)ethyl)ethyl]-2,4-decadienamide	Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011
P. capense L.	4, 5-dihydropiperine; Kaousine, , apigenine dimethylether, and piperchabamide A	Mgbeahuruike *et al.*, 2017
*P. chaba*Hunter	(−)-Sesamin	Mgbeahuruike *et al.*, 2017
P. cubeba L	Cubebin; hinokinin; 1-[(2E, 4Z,6E)-2,4,6-dodecatrienoyl] pyrrolidine	Mgbeahuruike *et al.*, 2017
P. galeatum (Miq.) C.DC.	cyclostachine-A, piperine, piperolein-B; 1-(30-hydroxy-50-methoxycinnamoyl)-piperidine	Chahal *et al.*, 2011
*P. guineense*Schum et Thonn	Piperine; 4, 5-dihydropiperine, guineensine Piperarborenine E, Piperlongumine, 1-[(2E, 4Z,6E)-2,4,6-dodecatrienoyl] pyrrolidine, Chavicine, Pipperine	Mgbeahuruike *et al.*, 2017; Gbadamosi 2015
P. hispidum Sw	N-[7-(30,40-methylenedioxyphenyl)-2(Z), 4(Z) heptadienoyl] pyrrolidine; (3Z,5Z)-N-isobutyl- 8-(30,40-methylenedioxyphenyl)- heptadienamid	Chahal *et al.*, 2011
P. hostmannianum (Miq.) C.DC	Prenyl methyl benzoate, chromenes and dihydrobenzopyran	Chahal *et al.*, 2011

P. longum L.	Piperine, Pipernonaline; Piperarborenine E; piperoctadecalidine, and piperlongumine,	Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011
P. nigrum L.	Chavicine; 4, 5-dihydropiperine; piperine; Pipercide; piperetine Piperlongumine; 1-[(2E, 4Z,6E)-2,4,6-dodecatrienoyl] pyrrolidine; 2E, 4E, 8Z-N-isobutyleicosatrienamide ; pellitorin, trachyone, pergumidiene and isopiperoleinB trachyone	Srivastava *et al.*, 2017; Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011
P. ovatum Vahl	piperovatine and piperlonguminine	Mgbeahuruike *et al.*, 2017; Chahal *et al.*, 2011
P. regnelli (Miq.) C. DC.	Aduncamide, Conocarpan; Eupomatenoid-5	Mgbeahuruike *et al.*, 2017; Chahal*et al.*, 2011
P. retrofractum Vahl	Cubebin , Pipernonaline; 1-[(2E, 4Z,8E)-9-(3,4-mehtylenedioxyphenyl)-2,4,8-nonatrienoyl] pyrrolidine; 1-[(2E, 4Z,6E)-2,4,6-dodecatrienoyl] pyrrolidine; (−)-Sesamin	Mgbeahuruike *et al.*, 2017
P. sarmentosum Roxb	Cubebin	Mgbeahuruike *et al.*, 2017
P. tuberculatum Jacq	8(Z)-N- (12,13,14-trimethoxycinnamoyl)-3-pyridin-2-one	Chahal *et al.*, 2011

In addition, phenolic compounds such as flavonoids (flavones or isoflavones), phenolic acids (vanillic, caffeic, ferulic, protocatechuic and rosmarinic acid), tannins, stilbenes and lignans have also been reported from *Piper* species. Most *Piper* species contain flavonoids such as quercetin, kaempferol, apigenin and luteolin or 5-O-caffeoylquinic acid, 4-p-coumaroylquinic acid, 5-p-coumaroylquinic acid, chavibetol and hydroxychavicol. The literature shows that phenolic compounds are widely studied and reported to have beneficial effects on human health, such as anti-cancer, anti-microbial and anti-mutagenic properties (Mgbeahuruike *et al.*, 2017).

