**Plant**
2018; 6(3): 53-59
http://www.sciencepublishinggroup.com/j/plant
doi: 10.11648/j.plant.20180603.11
ISSN: 2331-0669 (Print); ISSN: 2331-0677 (Online)

**Review Article**

# *Isolona hexaloba* Engl. & Diels: Phytochemistry, Pharmacology and Future Directions: A Mini-Review

**Lengbiye Moke[1], Gédéon Bongo[1], Kongumbeti Goga[1], Jeff Iteku[1], Inkoto Liyongo[1], Claudine Tshiama[3], Ngunde Ngunde[1], Koto-te-Nyiwa Ngbolua[1], Pius Mpiana[2, *]**

[1]Department of Biology, University of Kinshasa, Kinshasa, Democratic Republic of the Congo

[2]Department of Chemistry, University of Kinshasa, Kinshasa, Democratic Republic of the Congo

[3]Teaching and Administration in Nursing Care, Higher Institute of Medical Techniques, Kinshasa, Democratic Republic of the Congo

## Email address:

pt.mpiana@unikin.ac.cd (P. Mpiana)

[*]Corresponding author

## To cite this article:

Lengbiye Moke, Gédéon Bongo, Kongumbeti Goga, Jeff Iteku, Inkoto Liyongo, Claudine Tshiama, Ngunde Ngunde, Koto-te-Nyiwa Ngbolua, Pius Mpiana. *Isolona hexaloba* Engl. & Diels: Phytochemistry, Pharmacology and Future Directions: A Mini-Review. *Plant*. Vol. 6, No. 3, 2018, pp. 53-59. doi: 10.11648/j.plant.20180603.11

**Received**: June 9, 2018; **Accepted**: September 30, 2018; **Published**: October 29, 2018

**Abstract:** The aim of this review was to provide an updated knowledge on the Phytochemistry and Pharmacognosy of *Isolona hexaloba* Engl. & Diels. A literature search was conducted to obtain information about the phytochemistry and pharmacognosy of *Isolona hexaloba* from various electronic databases (PubMed Central, PubMed, Science Direct and Google scholar). The scientific name of this plant species was used as a keyword for the search, along with the terms phytochemistry and pharmacognosy. The chemical structures of the *Isolona hexaloba* and *Isolona genus* naturally occurring compounds were drawn using ChemBioDraw Ultra 12.0 software package. The findings revealed that this plant is traditionally used as a purgative and in treating sores, smoke from the bark as a strained muscle relaxant, infectious and parasitic pathologies, loss of appetite, rheumatism, intestinal cramps, headache, back pains, sexual weakness. This plant is reported to possess various biological properties like antioxidant, antimicrobial, antihyperglycemic, antileishmanial and antimalarial. These properties are due to the presence of numerous naturally occurring phytochemicals like flavonoids, alkaloids, tannins, saponins, reducting sugars, coumarins, terpenes and steroids. The present mini-review revealed that *Isolona hexaloba* Engl. & Diels is a good candidate for Tropical Plants Screening Research program for the development of lead compounds against genetic and parasitic diseases such as the evaluation of the anthelminthic activity.

**Keywords:** *Isolona hexaloba*, Phytochemistry, Pharmacognosy, Anthelminthic Activity

## 1. Introduction

### *1.1. Background*

The World Health Organization (WHO) recognizes that traditional and complementary medicines (TCM) are a vital part of the global health care system [1]. In Africa, it is estimated that over 80% of the population continues to rely on medicinal plant for their primary health care needs [2]. In the Democratic Republic of the Congo (DRC), medicinal plants represent the key product for both urban and rural populations for their health care needs because the costs of conventional drugs are often unaffordable. These medicinal plants have found to have therapeutic value which fights against major health problems [3]. *Isolona hexaloba* (*I. hexaloba*) Engl. & Diels is a tree of the *Isolona* genus Engl. which belongs to Annonaceae family, Monodoroideae sub-family and is used in DRC and Republic of the Congo as a purgative and in treating sores, and the smoke from the bark as a strained muscle relaxant. However, it was reported to contain various secondary metabolites such as the alkaloids in the root bark [10] and terpenes [4]. Some different species of the *Isolona* genus (Annonaceae) have been extensively studied from both chemical and pharmacological points of view as *I. cauliflora*

[8], *I. ghesquiereina* [9], *I. zenkiri, I. pilosa* [10] and some compounds identified in several *Isolona* species displayed the antimalarial and antitrypanosomial properties [11]. The present review aimed to provide updated information on the phytochemistry and pharmacognosy of this useful medicinal plant species and its integration in a future program of Tropical Plants Screening Research for anthelminthic properties mainly on animals.

