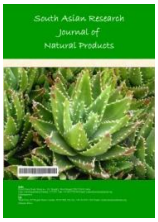

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A Mini Review on the Phytochemistry and Pharmacology of *Aframomum alboviolaceum* (*Zingiberaceae*)

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Authors' contributions

The present study was carried out in collaboration among all authors. Authors CLI, KNN and PTM wrote the first draft of the manuscript, Authors JTK and FLL collected information on plants bioactivity. Authors DSTT and DDT collected information on plant phytochemistry. The selection of the final list of references was made by Author JTK and CLI in order to include or exclude any potential articles according to the various inclusion and exclusion criteria outlined above. All authors read and approved the final manuscript.

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ABSTRACT

Background and Aims: Given the importance of finding a new Improved Traditional Medicine (ITM) based on medicinal plants, we reviewed the traditional uses, phytochemical composition, biological properties and toxicity of *Aframomum alboviolaceum* (*Zingiberaceae*), a plant species widely used in traditional African medicine as nutraceutical.

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Study Design: Multidisciplinary advanced bibliographic surveys and dissemination of the resulted knowledge.
Methodology: A non-exhaustive literature review for relevant articles and books published in the last twelve years was conducted in January 2021 on various electronic databases: Science Direct, Pubmed, Web of Science, Scopus, Google Scholar, POPLINE and System for Information on gray Literature in Europe. As search strategy, the scientific name of this plant was used as a keyword, with the terms phytochemistry and Pharmacology.
Results: In this literature review the results obtained show that *A. alboviolaceum* is rich in essential oils with a high concentration of β-pinene (51,6% This plant is also rich in macronutrients such as Carbohydrate, Lipids, Proteins, Ash, Magnesium, Phosphorus and Calcium. The presence of these compounds, such as essential oils, gives it anti-sickling, anti-oxidant, antimicrobial, anti-cancer and anti-malaria properties. Given the presence of the monoterpenes identified in this species including β-pinene (51,6%) which has already proven its anti-inflammatory properties by inhibiting the expression of pro-inflammatory molecules (IL-1β, IL-6 and TNF-α), cyclooxygenase-2 (Cox-2) and activation of the nuclear transcription factors Kappa B (NF-KB), we anticipate that *A. alboviolaceum* could be effective against inflammatory as well.
Conclusion: To our knowledge anti-inflammatory activity of this plant species and its effects on cell division have not been tested. With this in mind, we would like to evaluate the anti-inflammatory activity *in vitro* and *in vivo* of this plant species harvested in Democratic Republic of the Congo but also its genotoxic activity in our further studies.

Keywords: Edible plant; natural products; bioactivity; ethnopharmacology; nutraceuticals.

1. INTRODUCTION

The inflammatory is the response of living, vascularized tissue to aggression. This response involves phenomena of immunity, resistance to aggression [1]. It can be classified as either acute or chronic, and involves a cascade of biochemical events comprising the local vascular system, the immune system, and different cell types found in the injured tissue [2]. Inflammation is a protective measure taken by the body to eliminate harmful stimuli [3]. However, the use of anti-inflammatory substances can be an effective tool in the therapeutic treatment of diseases. In this context, medicinal plants and their isolated compounds are used worldwide in traditional medicine to treat various diseases [4-7] as well as inflammatory conditions such as lung and skin inflammations. In the ongoing search for new bioactive natural products against inflammation, essential oils and their isolated components, namely monoterpenes, have been reported [3]. *A. alboviolaceum* (*Zingiberaceae*) is widely distributed throughout Africa [8]. Its ethnobotanical uses are well reported [9-11]. The analysis of *A. alboviolaceum* extracts revealed the presence of several compounds like flavonoids, iridoids, phenolic acids, anthocyanins, coumarins, anthraquinones, tannins, alkaloids, tri-terpenes in this vegetal species [10,12]. It has been demonstrated that *A. alboviolaceum* extracts possess several biological properties including antimalarial, anti-sickling, antimicrobial, anticancer, and antioxidant properties [13-15]. Inflammation involves serious complications such as increased blood flow, high cell metabolism, and vasodilation, release of soluble mediators, fluid extravasation and cell influx [2]. It is now widely accepted that inflammation plays a major role in the pathogenesis and physiopathological consequences of sickle cell disease. The increase in the number of leukocytes (hyperleukocytosis) and their state of activation are markers of the pro-inflammatory state associated with sickle cell disease [16]. The fact that extracts of *A. alboviolaceum* have already shown anti-sickle cell activity [13,17], may help to anticipate that it also has anti-inflammatory properties. Indeed, the presence in this plant of monoterpenic compounds such as β-pinene and 1,8-cineole which have already shown anti-inflammatory properties by inhibiting the expression of pro-inflammatory molecules (IL-1β, IL-6 and TNF-α), cyclooxygenase-2 (Cox-2) and activation of Kappa B nuclear transcription factors (NF-KB) [3] helps us to anticipate that this species would have some potency or activity against inflammations and therefore this plant is a potential candidate in the fight against inflammations. In this literature review, we present data on *A. alboviolaceum* and its main compounds that could justify their use in the treatment of inflammatory diseases in traditional medicine in the Democratic Republic of Congo. In addition, the objective of this study is to review the literature on the traditional use, phytochemistry, biological properties and toxicity