Furthermore, essential oils are also among the major phytocompounds from *Piper* species. Although their composition varies depending on the species and their origins (Lima *et al.*, 2019). It should be noticed that post-harvest processing can also influence the chemical composition of essential oils of *Piper* species. Moreover, the work of Lima *et al.* (2019), revealed that fresh leaves of *P. klotzschianum* present high contents of germacrene D, bicyclogermacrene, (*E*)-caryophyllene, compared to dried leaves. The same is true for fresh leaves of *P. arboreum*, of which analyses reported by Lima *et al.* (2019), showed that they have high contents of bicyclogermacrene.

The major chemical constituents of the essential oils of some *Piper* species is presented in Table 5.

Table 5. Origin biologically active alkaloids from Piper species**.**

Species	Constituents of essential oils	Percentage contents	References
P. acutilimbum C.DC	γ-eudesmol, Germacrene B, α-muurolol, β-longipinene, 1-*epi*-cubenol	5-7.5	Araujo *et al.*, 2018
Piper amalago L.	Elemene, limonene, β-copaen-4-α-ol, eudesmol, amorphene	20-40	Araujo *et al.*, 2018
	E-caryophyllene, bicyclogermacrene, caryophyllene oxide, zingiberene, epi-α-cadinol, n-hexyl-benzoate, β-phellandrene, germacrene D, camphene, limonene, spathulenol, α-cadinol, murolene, (E)-methyl geranate, nerolidol, α-muurulene, germacrene D-4-ol, β-cedrene, sabinene, myrcene, γ-muurolene	10-19	Araujo *et al.*, 2018
		5-9	Araujo *et al.*, 2018
	α-phellandrene, spathulenol	10-20	Araujo *et al.*, 2018
P. arboreum Aublet	Bicyclogermacrene; *E*)-caryophyllene	15-28	Lima *et al.*, 2019
P. bellidifolium Yunck	*E*)-nerolidol; aromadendrene, α-copaene	10-20	Araujo *et al.*, 2018
P. borbonense (Miq) C.D.C	Spathulenol, Bicyclogermacrene	16-27	Soidrou *et al.*, 2019
	α-Bisabolol, (*E*,*E*)-α-Farsenene	24-32	Soidrou *et al.*, 2019