### *1.2. Botany and Geographical Distribution*

*I. hexaloba* Engl. & Diels (figure 1) is a tree of 10 – 40 m high, with a trunk of 60 cm diameter. It grows in dense and humid forests of tropical Africa and has a soft bark of 1 cm of thickness. *I. hexaloba* is characterized by the horizontal positions of its flower, and its ovoidal to sub globular fruits with bumps and longitudinal ribs. Leaves are 6 – 30 cm long, 3 – 10 cm large and sub coriaceous [12]. *Isolona* genus belongs to the Annonaceae family, in Monodoroideae sub-family. This genus has 20 species which are originated from tropical Africa and Madagascar. Among the 20 species of this genus, most of species possess medicinal virtues. *I. hexaloba* Engl. & Diels is found in tropical and sub-tropical regions namely in DRC, Gabon, Cameroon, Ghana, Tanzania and Republic of the Congo.

***Figure 1.*** *Leaves of Isolona hexaloba Engl. & Diels.*

### *1.3. Ethnobotany*

*I. hexaloba* Engl. & Diels is a multipurpose plant with high traditional and medicinal uses for the maintenance of free health life. Traditionally, this plant is used in DRC as a purgative and in treating sores, smoke from the bark is used as a strained muscle relaxant [8] and infectious and parasitic pathologies [15], loss of appetite, rheumatism, intestinal cramps, headache, back pains and sexual weakness [16]. However, in the Ivory Coast *I campanulata* Engl. & Diels is used as an aphrodisiac and for increasing fertility in sterile women [6-7]. In contribution to systematic chemical studies of African medicinal plants, an extensive survey of literature revealed the structure determination of the methyl 7-(5',5'-dimethyltetrahydrofuran-2'-yl)-3-methylocta-2,6-die neoate (cazolobine), a new sesquiterpene isolated from the root of *I hexaloba* Engl. & Diels while the major secondary metabolite group identified was the alkaloids as reported in several studies [10].

## 2. Method

A literature search was conducted in order to obtain information on the phytochemistry and pharmacognosy of *I. hexaloba* Engl. & Diels from various electronic databases (PubMed Central, PubMed, Science Direct and Google scholar). The scientific name of this plant species was used as the keyword for the search, along with the terms phytochemistry and pharmacognosy. Different chemical structures of the *I. hexaloba* Engl. & Diels naturally occurring compounds were drawn using ChemBioDraw Ultra 12.0 software package.

## 3. Results and Discussion

### *3.1. Phytochemistry*

The phytochemistry screening of *I. hexaloba* Engl. & Diels revealed the presence of various secondary metabolites such as the alkaloids found in the root bark [10]. The column chromatography of dichloromethane extract of *I. hexaloba* root yielded cazolobine (Sesquiterpene) ($C_{16}H_{26}O_3$) as pale yellow viscous oil [4]. Many phyto-constituents were identified from *Isolona* genus and it is considered as a source of bisbenzylisoquinolines alkaloids and contains also monomeric, dimeric mono- as well as diprenylatedindoles and most of these compounds were isolated from the stem bark and root bark of the plant. Amongst these isolated compounds, were found alkaloids notably cycleanin, isochondodendrine, mono-O-methylisochondodendrine, norcycleanine, curine, guattegaumerine, atherospermidine, liriodenine, lysicamine, 5- (3-oxo-but-1-enyl)- indole, 5-formyl-indole [5], as well as tannins, flavonoids, terpenoids (cazolobine), phytosterols (campesterol, ß-sitosterol and stigmasterol) and fatty acids (linoleic acid, palmitic acid and stearic acid) have already been isolated from *I. hexaloba* Engl. & Diels [24] as shown below (table 1).