of *A. alboviolaceum*. The results obtained in this literature review will enable us to guide our future work to develop an improved traditional herbal medicine to combat inflammatory diseases.

2. METHODOLOGY

2.1 Search Strategy

A non-exhaustive literature searches for relevant articles and books published in the last twelve years was conducted in January 2021 on various electronic databases: Science Direct, Pubmed, Web of Science, Scopus, Google Scholar, POPLINE and System for Information on gray Literature in Europe. As search strategy, the scientific name of this plant was used as a keyword, with the terms phytochemistry and Pharmacology. The chemical structures of *A. alboviolaceum* naturally occurring compounds were drawn using ChemBioDraw Ultra 12.0 software package.

2.2 Eligibility Criteria

In this literature mini-review, the selection of included studies was limited to studies with the inclusion criteria of: (i) Phytochemistry data of *A. alboviolaceum*, (ii) Ethno pharmacological uses of this plant species in the past and clinical application, (iii) Pharmacological properties of *A. alboviolaceum* in human, in vitro assay, or in vivo model. In the present research, the studies obtained were excluded based on several criteria such as unreliably extracted data, only-abstract available, (iv) Overlapped data sets, reviews, thesis, editorials and book chapters.

2.3 Screening Methods

In this mini-review, a manual search was conducted to identify references more relevant to this study. The selection of the final list of references was made by three independent reviewers from our research team in order to include or exclude any potential articles according to the various inclusion and exclusion criteria outlined above. The selection of the full text was carried out by three other authors. Disagreements were resolved by consensus with the authors through exchange of ideas and consultation.

2.4 Quality Assessment

Uploaded articles have been classified into two categories, in vivo studies and in vitro studies to assess the risk of bias.

2.5 Data Extraction

Two authors voluntarily extracted data from the included studies. The extracted data were based on the first author, year of publication, plant parts used, extraction methods and detailed results of in vitro tests or in vivo experiments (types of tests, animal strains, microorganisms, doses, concentration of reference molecules and plant extracts). References in other languages have been translated into English by a member of our research team.

3. RESULTS AND DISCUSSION

In the present study we had uploaded a total of 80 articles talking about this plant and synonyms, after this initial search we then selected 62 articles included for filtering after eliminating duplicates. Subsequently, 45 articles were included for full-text filtering. Finally, 30 articles were included for the editorial staff of our journal. These different articles were characterized according to the activities of *A. alboviolaceum* as detailed in the following selections.