P. capens L	Pinene, *β*-caryophyllene	12-32	Soidrou *et al.*, 2019
	β-pinene	33-59	Soidrou *et al.*, 2019
	β- pinene	50	Wansi *et al.*, 2019
	β- pinene	61,4	Wansi *et al.*, 2019
P. consanguineum Kunth	γ-eudesmol, γ-cadinene	11-18	Araujo *et al.*, 2018
P. dilatatum Rich	Germacrene D, bicyclogermacrene	30-34	Lima *et al.*, 2019
P. durilignum C.DC	Germacrene D, limonene	10-11	Araujo *et al.*, 2019
P. fimbriulatum C.DC	*E*)-caryophyllene, germacrene D	11.3-12.8	Lima *et al.*, 2019
P. gaudichaudianum Kunth	*E*)-Caryophyllene and bicyclogermacrene	7-8	Lima *et al.*, 2019
P. galeatum (Miq.) C.DC.	b-elemene, d-elemene, a-humulene, b-caryophyllene, a-copaene, a-ionone, 10-(acetylmethyl)-3-carene, dihydrocarvyl acetate, 1-p-menthen-8-yl acetate and linalyl acetate	nd	Chahal *et al.*, 2011
	b-sitosterol,	nd	Chahal *et al.*, 2011
P. goesii Yunck	Germacrene D	28.9	Lima *et al.*, 2019
P. guineense Schum et Thonn	germacrene D	20-25	Wansi *et al.*, 2019
	Limonene, β-caryophyllene, linalool	15,8-41.8	Wansi *et al.*, 2019
	Limonene, *Z, E*)-α- farsenene	19.7-28.7	Wansi *et al.*, 2019
P. hispidum Sw	Germacrene D, δ-3-carene, (*E*)-caryophyllene	13.8-33.9	Chahal *et al.*, 2011
	germacrene D, *E*)-caryophyllene, δ-cadinene	10.6-18.8	Lima *et al.*, 2019
P. klotzschianum C.DC	*E*)-caryophyllene, bicyclogermacrene, (*E*)-caryophyllene	14.6-22.8	Lima *et al.*, 2019
	Bicyclogermacrene, β-Pinene, *E*)-caryophyllene	11.9-27.2	Lima *et al.*, 2019
P. maingayi Hook F.	β-caryophyllene, δ-cadinene	22.6-39.6	Hashim, 2018
	Caryophyllene and α-cedrene	8.4-26.2	Hashim, 2018
P. magnibaccum C.DC	Germacrene D and β-caryophyllene	8.5-40.8	Hashim 2018
P. nigrum L.	α-selinene, β-selinene	14.6-16.5	Wansi *et al.*, 2019 ; Srivastava, 2017
	δ-3-carene, limonene, sabinene, β-caryophyllene	11.2-18.5	Wansi *et al.*, 2019; Srivastava, 2017
	δ-3-carene, %), β-caryophyllene	14.4-36	Wansi *et al.*, 2019
P. rupestres Kunth	germacrene D	15.0	Lima *et al.*, 2019
P. sarmentosum Roxb	(*E*)-caryophyllene	13.9	Lima *et al.*, 2019
	Spathulenol, myristicin, β-caryophyllene, (E,E)-farnesol	10.5-20.9	Seyyedan *et al.*, 2013
P. stylosum Miq.	Aromadendrene, sabinene, caryophyllene	11.5-26.6	Salleh *et al.*, 2019
	aromadendrene	6.7-18.8	Salleh *et al.*, 2019

4. Conclusion

The present work has enabled us to compile data on the uses, biological activities and chemical composition of *Piper* species. The species from *Piper* genus are widely used both as a condiment and as medicines to relieve several health problems. The leaves of some species are used as a wrapper for seasoning certain traditional dishes while other species are used to prevent bad breath but also as insecticide, aphrodisiac, appetite stimulant or against the bites of venomous

animals. Several biological activities are reported in the literature concerning extracts of the *Piper* genus and some isolated compounds from different species. Alkaloids are the most important group of metabolites of the *Piper* genus and piperine is the most mentioned alkaloid in the literature. We suggest that future studies could scientifically justify the uses of *Piper* species that have not been subject to in-depth scientific investigations, or identify their active principles and then determine their mechanisms of action. Studies aimed at highlighting probable synergies of action between different active ingredients of *Piper* species are needed.

5. References

Ahmad, N., Faza, H., Haider Abbasi, H. B., Farooq, S., Ali, M. and Ali Khan, A. M. 2012. Biological role of *Piper nigrum* L. (Black pepper): A review. *Asian Pacific Journal of Tropical Biomedicine*, S1945-S1953.

Amujoyegbe, O. O., Idu, M., Agbedahunsi, J. M. and Erhabor, J. O. 2016. Ethnomedicinal survey of medicinal plants used in the management of sickle cell disorder in Southern Nigeria. *Journal of Ethnopharmacology*, 185: 347–360.

Angone, A. R. R. R., Aworet, Samseny S. C. and Mve Mba, M. E. 2014. Quelques propriétés des huiles essentielles des plantes médicinales du Gabon. Phytothérapie Lavoisier SAS, 2014: 1-6.

Araujo- Baptista, L. M., Rondón Rivas, M. E., Cruz, Tenempaguay T. R. E., Guayanlema Chávez, G. J. D., Vargas Córdova, C. A. and Morocho Zaragocin, S. V. 2019. Antimicrobial activity of the essential oil of *Piper amalago* L. (PIPERACEAE) collected in coastal Ecuador. *Pharmacology*online, 3(3): 15-27.