***Table 1.*** *Geographical Distribution, pharmacological activity and used plant part of 19 biologically active compounds isolated from Isolona genus (Annonaceae).*

| Biologically active compounds | Species name | Used part of the plant | Pharmacological activity | Geographical distribution | Reference |
|---|---|---|---|---|---|
| methyl 7-(5',5'-dimethyltetrahydrofuran-2'-yl)-3-methylocta-2,6-dieneoate (cazolobine) | *Isolona hexaloba* | Root | muscle relaxant [4] | Gabon | [4] |
| Isochondodendrine | *Isolona hexaloba* | Root+stem | antihypertensive activity [23]. | DRC | [36] |
| | *Isolona ghesquieri* | Stem bark | - | Madagascar | [44] |
| | *Isolona pilosa* | Bark | - | Ghana | [31] |
| Isopiline | *Isolona pilosa* | Stem bark | - | Ghana | [31] |
| Lirinidine | *Isolona zenkeri* | Leaf | melanogenesis inhibitory activity in B16 melanoma cells [20]. | Taiwan | [39] |
| Liriodenine | *Isolona campanulata* | Stem bark | Analgesic [29], Antibacteriel [29], Anticrustacean [41], antifungic [29], antileishmanial [27], Trypanocidal [28], antimicrobial, antioxidant, antitumor activities [19]. | Ghana | [31] |
| | *Isolona maitlandii* | Bark | - | Tanzania | [32] |
| Lysicamine | *Isolona maitlandii* | Stem bark | Anticrustacean [41], cytotoxic [35]. melanogenesis inhibitory activity in B16 melanoma cells [40] | Venezuela | [32] |
| | *Isolona maitlandii* | Stem bark | | Ghana | [32] |
| N-methylcrotsparine | *Isolona zenkeri* | Leaf | - | DRC | [36] |
| Norcycleanine | *Isolona hexaloba* | Root+stem bark | - | DRC | [36] |
| (R)-5-(3-Methyl-1,3butadienyl)-3-(2,3-epoxy-3methylbutyl)-indole (+)-Nomuciferine | *Isolona pilosa* | Trunk bark | Antileishmanial [28], antidepressive effect [30], CD45 protein tyrosine phosphatase inhibitior [33], antimicrobial, antioxidant, antitumor activities [19]. | Ghana | [31] |
| Oleic acid (R)-3-hydroxy-3-methyl-2-[6-(3-methyl-2buthyl)-indole-3-yl]butyl ester | *Isolona maitlandii* | Stem bark | - | Ghana | [32] |
| Oliverine | *Isolona campanulata* | Stem bark | antimicrobial, antioxidant, antitumor activities [19]. | Cameroon | [42] |
| Oliverine N-oxide | *Isolona campanulata* | Bark | - antimicrobial, antioxidant, antitumor activities [19]. | Ghana | [31] |
| Palmitic acid (R)-3hydroxy-3-methyl-2-[6-(3-methyl-2-butenyl)-indole-3-yl] butyl ester | *Isolona maitlandii* | Stem bark | melanogenesis inhibitory activity in B16 melanoma cells [20] | Ghana | [32] |
| Pellitorine | *Isolona maitlandii* | Stem bark | - | Ghana | [32] |
| (+)-Pronuciferine | *Isolona pilosa* | Trunk bark | melanogenesis inhibitory activity in B16 melanoma cells [20] | Ghana | [31] |
| Roemerine | *Isolona pilosa* | Bark+leaf | CD45 protein tyrosine phosphatase inhibitior [33], Cytotoxic [43] Vascular activity [21]. | Ghana | [37] |
| | | Stem bark | - | Tanzania | [31] |
| Unonopsine | *Isolona maitlandii* | Stem bark | Antiprotozoal Activity [22], Antileishmanial activity [45] | Ghana | [32] |
| Zenkerine | *Isolona pilosa* | Trunk bark | Antiplasmodial activity [18]. | Ghana | [31] |
| | *Isolona zenkeri* | Leaf | - | Taiwan | [36] |

Different chemical structures of various compounds isolated from the *Isolona* genus (Annonaceae) are given in Figure 2.