3.1 Botanical Description

A. alboviolaceum (syn; *A. latifolium*) is an herbaceous plant with creeping rhizomes relatively deeply buried, throwing up stems to 3 m high. Leaves stalk less with narrowly lanceolate blade, hairless, but with a slightly scabrous margin of about 20x4.5 cm. Ligule bifid, acutely lobed, about 1 cm long and 2 mm wide at the base. Inflorescence in pauciflorous, solitary or paired spikes at base of stems; stalk a few cm (0.6 in.) short, so that the flower appears at or slightly above ground level. Lower subtending bracts green, upper ones reddish-tinged and reaching 20-30x15 mm. Calyx spathacate, laterally split, 3 cm (0.5 in.) long. Corolla pink to pale-purple, acutely lobed, ca. 4 cm (0.5 in.) long. Beautiful of the same hue, spreading, obtusely rounded at the top, with sinuous margins. Staminal connective with almost no median lobe, truncate, hairless ovary, red and black fruit [8]. The Fig. 1 gives the different parts *A. alboviolaceum.*

3.2 Traditional Uses

The traditional use of *A. alboviolaceum* according contry and used part (s) are given in the Table 1.

3.3 The Microscopic Features

The microscopic study of *A. Alboviolaceum* revealed the presence of fibers, non-glandular

hairs, paracytic stomata, fragments of spiral bundles, fragments of punctuated vessels, parenchyma with numerous starch grains, secreting hairs, as well as lignified fibers [12]. The microscopic features of *A. alboviolaceum* are shown in Fig. 2 below.

Fig. 1. A (Seeds), B (Flower), C (Leaves) and D (rhizome) of *A. alboviolaceum*

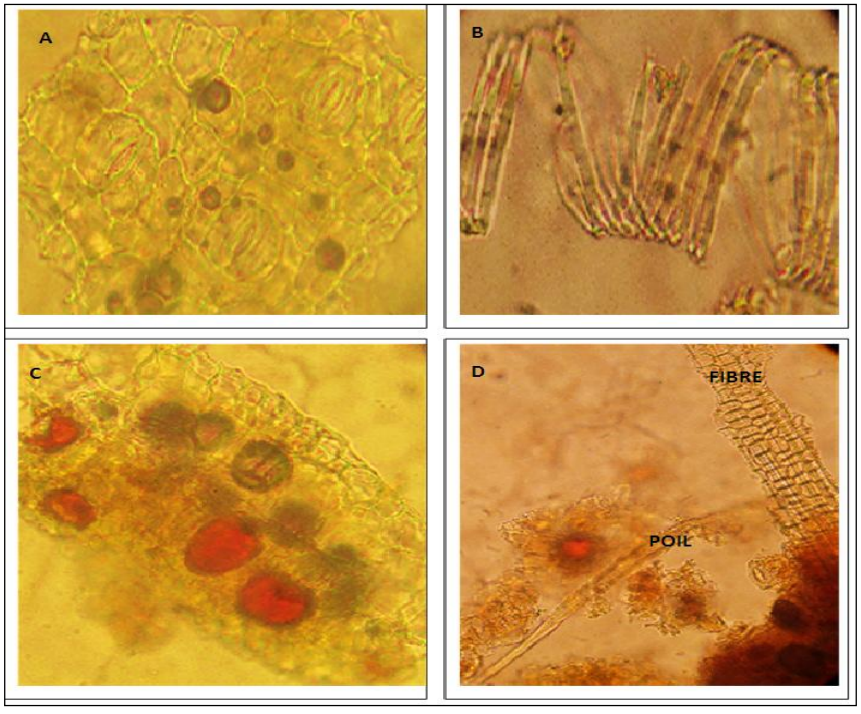

Fig. 2. Microscopic features of *A. alboviolaceum*: (A) Paracytic stomata, (B) fragments of spiral vessels, (C) fragments of suber and (D) fibers and secretory hairs [12]