Bastos, M., Houly, R., Conserva, L., Andrade, V., Rocha, E. and Lemos, R. 2011. Antimicrobial and wound healing activities of *Piper hayneanum*. *Journal of Chemical and Pharmaceutical Research*, 3: 213-222.

Bekele, D., Petros, B., Tekie, H., and Asfaw, Z. 2014. Larvicidal and adulticidal effects of extracts from some indigenous plants against the malaria vector, *Anopheles Arabiensis* (Diptera: Culicidae) in Ethiopia. *Journal of Biofertilizers and Biopesticides*, 5(2): 1-8.

Bezerra, D. P., Pessoa, C., Moraes, M. O. D., Silveira, E. R., Lima, M. A. S., Martins Elmiro, F. J. and Costa-Lotufo, L. V. 2005. Antiproliferative effects of two amides, piperine and piplartine, from *Piper* species. *Zeitschrift für Naturforschung*. 60: 539-543.

Bobasa, E. M., Biniyam, G., Alemu, S. T. Shibiru T, Berkessa,, Moti M. Y., Gemechu, Fanta F. G., Fufa, Gemechu G. Z., Cari, W.ote A., Rike. 2018. Antimalarial activity of selected Ethiopian medicinal plants in mice. *Journal of Pharmacy and Pharmacognosy Research*, 6 (1): 57-64.

Bosquiroli, L. S., Demarque, D. P., Rizk, Y.S., Cunha, M. C., Marques, M. C. S., Maria de Fátima, C. M., Kadri, M. C., Carollo, C. A. and Arruda, C.C. 2015. In vitro anti-leishmania infantum activity of essential oil from *Piper angustifolium***.** *Revista Brasileira de Farmacognosia*, 25: 124-128.

Calderón, A. I., Romero, L. I., Ortega-Barría, E., Solís, P. N., Zacchino, S., Gimenez, A., Pinzón, R., Cáceres, A., Tamayo, G., Guerra, C., Espinosa, A., Correa, M. and Gupta, M. P. 2010. Screening of Latin American plants for antiparasitic activities against malaria, Chagas disease, and leishmaniasis. *Pharmacology and Biology*, 48(5): 545-53.

Chahal, J., Ohlyan, R., Kandale, A., Walia, A., Puri, S. 2011. Introduction, phytochemistry, traditional uses and biological activity of genus *Piper:* A review. *International Journal of Current Pharmaceutical Review and Research*, 2(2): 130-144.

Choudhary, N. and Singh, V. 2018. A census of *P. longum*'s phytochemicals and their network pharmacological evaluation for identifying novel drug-like molecules against various diseases, with a special focus on neurological disorders. *PLoS ONE*, 13(1): e0191006.

Conde-Hernández, L. A. and Guerrero-Beltrán, J. Á. Total phenolics and antioxidant activity of *Piper auritum* and *Porophyllum ruderale*. *Food Chemistry*, 142: 455-60.

Cruz, S. M., Cáceres, A., Álvarez, L., Morales, J., Apel, M. A., Henriques, A. T., Salamanca, E., Giménez, A., Vásquez, Y. and Gupta, M. P. 2011. Chemical composition of essential oils *of Piper jacquemontianum* and *Piper variabile* from Guatemala and bioactivity of the dichloromethane and methanol extracts. *Revista Brasileira de Farmacognosia*, 21 (2011): 587-593.

De Feo, V. 2003. Ethnomedical field study in northern Peruvian Andes with particular reference to

divination practices. *Journal of Ethnopharmacology*, 85(2-3): 243–256.

Debebe, E., Dessalegn, T. and, Melaku, Y. 2018. Chemical constituents and antioxidant activities of the fruits extracts of P*iper capense. Bulletin of the Chemical Society of Ethiopia*, 32(1): 167-174.

Diame, G. L. A. 2010. Ethnobotany and ecological studies of plants used for reproductive health: A case study at Bia biosphere reserve in the western region of Ghana. Final report: Ethnobotany and ecology of plants for reproductive health, University of Cape Coast Ghana. 2010. Pp. 125.