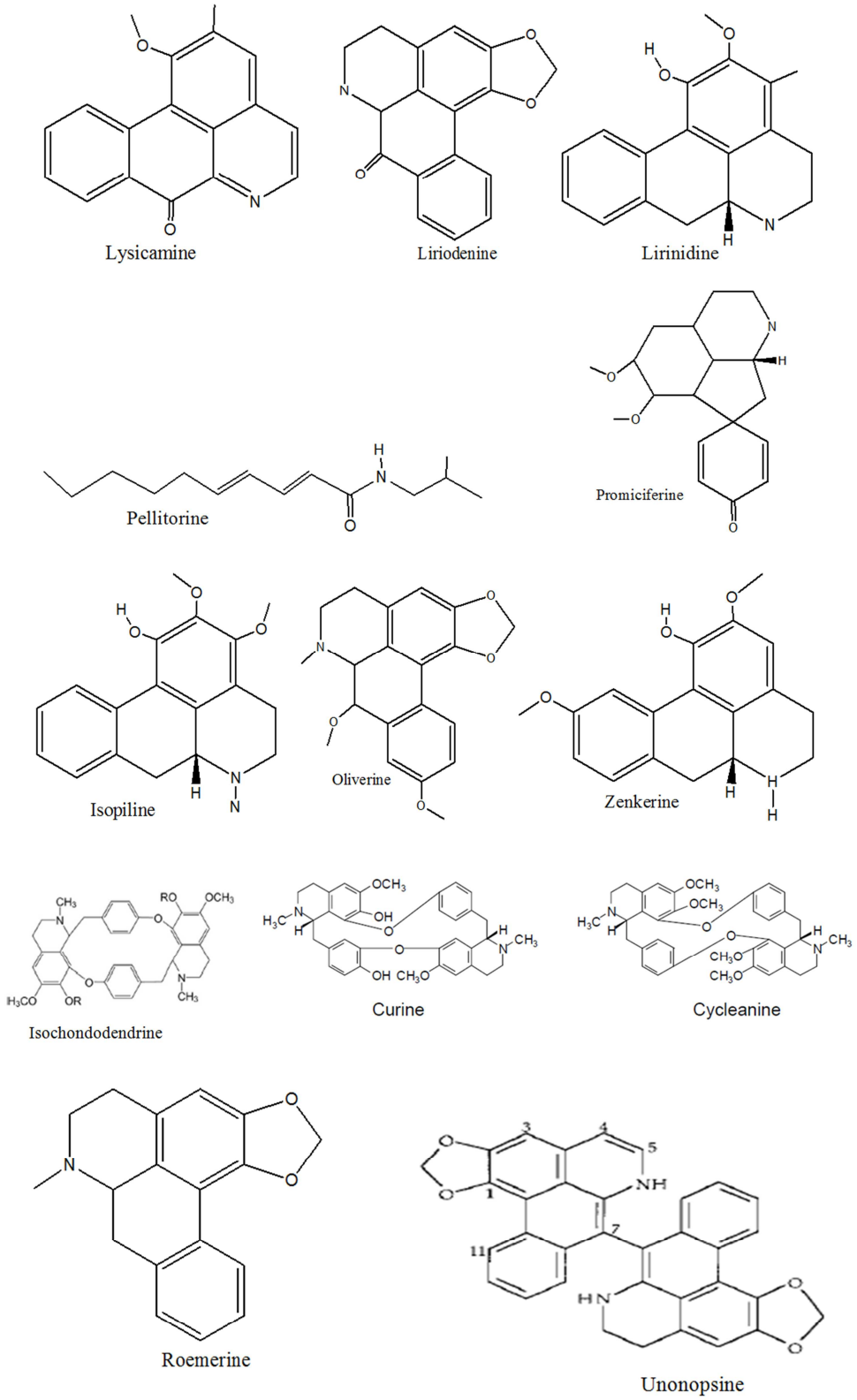


***Figure 2.*** *Different chemical structures of active compounds isolated from Isolona* genus *Engl. & Diels.*

### *3.2. Pharmacological Activities of I. Hexaloba Engl. & Diels.*

#### *3.2.1. Antileishmanial Activity*

The African family plant which has the best antileishmanial effect is the Annonaceae family. Plants belonging to this family seem to have some medicinal properties and contain chemical compounds that have leishmanicidal effects. Plants of this family include *Pistacia atlantica, Anonidium mannii, Enantia chlorantha, Isolona hexaloba, Annona glauca,*

*Annona senegalensis and Annickia kummeriae.* [13]. The aqueous decoction of root bark of *I. hexaloba* from DRC revealed the antileishmanial activity with an $IC_{50}$ of 8.00 $\mu g.mL^{-1}$ [14].