3.4 Phytochemical Constituents

Inkoto et al. [12] investigated the phytochemical composition of *A. alboviolaceum* leaves by Thin Layer Chromatography. Thin layer chromatographic analysis revealed the presence of various compounds like flavonoids, iridoids, phenolic acids, anthocyanins, coumarins, anthraquinones, tannins, and the absence of alkaloids in this species. Djeussi et al. [10] reported that fruits of *A. alboviolaceum* contain anthocyanins, flavonoids, alkaloids, polyphenols and tri-terpenes. It has also been shown that the leaves essential oils extract of this plant species contain 1,8-cineole . Its exceptionally contain terreyol, bergamotols 1 and 2, β-bisabolol [24]. Kunle and Egharevba [25] reported the major components of *A. alboviolaceum* including 12-dien-16-oate, (E)-labda-8(17), 15-epoxylabd-8(17), 12-diene-15, methyl (E)-14, 16-dial; (E)-β-17-epoxy-labd-12-ene-15 and16-dial. The hydro-distilled leaf and rhizome oils of *A. alboviolaceum* were analyzed by GC and GC/MS. Seventeen and twenty-nine compounds were identified in the leaf and rhizome oils respectively. The major compounds in the leaf oil were beta-pinene (58.5%), beta-caryophyllene (14.2%), alpha-pinene (7.3%) and trans-sabinyl acetate (5.6%). The rhizome oil was dominated by beta-pinene (23.8%), 1,8-cineole (22.5%), alpha-terpineol (5.0%), gamma-terpinene (4.9%), alpha-pinene (4.6%) and limonene (4.6%).

3.4.1 Macronutriments

In D.R. Congo, proximate analysis of *A. alboviolaceum* revealed the presence of carbohydrate (52.37% with 3.86% of dietary fiber); lipids (10.58%); humidity (30.68%); protein (5.19%), ash (1.18%), magnesium (0.29%), phosphorus (0.14%), calcium (0.72%). The calculated energy value is 325.46 Kcal / 100 g [26]. Certain trace elements, such as magnesium, play several roles in the body. Among them, others are like co-factors, such as magnesium [27]. The presence of these elements in the plant reinforces its biological properties.

Table 2 gives the chemical composition of essential oils from leaves *A. alboviolaceum.*

Fig. 3 gives the different identification methods of the essential oil compounds of *A. alboviolaceum.*

This figure shows that three methods have been used in identification of essential oil compounds of this plant. Among these methods, identification method based on comparison of mass spectrum with literature data (1) and identification method based on comparison of retention index with those of published data (2) are the most used with at least 43% each.

Fig. 4 gives major essential oil compounds identified from the *A. alboviolaceum* leaves

It results in the present figure that among the secondary metabolites identified in the different parts of this plant, 11 are predominantly β-pinene (D: 55%), followed respectively by (E)-β-Cariophyllene (H: 13%), Sabinene (C: 8%), α-Pinene (B: 7%), α-Humulene (I: 5%), β-Phellandrene (F: 3%), Myrtenyl acetate, Germacrene D and Caryopphyllene (G, J and K: 2% each), α-Thujene and Limonene (A and E: 1% each).

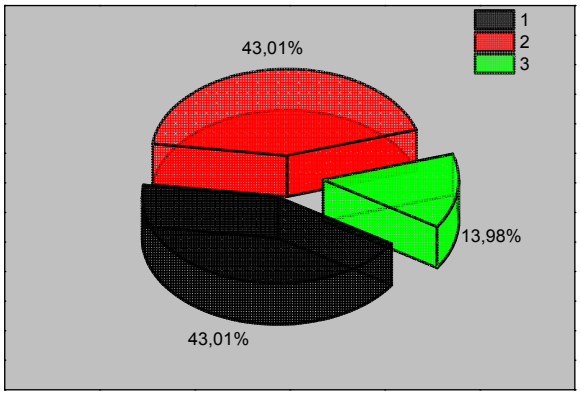

Fig. 3. Different identification methods of the essential oil compounds

Table 1. Summary of the traditional use of *A. alboviolaceum*

Country	Part use	Utilization	Reference
Cameroon	All parts	Diuretic, anti-malaria, anti-helminthic, anti-parasitic and fever	[10,18,19]
Ivory Coast	Rhizomes	As a Food	[20]
Nigeria	Fruits	Women, especially pregnant women and children	[21]
India	Roots and Leaves	Dysmenorrhea, fever, headache and cough	[22]
DRC	Leaves	Vision problems, fever, headache, gastritis, cough, amoebic dysentery and haemorrhoids	[11, 23]
		hypertension, malaria, headaches, myoma, gastritis and pruritis, to relieve headaches, pruritus and filarial	[9]