Estevez, Y., Castillo, D., Pisango, M. T., Arevalo, J., Rojas, R., Alban, J., Deharo, E., Bourdy, G. and Sauvain, M. 2007. Evaluation of the leishmanicidal activity of plants used by Peruvian Chayahuita ethnic group. *Journal of Ethnopharmacology*, 114(2): 254-259.

Fankam, A. G., Kuete, V., Voukeng, I. K., Kuiate, J. R. and Pages, J. M. 2011. Antibacterial activities of selected Cameroonian spices and their synergistic effects with antibiotics against multidrug-resistant phenotypes. *BMC Complementary and Alternative Medicine*, 11 (104): 1-11.

Ganesh, P., Suresh, Kumar K. R. and, Saranraj, P. 2014. Phytochemical analysis and antibacterial activity of Pepper (*Piper nigrum* L.) against some human pathogens. *Central European Journal of Experimental Biology*, 3(2): 36-41.

Garavito, G., Rincón, J., Arteaga, L., Hata, Y., Bourdy, G., Gimenez, A., Pinzón, R. and Deharo, E. 2006. Antimalarial activity of some Colombian medicinal plants. *Journal of Ethnopharmacology*, 107(3): 460-462.

Gbadamosi, I. T. 2015. An inventory of ethnobotanicals used in the management of sickle cell disease in Oyo State, Nigeria. *Botany Research International*, 8(4): 65-72.

Gontijo C. D., Alves do Nascimento, M. F., Rody, H. V. S., Magalhães, R. A., Margalho, L. F., Brandão, G. C. and de Oliveira, A. B. 2021. In vitro antiplasmodial activity, targeted LC–MS metabolite profiling, and identification of major natural products in the bioactive extracts of *Palicourea* and *Psychotria* species from the Amazonia and Atlantic Forest biomes, Brazil. *Metabolomics*, 17(9): 81-86.

Hashim, N. A. B. 2018. *Phytochemicals and bioactivities of Piper maingayi HK. F., P. magnibaccum C.DC and P. caninum blume species*. Doctoral thesis, Universiti Teknologi Malaysia.

Iwu, M. M. 2014. Pharmacognostical profile of selected medicinal plants In: Handbook of African Medicinal Plants CRC Press.

Li, Y., Zhang, J. J., Xu, D. P., Zhou, T., Zhou, Y., Li, S. and Li, H. B. 2016. Bioactivities and Health Benefits of Wild Fruits. *International Journal of Molecular Sciences*, 17(1258): 1-27.

Lima, C. N. F, Ferreira de Lima, L., Bezerra, Correia C. D., Tavares de Sousa, M.achado S., Pereira de Sousa, J., Soares, Santos S. E., Gyllyandeson, de AraújoA. D., Alencar de Menezes, I. R., Francisco Bezerra, F., Felipe, C., Melo Coutinho, H. D. and Kernto, M. R. 2020. Systematic review: Medicinal use and scientific elucidation of the *Piper* genus for the treatment of symptoms and inflammatory diseases. *Journal of Medicinal Plants Research*, 14(2): 62-72.

López, A., Ming, D. S. and Towers, G.N. 2002. Antifungal activity of benzoic acid derivatives from *Piper lanceaefolium. Journal of Natural Products*, 65: 62-64.

Maryo, M., Nemomissa, S. and Bekele, T. 2015. An ethnobotanical study of medicinal plants of the Kembatta ethnic group in Enset-based agricultural landscape of Kembatta Tembaro (KT) Zone, Southern Ethiopia. *Asian Journal of Plant Science and Research*, 5(7): 42-61.

Mgbeahuruike, E. E., Yrjönen, T., Vuorela, H., Holm, Y. 2017. Bioactive compounds from medicinal plants: Focus on *Piper* species. *South African Journal of Botany*, 112: 54–69.