### *3.2.2. Antiplasmodial Activity*

Relying on an ethnopharmacological survey conducted in the Bolongo area, Bandundu province, the antiplasmodial potential of 33 selected medicinal plants was evaluated [16]. To mimic the traditional methods of preparation, lyophilized aqueous extracts were used during this screening assay. Out of all the extracts tested, 9 aqueous decoctions were found to have pronounced activity against the chloroquine and pyrimethamine-resistant K1strain of *P. falciparum*. Among them, the aqueous extracts from *Quassia africana* root bark and stem bark were the most active ones ($IC_{50}$‹1.5 $mg.mL^{-1}$). The 7 other extracts (5 $mg.mL^{-1}$ ‹$IC_{50}$‹15 $mg.mL^{-1}$) included *A. cordifolia* leaves*, Enantia chlorantha* stem bark, *Harungana madagascariensis* stem bark, *Isolana hexaloba* root bark, *Ocimum gratissimum* leaves, *Piptadeniastrum africanum* stem bark, *Psidium guajava* leaves and *Triclisia dictyophilla* leaves [17].

### *3.2.3. Antioxidant and Antihyperglycemic Activities*

Ngombe *et al.* [24] reported that the antioxidant and antihyperglycemic activities of crude extracts of *I. hexaloba* using DPPH scavenging method and glucose overloaded hyperglycemic rat models at dose levels of 200 and 400 mg/kg of body weight. The results showed that the total ethanolic extract and its fractions have an antioxidant potential. These results are promising especially as the potential antioxidant of plant extracts help to maintain health and to protect against coronary heart disease and diabetes in particular has a strong interest among scientists [25]. The phytochemical analysis of total crude extract showed presence of flavonoids, alkaloids, tannins, saponins, reducting sugars, coumarins, terpenes and steroids. It is known that flavonoids are potent antioxidants and are known to modulate the activities of various enzymes due to their interaction with various biomolecules. The activity of this biologically active compound could be attributed to the presence of these substances.

## 4. Conclusion

The present mini-review was undertaken with the aim of providing highlight and updated information on the medically and scientific evidence supporting the multiple uses of *I. hexaloba* in Traditional Medicine. Medicinal plant species are rich in secondary metabolites of pharmaceutical relevance. The advantages of their therapeutic uses in various ailments are their safety besides being economical, effective and available.

*I. hexaloba* Engl. & Diels. is pharmacologically and chemically much studied plant species but limited to only some activities, although the diversity of secondary metabolites present in the plant species especially alkaloids, saponins tannins, flavonoids, terpenoids (cazolobine), phytostérols and fatty acids have already been isolated from it. This makes it a good candidate for the development of new lead compounds against genetic and parasitic diseases such as the evaluation of anthelminthic activity. Plant species from Annona genus are also good drug candidates for external use like wound healing medicines.

## References


[1] Ngbolua K. N., Mihigo S. O., Mpiana P. T., Inkoto C. L., Masengo C. A., Tshibangu D. S. T., Gbolo B. Z., Baholy R. and Fatiany P. R. Ethnopharmacological, survey and ecological studies of some plants used in traditional medicine in Kinshasa city (Democratic Republic of the Congo). *Tropical Plant Research*, 2016, 3(2):413-427.

[2] Bongo G. N., Ngbolua K. N., Masengo C. A., Karume K. L., Mukiza J., Tshilanda D. D., Tshibangu D. S. T., Ngombe N. K., Mbemba T. F. and Mpiana P. T. Pharmacological screening of *Gymnanthemum coloratum* (Willd.) H. Rob. & B. Kahn (Compositae) and *Terminalia ivorensis* A. Chev. (Combretaceae) from DR Congo: Spotlight on the antisickling, antibacterial and antidiabetic activities. *Tropical Plant Research*, 2017, 4(3): 441–448.

[3] Ngbolua K. N., Mandjo B. L., Munsebi J. M., Masengo C. A., Lengbiye E. M., Asamboa L. S., Konda R. K., Dianzuangani D. L., Ilumbe M., Nzudjom A. B., Kadimanche M. and Mpiana P. T. Etudes ethnobotanique et écologique des plantes utilisées en médecine traditionnelle dans le District de la Lukunga à Kinshasa (RD du Congo). *International Journal of Innovative Science Research*, 2016, 26(2):612-633.

[4] Hilarion M., Isabelle C., Hassan O., Elisabeth S., Adam D. and Abdelhakim E. Cazolobine, a New Sesquiterpene from *Isolona hexaloba* (Annonaceae). *Z. Naturforsch*, 2004, 59b:1118 – 1120.