Table 2. Chemical composition of essential oils from leaves of *A. alboviolaceum* [20]

N°	Compounds	Method of identification	%	N°	Compounds	Method of identification	%
01	α-Thujene	1 and 2	1.0	21	Myrtenol	1 and 2	0.2
02	α-Pinene	1, 2 and 3	6.7	22	Bornyl acetate	1, 2 and 3	0.1
03	Camphene	1, 2 and 3	0.1	23	*cis*-Sabinyl acetate	1 and 2	0.1
04	Sabinene	1, 2 and 3	7.6	24	*trans*-Sabinyl acetate	1 and 2	0.3
05	β-Pinene	1, 2 and 3	51.6	25	Myrtenyl acetate	1 and 2	1.7
06	Myrcene	1, 2 and 3	0.6	26	α-Copaene	1 and 2	0.2
07	α-Phellandrene	1 and 2	0.1	27	β-Bourbonene	1 and 2	0.2
08	α-Terpinene	1 and 2	0.2	28	(E)-β-Caryophyllene	1, 2 and 3	12.3
09	*p*-Cymene	1, 2 and 3	0.3	29	α-Humulene	1, 2 and 3	5.1
10	Limonene	1, 2 and 3	1.0	30	*allo*-Aromadendrene	1 and 2	0.1
11	β-Phellandrene	1 and 2	3.1	31	Germacrene D	1 and 2	1.7
12	(*E*)-β-Ocimene	1, 2 and 3	0.1	32	α-Selinene	1 and 2	0.1
13	Y-Terpinene	1 and 2	0.4	33	Valencene	1 and 2	0.3
14	*cis*-Sabinene hydrate	1 and 2	0.1	34	gamma-Cadinene	1 and 2	0.1
15	Terpinolene	1 and 2	0.2	35	$^{\delta}$-Cadinene	1 and 2	0.4
16	*trans*-Sabinene hydrate	1 and 2	0.1	36	Caryophyllene oxide	1 and 2	1.6
17	*trans*-Pinocarveol	1 and 2	0.1	37	Humulene epoxide II	1 and 2	0.4
18	Terpinen-4-ol	1, 2 and 3	0.7	38	Caryophylla-4(12),8 (13) dien-5-ol	1 and 2	0.1
19	α-Terpineol	1, 2 and 3	0.2	39	*Epi*-α-muurolol	1 and 2	0.4
20	1,8-cineole	1 and 2	0.2	40	14-hydroxy-9-epi (*E*)-Caryophyllene	1 and 2	0.1
Total	99,7%						

Legend: 1: Identification method based on comparison of mass spectrum with literature data, 2: identification method based on comparison of retention index with those of published data; 3: Identification method based on co-injection with authentic sample.

3.5 Bioactivities of *A. alboviolaceum*

Table 3 *gives the* Model system used, pharmacological action and plant part of biologically active compounds isolated or identified from *A. alboviolaceum.*

3.5.1 Anti-sickling activity

The anti-sickling activity of the ethanolic extract and dichloromethane fraction of the leaves of *A. alboviolaceum* was evaluated by the Emmel test on the blood of sickle cell subjects [13,17]. The results obtained in this study reported that all tested extracts possess a high anti-sickling activity. Certain mineral elements, including magnesium, play an important role in sickle cell disease. Magnesium, in addition to being a co-factor of enzymes, reduces the number of abnormal erythrocytes in sickle cell patients and improves the hydration of red blood cells [27]. Apart from secondary metabolic changes such as anthocyanins, which are endowed with anti-sickling properties, the anti-sickling activity obtained in the leaf extracts of this species could also be due to the presence of this trace element.

3.5.2 Anti-microbial activity

Labdanes isolated from fruits extract of this plant showed a modest *in vitro* activity against a chloroquine sensitive *Plasmodium falciparum* strain [15]. Abreu and Noronha [28] demonstrated the antimicrobial activity of volatile compounds from the rhizomes of *A. alboviolaceum*. Extracts of this plant showed interesting antibacterial activity spectra against gram-negative bacteria [10]. Kwazou et al. [14] reported that the essential oil of this plant exhibited a significant antifungal activity against *Aspergillus flavus*.