Ngbolua, K. N., Inkoto, C. L.., Mongo, N. L., Ashande, C. M., YB. Masens, Y. B. and Mpiana, P. T. 2019. Étude ethnobotanique et floristique de quelques plantes médicinales commercialisées à Kinshasa, République Démocratique du Congo. *Revue Marocaine des Sciences Agronomiques et Vétérinaires*, 7(1): 118-128.

Njeri, L. K., Njagi, E. N. M. 2017. Anti-diabetic activity in mice of *Piper Capence* used traditionally in the management of diabetes mellitus in Kenya. *Journal of Diabetes and Metabolism*, 8: 737.

Nkeoua, G. and Boundzanga, G. C. 1999. Données sur les Produits forestiers non ligneux en République du Congo. Projet GCP/INT/679/EC Programme de partenariat – EC – FAO, République du Congo.

Osorio, J. R., Colmenares, Dulcey D. A. J., Mora, E. E., Sánchez, A.ndica R. 2013. Extraction, chemical composition and antimicrobial activity of the essential oils of Pipilongo (*Piper tuberculatum*) using supercritical carbon dioxide. Exactas Universidad del Valle, Facultad de Ciencias Naturales, 17: 45-56.

Otero, R., Núñez, V., Barona, J., Fonnegra, R., Jiménez, S., Osorio, R., M. Saldarriaga, M. and Dıaz, A. 2000. Snakebites and ethnobotany in the northwest region of Colombia: part III: neutralization of the haemorrhagic effect of *Bothrops atrox* venom. *Journal of Ethnopharmacology*, 73: 233-241.

Pandey, P., Singhal, D., Khan, F. and Arif, M. 2021. An i*n Silico* screening on *Piper nigrum*, *Syzygium aromaticum* and *Zingiber officinale roscoe* derived compounds against SARS-CoV-2: A drug repurposing approach. *Biointerface Research in Applied Chemistry*, 11(4): 11122-11134.

Pedersen, M. E., Metzler, B., Stafford, G. I., Van Staden, J., Jäger, A. K. and Rasmussen, H. B. 2009. Amides from *Piper capense* with CNS Activity –A Preliminary SAR Analysis. *Molecules, 14*: 3833-3843.

Pereira, F. G., Dias dos Santos, P. R., Guimarães, E. F., Auxiliadora, C. K. M. and Coelho Kaplan M. 2016. Composition of the essential oils from leaves of *Piper lepturum* Kunth (C.DC.) var. lepturum and *Piper lepturum* var. angustifolium (Miq.) Yunck. from Brazil. *Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas*, 15 (2): 88-93.

Priya, N. C. and Saravana Kumari, S. P. 2017. Antiviral activities and cytotoxicity assay of seed extracts of *Piper longum* and *Piper nigrum* on human cell lines. *International Journal of Pharmaceutical Sciences Review and Research*, 41(1): 197-202.

Reshmi, S. K., Suganya, S. and Devi, P. 2010. Isolation of piperdine from *Piper nigrum* and its antiproliferative activity. *Journal of Medicinal Plants Research*, 4(15): 1535-1546.

Rusaati, B. I. W., Gendusa, A. P., Joo, S. H., Park, J. W., Masumbuko, N. C., Iragi, K. G., Ngbolua, K. T. N., Furaha, M. A., Rolly, N. K. and, Kang, J. W. 2021. A systematic review of antimalarial medicinal plants in Democratic Republic of the Congo. *Bois et Forêts des Tropiques*, 347: 11-27.

Salehi, B., Amiruddin, Zakaria Z. Z., Gyawali, R., Salam, Ibrahim I. A., Rajkovic, J., Zabta Shinwari, Z. K., Tariq Khan, T., Sharifi-Rad, J., Ozleyen, A., Turkdonmez, E., Valussi, M., Boyunegmez, Tumer T. T., Monzote, Fidalgo F. L., Martorell, M. and, William Setzer, W. N. 2019. Review piper species: A comprehensive review on their phytochemistry, biological activities and applications. *Molecules,* 24: 1364-1368.