[5] Ana Silvia S. C. L., Jackson R. G. S. A., Emídio V. L. C., Josean F. T. and José-Maria B. F. Alkaloids of the Annonaceae: Occurrence and a Compilation of Their Biological Activities. *The Alkaloids*, 2014, 74:1099-4831. http://dx.doi.org/10.1016/bs.alkal.2014.09.002.

[6] Kerharo J. and Bouquet A. Plantes Médicinales et Toxiques de la Cote d'Ivoire et Haute-Volta, Vigot Freres, Paris, 1950.

[7] Vollesen K. Annotated check-list of the vascular plants of the Selous Game Reserve, Tanzania. *Opera Botanica*, 1950, 59:1.

[8] Makangara J. J., Henry L., Jonker S. A. and Nunya M. H. H. *Phytochemistry*, 2004, 65:227.

[9] Mambu L., Martin M. T., Razafimahefa D., Ramanitrahasimbola D., Rasoanaivo P. and Frappier F. Spectral characterization and anti plasmodial activity of bisbenzyl isoquionlines from *Isolona ghesquiereina Planta Medica*. 2000, 66:537-540.

[10] Hocquemiller, R., Cabalion, P., Foumet, A., Cave, A. Alkcaloids of Annonaceae. XLIX. Alkaloids of *Isolona hexaloba, I. zenkeri* and *I. pilosa*. *Planta Medica*, 1984, 50:23-25.

[11] Hocquemiller R., Cabalion P., Bruneton J. and Cavé A. Annonaceae alkaloids. XXiπ. Bark allcaloids from *Isolona campanulata* Engler et Diels. *Planta Medica Phytotherapy*, 1978, 12:230-234.

[12] Le Thomas A. Annonacees, in Flore du Gabon, A. *Aubreville* 16, 355 (1969).

[13] Abdeslam E., Abdelhakim B., Hajiba F., Meryem M., Houria E. B., Nadia D., Abderrahim S. and Youssef B. Antileishmanial activity of medicinal plants from Africa: A review. *Asian Pacific Journal of Tropical Disease*, 2017, 7(12):826-840.

[14] Musuyu M. D., Fruth B. I., Nzunzu L. J., Mesia G. K., Kambu O. K. and Tona G. L. *In vitro* antiprotozoal and cytotoxic activity of 33 ethnopharmacologically selected medicinal plants from Democratic Republic of Congo. *Journal of Ethnopharmacology*, 2012, 141: 301-8.

[15] Ngbolua K. N., Mpiana P. T., Mudogo V., Ngombe N. K., Tshibangu D. S. T., Ekutsu E., Kabena O. N., Gbolo B. Z. and Muanyishayi C. L. Ethno-pharmacological survey and floristical study of some medicinal plants traditionally used to treat infectious and parasitic pathologies in the Democratic Republic of Congo. *International Journal of Medicinal Plants. Photon,* 2014, 106:454-467. ISJN: 6672-4384.

[16] Muganza D. M., Fruth B. I., Lami J. N., Mesia G. K., Kambu O. K., Tona G. L., Cimanga K. R., Cos P., Maes L., Apers S. and Pieters L. *In* vitro antiprotozoal and cytotoxic activity of 33 ethnopharmacologically selected medicinal plants from Democratic Republic of Congo. *Journal of Ethnopharmacology*, 2012, 141:301–308.

[17] Memvanga P. B., Tona G. L., Mesia G. K., Lusakibanza M. M., Cimanga R. K. Antimalarial activity of medicinal plants from the Democratic Republic of Congo: A review. *Journal of Ethnopharmacology*, 2015, 169:76-98. doi.org/10.1016/j.jep.2015.03.075

[18] Akendengue B., Ngou-Milama E., Roblot F., Laurens A., Hocquemiller R., Grellier P. and Frappier F. Antiplasmodial activity of *Uvaria klaineana*. *Planta Medica*, 2002, 68:167-169.

[19] Agnieszka K. R. F., Telma M. K., Adilson S., Damila R. M., Marcos N. E., Patricia S. L., Ivana B. S. and Paulo R. H. M. Antimicrobial, antioxidant, antitumor activities of *Guatteria elliptica* R. E. Fries (Annonaceae) alkaloids and their safety. *International Journal of Scientific & Engineering Research*, 2017, 8(7):1130-1135.