In another study, Ogunmola and Amusat [29] reported that peperitone, the essential oil identified in the leaves of this plant showed strong antimicrobial potential against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Candida albicans*, *Escherichia coli*, *Bacillus subtilis* and *Aspergillus niger* at 100%, 50% and 25% and moderate inhibition at 12.5 and 6.25%.

3.5.3 Cytotoxicity and anticancer activity

The work of Kuete et al. [30] showed that species of the genus *Aframomum* including *A. alboviolaceum* showed remarkable toxicity activity towards cancer cells. In the recent study on the cytotoxicity of *A. alboviolaceum* towards multi-factorial drug resistant cancer cell lines reported cytotoxic potential of *Aframomum* species and highlights the good activity of *A. alboviolaceum* on sensitive and drug-resistant cancer cell lines.

3.5.4 Anti-oxidant activity

The antioxidant activity was demonstrated by Bongo et al. [13]. These authors reported the ethanolic extracts of *A. alboviolaceum* showed IC_{50} values < 100 µg/mL in the ABTS test.

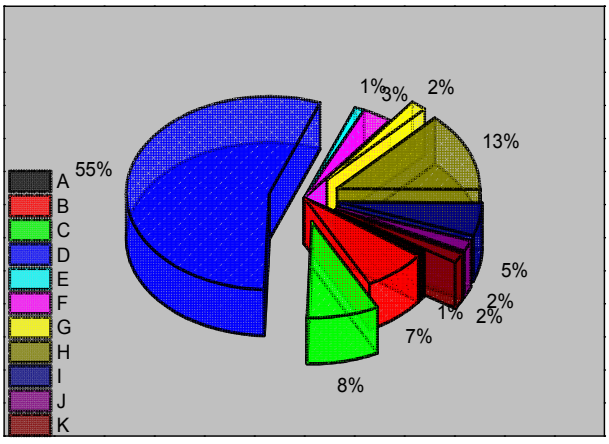

Fig. 4. Major essential oil compounds identified from *A. alboviolaceum* leaves

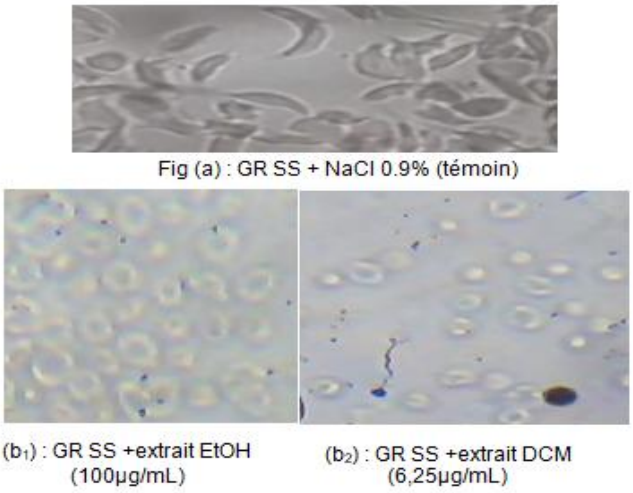

Fig. 5. *Antisickling test Microscopy*: untreated erythrocytes (a); erythrocytes treated with EtOH extract 100µg/mL (b1) and DCM fraction 6.25µg/mL (b2) of *A. alboviolaceum* [13]