Salehi, B., Zakaria, Z. A., Gyawali, R., Ibrahim, S. A., Rajkovic, J., Shinwari, Z. K., Khan, T., Sharifi-Rad, J., Ozleyen, A., Turkdonmez, E., Valussi, M., Tumer, T. B., Fidalgo, M. L., Martorell, M. and Setzer, W. N. 2019. *Piper* species: A comprehensive review on their phytochemistry, biological activities and applications. *Molecules*, 24(7):1364.

Salleh, W. M. N. H. W., Ahmad, F. and Khong H.K 2014. Chemical composition of Piper stylosum Miq. and piper ribesiodes wall essential oils, and their antioxidant, antimicrobial and tyrosinase inhibition activities. *Boletin Latinoamericano y del Caribe de Plantas Medicinales y Aromaticas*, 13(5): 488-497.

Salleh, W. M. N. W., Athirah Hashim, A. N., Khamis, S. 2019. Chemical constituents and lipoxygenase inhibitory activity of *Piper stylosum* MIQ. *Bulletin of the Chemical Society of Ethiopia*, 33(3): 587-592.

Sawadogo, R. W., Schumacher, M., Teiten, M. H. and Diederich, D. M. 2012. Traditional West African pharmacopeia, plants and derived compounds for cancer therapy. *Biochemical Pharmacology*, 84: 1225–1240.

Seyyedan, A., Yahya, F., Kamarolzaman, M. F. F., Suhaili, Z., Desa, M. N. M., Khairi, H. M., Somchit, M. N., Fatimah, C. A., Teh, L. K., Salleh, M. Z. and Zakaria, Z. A. 2013. Review on the ethnomedicinal, phytochemical and pharmacological properties of *Piper sarmentosum*: scientific justification of its traditional use. *Tang Humanitas Medecine*, 3(3): 1-32.

Siddiqui, B. S., Gulzar, T., Mahmood, A., Begum, S., Khan, B., Rasheed, M., Afshan, F., Rajput Tariq, R. M. 2005. Phytochemical studies on the seed extract of *Piper nigrum* Linn., *Natural Product Research: Formerly Natural Product Letters*, 19(7): 703-712.

Silva, M. A., da Fialho, S. N., Martinez, L. D. N., Facundo, V. A., da Silva, F. B., Kaplan, M. A. C., Marques, A. M., Bastos, I. D. S., Orlandi, P. P., Pessoa, C. D. Ó, Abreu, B. B. D., Oliveira, F. D. C. E. D., Teles, C. B. G. and Kuehn, C. C. 2020. Chemical composition and biological activities of the leaf extract and essential oil from *Piper alatabaccum* (Piperaceae) fruits. *South American Journal of Basic*

Education, Technical and Technological, 7(1): 163-185.

Soidrou, S. H., Farah, A., Satrani, B., Ghanmi, M., Lachkar, M. and, Himidi H. A. 2019. Chemical composition, antioxidant and antimicrobial activity of essential oils isolated from two piper species collected in Comoros. *International Journal of Pharmacognosy and Phytochemical Research*, 11(4): 315-322.

Sonibare, M. A., Moody, J. O. and Adesanya, E. O. 2009. Use of medicinal plants for the treatment of measles in Nigeria. *Journal of Ethnopharmacology*, 122: 268-272.

Srivastava, A. K. and Kumar Singh, K. V. 2017. Biological action of *Piper nigrum* - the king of spices. *European Journal of Biological Research*, 7(3): 223-233.

Stojanovi´c-Radi,´ Z., Pej˘ci´, M., Dimitrijevi´, M., Aleksi´c, A., Nanjangud Anil Kumar, N. A. V, Salehi, B., Cho, W. C. and Sharifi-Rad, J. 2019. Piperine- a major principle of black pepper: A review of its bioactivity and studies. *Applied Sciences*, 9: 4270.