[20] Seikou N., Souichi N., Genzo T., Yoshimi O., Nami Y., Katsuyoshi F., Takahiro M., Rika S., Tomoe O., Keiko O., Shino N., Hisako M., Hisashi M., Osamu M. and Masayuki Y. Alkaloid constituents from flower buds and leaves of sacred lotus (*Nelumbo nucifera*, Nymphaeaceae) with melanogenesis inhibitory activity in B16 melanoma cells. *Bioorganic & Medicinal Chemistry*, 2013, 21:779–787. doi.org/10.1016/j.bmc.2012.11.038

[21] Valiente M., D'ocon P., Noguera M. A., Cassels B. K., Lugnier C. and Ivorra M. D. Vascular activity of (-)-Anonaine, (-)-Roemerine and (-)- Pukateine, Three Natural 6a (R)-1,2-Methylenedioxyaporphines with different Affinities for $\alpha_1$-Adrenoceptor Subtypes. *Planta Medica*, 2004, 70:603-609. doi 10.1055/s2004-82781.

[22] Anne-Isabelle W., Andre´ C., Hocquemiller R., Christian B., Victoria M. and Alain F. Antiprotozoal Activity of Aporphine Alkaloids Isolated from *Unonopsis buchtienii* (Annonaceae). *Phytotherapy Research*, 1999, 13:175–177.

[23] Lazare B., Mathieu N., Sylvain I., Noufou O., Geoffroy G. O., Mohamed B. B., Sylvin O. and Innocent G. Study on antihypertensive activity of an aqueous extract of *Anogeissus leiocarpus* (AEAL) DC Guill et Perr bark of trunk in LNAME-induced hypertensive rats. *Biochemical Pharmacology*, 2017, 139:105–14. doi:10.1016/j.bcp.2017.06.074.

[24] Ngombe K. N., Mbombo M. P., Maloueki M., Musuyu M. D., Mutwale K. P., Tujibikila M. A., Ngbolua K. N. J. C. and Kalenda D. T. Antioxidant and antihyperglycemic potential of *Isolona hexaloba* (Pierre) Engl. & Diels (*Annonaceae*) Leaves: A Preliminary Study. *International Journal of Medicinal Plants, Photon*, 2013, 105:242-249.

[25] Exarchou V., Nenadis N., Tsimidou G., Gerothanassis I. P., Troganis A. and Boskou D. Antioxidant activities and phenolic composition of extracts from Greek oregano, Greek sage and summer savory. *Journal Agricultural & Food Chemistry*, 2002, 50(19):5294- 5299.

[26] Hsieh T. J., Chang F. R., Chia Y. C., Chen C. Y., Lin H. C., Chiu H. F. and Wu Y. C. J. Cytotoxic constituents of the fruits of *Cananga odorata. Journal of Natural Products*, 2001, 64(5):616-619.

[27] Costa E. V., Pinheiro M. L. B., Xavier C. M., Silva J. R. A., Amaral A. C. F., Sousa A. D. L., Barison A., Campos F. R., Ferreira A. G., Machado G. M. C. and Leon L. L. P. J. A pyrimidine-beta-carboline and other alkaloids from *Annona foetida* with antileishmanial activity. *Journal of Natural Products*, 2006, 69(2):292-4.

[28] Costa E. V., Pinheiro M. L. B., Souza A. D. L., Barison A., Campos F. R., Valdez R. H., Ueda-Nakamura T., Dias Filho B. P. and Nakamura C. V. Trypanocidal Activity of Oxoaporphine and Pyrimidine-β-Carboline Alkaloids from the branches of *Annona foetida* Mart. (2011). *Molecules*, 2011, 16:9714-9720.

[29] Leboeuf M., Cavé A., Forgacs P., Tiberghien R., Provost J., Touché A. and Jacquemin H. Alcaloides des Annonacées XL: étude chimique et pharmacologique des alcaloides de l'*Annona montana* Macf. *Plantes Médicinales et Phytothérapie,* 16(4):169-184.

[30] Hasrat J. A., De Bruyne T., De Backer J. P., Vauquelin G. and Vlietinck J. J. Isoquinoline derivatives isolated from the fruit of *Annona muricata* as 5-H Tergic 5-HT1A receptor agonists in rats: unexploited antidepressive (lead) products. *Journal of Pharmacy and Pharmacology*, 1997, 49(11):1145-9.