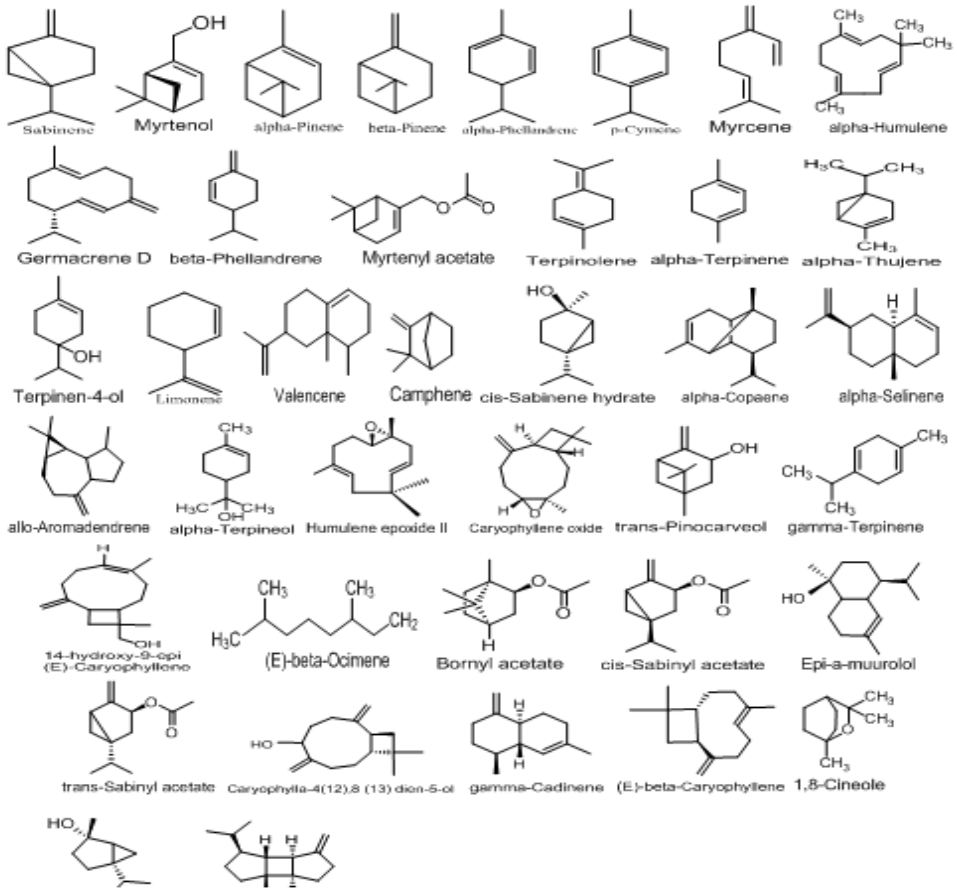

Fig. 6. Chemical structure of compounds identified from the essential oils of *A. alboviolaceum* leaves

Table 3. Model system used, pharmacological action and plant part of biologically active compounds isolated or identified from *A. alboviolaceum*

Parts	Extract or molecules	System model	Biological activity	Reference
Leaves	Ethanolic extract and dichloromethane fraction	Sickle cell	Anti-sickling activity	[13,17]
Fruits and leaves	Labdanes	Plasmodium falciparum	Anti-malaria activity	[15]
Rhizomes	-	*Pseudomonas aeruginosa, Staphylococcus aureus*, *Candida albicans*, *Escherichia coli, Bacillus subtilis* and *Aspergillus niger*	Antibacteria activity	[28].
Seeds	Essential oils	Aspergillus flavus	Anifongical activity	[14]
Leaves and seeds	-	Cancer cell lines	Anticancer activity	[29]
Leaves	Ethanolic extract, dichloromethane fraction		Antioxidant activity	[13]

4. CONCLUSION

In this study, it was a question of carrying out a bibliographical study on the traditional uses, phytochemical data, biological properties and toxicity of the plant *A. alboviolaceum* used in traditional African medicine as a nutraceutical. The various bibliographical data obtained in this study show that:

- Traditionally this plant is used in most African customs;
- *A. alboviolaceum* is rich in essential oils with a high concentration of β-pinene (51,6%).
- *A. alboviolaceum* is rich in macronutrients such as Carbohydrate, Lipids, Protein, Ash, Magnesium, Phosphorus and Calcium.

The presence of phyto-compounds, such asessentials oils, phenolic acids and anthocyanin, would justify its anti- anti-sickling, anti-oxidant, antimicrobial, anti-cancer and anti-malaria power demonstrated by several authors. To our knowledge, the anti-inflammatory activity of this plant has not been evaluated. It is in this perspective that we wish to evaluate its anti-inflammatory activity in vitro and in vivo of this plant but also its genotoxic activity.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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