Tang, G. H., Chen, D. M., Qiu, B. Y., Sheng, L., Wang, Y. H., Hu, G. W., Zhao, F. W., Ma, L. J., Wang, H., Huang, Q. Q., Xu, J. J., Long, C. L. and Li, J. 2011. Cytotoxic amide alkaloids from *Piper boehmeriaefolium*. *Journal of Natural Products*, 74(1):45-49.

Torres-Pelayo, V. R., Fernandez, M. S., Carmona-Hernandez, O., Molina-Torres, J. and Lozada-Garcia, A. J. 2016. A phytochemical and ethno-pharmacological review of the genus Piper: As a potent bio-insecticide. *Research & Reviews. Research Journal of Biology*, 4(2): 51104-114.

Traoré, M. C. 2006. Etude de la phytochimie et des activités biologiques de quelques plantes utilisées dans le traitement traditionnel de la dysménorrhée au Mali. Doctoral thesis, University of Bamako. Doctoal dissertation, University of Bamako.

Tsai, I. L., Lee, F. P., Wu, C. C., Duh, C. Y., Ishikawa, T., Chen, J. J., Chen, Y. C., Seki, H., Chen, I. S. 2005. New cytotoxic cyclobutanoid amides, a new furanoid lignan and anti-platelet aggregation constituents from *Piper arborescens*. *Planta Medica*, 71(6): 535-542.

Umoh, I., Oyebadejo, S., Bassey, E. and Uko, U. 2013. Chronic consumption of *Abelmoschus esculentus* and *Piper guineense* induce testicular-toxicity in Wistar rats, histopathological finding. *Advances in Life Science and Technology*, 14: 98-106.

Valadeau, C., Pabon, A., Deharo, E., Albán-Castillo, J., Estevez, Y., Lores, F. A., Rojas, R., Gamboa, D., Sauvain, M., Castillo, D. and Bourdy, G. 2009. Medicinal plants from the Yanesha (Peru): evaluation of the leishmanicidal and antimalarial activity of selected extracts. *Journal of Ethnopharmacology*, 123(3): 413-22.

Voukeng, I. K., Kuete, V., Dzoyem, J. P., Fankam, A. G., Noumedem, J. A. K., Kuiate, J. R. and Marie, J. 2012. Antibacterial and antibiotic-potentiation activities of the methanol extract of some Cameroonian spices against Gram-negative multi-drug resistant phenotypes. *BMC Research Notes*, 5 (299): 1-10.

Wamba, B. E. N., Ghosh, P., Mbaveng, A. T., Bhattacharya, S., Debarpan, M., Depanwita, S., Mitra, Saunak S. M., Kuete, V. and Murmu, N. 2021. Botanical from *Piper capense* Fruit Can Help to Combat the Melanoma as Demonstrated by *In Vitro* and *In Vivo* Studies. *Evidence-Based Complementary and Alternative Medicine*, 1-15.

Wang, Y. H., Morris-Natschke, L. S., Yang, J., Niu, H. M., Long, C. L. and Lee, K. H. 2014. Anticancer principles from medicinal *Piper* Plants. *Journal of Traditional and Complementary Medicine*, 4(1): 8-16.

Wansi, J. D., Sewald, N., Nahar, L., Martin, C. and Sarker, S. S. 2019. Bioactive essential oils from the Cameroonian rain forest: A review - Part II. *Trends in Phytochemical Research*, 3(1): 3-52.

Xiang, C. P., Shib, Y. N., Liub, F. F., Lia, H. Z., Zhang, J. Y., Yang, C. R. and Xua, M. 2016. A survey of the chemical compounds of *Piper* spp. (Piperaceae) and their biological activities. *Natural Product Communications*, 11(9): 1403-1408.