[31] Hocquemiller R., Cabalion P., Bruneton J. and Cavé A. Annonaceae aUcaloids. XXiπ. Bark allcaloids from *Isolona campanulata* Engler & Diels. Planta Medica Phytotherapy, 1978, 12:230-234.

[32] Achenbach H. and Lowell M. Constituents of *Isolona maitlandii*. Phytochemistry, 1995, 40:967-973.

[33] Miski M., Shen X., Cooper R., Gillum A. M., Fisher D. K., Miller R. W. and Higgins T. Aporphine alkaloids, cd45 protein-tyrosine-phosphatase inhibitors from Rollinia-Ulei. *Bioorganic and Medicinal Chemistry Letters*, 1995, 5: 1519-1522.

[34] Cortes D., Torrero M. Y, Pilar-D'Ocon M., Luz-Candenas M., Cavé A. and Hadi A. H. A. Norstephalagine and atherospermidine: two smooth muscle relaxant aporphines from *Artabotrys maingayi. Journal of Natural Products,* 1990, 53(2):503-508.

[35] Silva D. B., Matos M. F. C., Nakashita S. T., Misu C. K., Yoshida N. C., Carollo C. A., Fabri J. R., Miglio H. S. and Siqueira J. M. Isolamento e avaliação da atividade citotóxica de alguns alcalóides oxaporfínicos obtidos de Annonaceae. *Quimica Nova,* 2007, 30:1809-1812.

[36] Hocquemiller, R., Cabalion, P., Foumet, A., Cave, A. Alkcaloids of Annonaceae. XLIX. Alkaloids of *Isolona hexaloba, I. zenkeri* and *I. pilosa*. *Planta Medica*, 1984, 50:23-25.

[37] Fechine I. M., Tavares J. F., Da-Silva M. S., Barbosa-Filho J. M., Agra M. F. and Da-Cunha E. V. L. Two new alkaloids from *Hornschuchia oblique. Fitoterapia*, 2003, 74(1-2):29-33.

[38] Montenegro H, Gutierrez M, Romero L, Barria EO, Capson TL and Rios LC. Aporphine alkaloids from *Guatteria spp.* with leishmanicidal activity. *Planta Medica*, 69(7):677-9.

[39] Chang F. R., Wei J. L., Teng C. M. and Wu Y. C. Two new 7-dehydroapormorphine alkaloids and antiplatelet action apomorphines from the leaves of *Annona purpurea. Phytochemistry*, 1998, 49: 2015-2018.

[40] Harrigan G. G., Gunatilaka A. A. L., Kingston D. G. I., Chan G. W. and Johnson R. K. J. Isolation of Bioactive and Other Oxoaporphine Alkaloids from two Annonaceaous Plants, *Xylopia aethiopica* and *Miliusa cf. banacea*. *Journal of Natural Products*, 1994, 57(1):68-73.

[41] Siqueira J. M., Bomm M. D., Pereira F. G., Garcez W. S. and Boaventura M. A. D. Estudo fitoquímico de *Unonopsis lindmanii* - Annonaceae, biomonitorado pelo ensaio de toxicidade sobre a *Artemia salina* leach. *Quimica Nova,* 21: 557-559.

[42] Titanji V. P. K., Evehe M. S., Ayafor J. F., Kimbu S. F. Novel *Onchocerca volvulus* filaricides from *Carapa procera, Polyalthia suaveolens* and *Pachypodanthium staudtii*. Acta Leidensia, 1990, 59:377-382.

[43] You M., Wickramaratne D. B. M., Silva G. L., Chai H., Chagwedera T. E., Farnsworth N. R., Cordell G. A., Kinghorn A. D. and Pezzuto J. M. J. Roemerine, an Aporphine Alkaloid from *Annona senegalensis* that reverses the Multidrug-Resistance Phenotype with Cultured Cells. *Journal of Natural Products*, 1995, 58(4):598-604.

[44] Hocquemiller R., Debitus C., Roblot F., Cavé A. and Jacquemin H. J. Alcaloïdes des Annonacées. XLVIII. Alcaloides des écorces de *Guatteria discolor Journal of Natural Products,* 1984, 47(2):353-362.

[45] Mishra B. B., Kale R. R., Singh R. K. and Tiwari V. K.. Alkaloids: future prospective to combat leishmaniasis. *Fitoterapia*, 2009, 80(2):81-90.