

**Review Article**

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

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**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, reducing 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 anthelmintic activity.

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

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## **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 antitrypanosomal 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 anthelmintic 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.

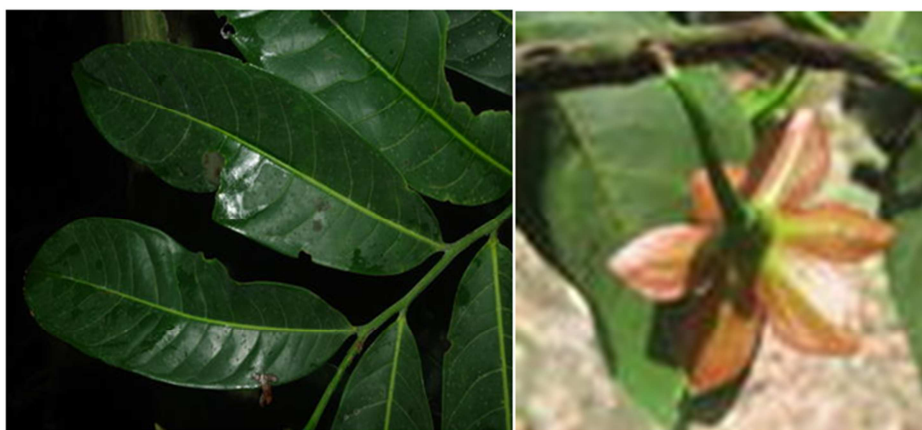


Figure 1. Leaves of *Isolona hexaloba* Engl. & Diels.

### 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-dieneoate (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,  $\beta$ -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 (cazoboline)	<i>Isolona hexaloba</i>	Root	muscle relaxant [4]	Gabon	[4]
Isochondodendrine	<i>Isolona hexaloba</i>	Root+stem	antihypertensive activity [23].	DRC	[36]
	<i>Isolona ghesquieri</i>	Stem bark	-	Madagascar	[44]
	<i>Isolona pilosa</i>	Bark	-	Ghana	[31]
Isopiline	<i>Isolona pilosa</i>	Stem bark	-	Ghana	[31]
Lirinidine	<i>Isolona zenkeri</i>	Leaf	melanogenesis inhibitory activity in B16 melanoma cells [20]. Analgesic [29], Antibacterial [29],	Taiwan	[39]
			Anticrustacean [41], antifungic [29], antileishmanial [27], Trypanocidal [28], antimicrobial, antioxidant, antitumor activities [19].		
Liriodenine	<i>Isolona campanulata</i>	Stem bark		Ghana	[31]
	<i>Isolona maitlandii</i>	Bark	-	Tanzania	[32]
Lysicamine	<i>Isolona maitlandii</i>	Stem bark	Anticrustacean [41], cytotoxic [35]. melanogenesis inhibitory activity in B16 melanoma cells [40]	Venezuela	[32]
	<i>Isolona maitlandii</i>	Stem bark		Ghana	[32]
N-methylcrotsparine	<i>Isolona zenkeri</i>	Leaf	-	DRC	[36]
Norcycleanine	<i>Isolona hexaloba</i>	Root+stem bark	-	DRC	[36]
(R)-5-(3-Methyl-1,3butadienyl)-3-(2,3-epoxy-3methylbutyl)-indole (+)-Nomuciferine	<i>Isolona pilosa</i>	Trunk bark	Antileishmanial [28], antidepressive effect [30], CD45 protein tyrosine phosphatase inhibitor [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	<i>Isolona maitlandii</i>	Stem bark	-	Ghana	[32]
Oliverine	<i>Isolona campanulata</i>	Stem bark	antimicrobial, antioxidant, antitumor activities [19].	Cameroon	[42]
			-		
Oliverine N-oxide	<i>Isolona campanulata</i>	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	<i>Isolona maitlandii</i>	Stem bark	melanogenesis inhibitory activity in B16 melanoma cells [20]	Ghana	[32]
Pellitorine	<i>Isolona maitlandii</i>	Stem bark	-	Ghana	[32]
(+)-Pronuciferine	<i>Isolona pilosa</i>	Trunk bark	melanogenesis inhibitory activity in B16 melanoma cells [20] CD45 protein tyrosine phosphatase inhibitor [33],	Ghana	[31]
			Cytotoxic [43] Vascular activity [21].		
Roemerine	<i>Isolona pilosa</i>	Bark+leaf		Ghana	[37]
		Stem bark	-	Tanzania	[31]
Unonopsine	<i>Isolona maitlandii</i>	Stem bark	Antiprotozoal Activity [22], Antileishmanial activity [45]	Ghana	[32]
Zenkerine	<i>Isolona pilosa</i>	Trunk bark	Antiplasmodial activity [18].	Ghana	[31]
	<i>Isolona zenkeri</i>	Leaf	-	Taiwan	[36]

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

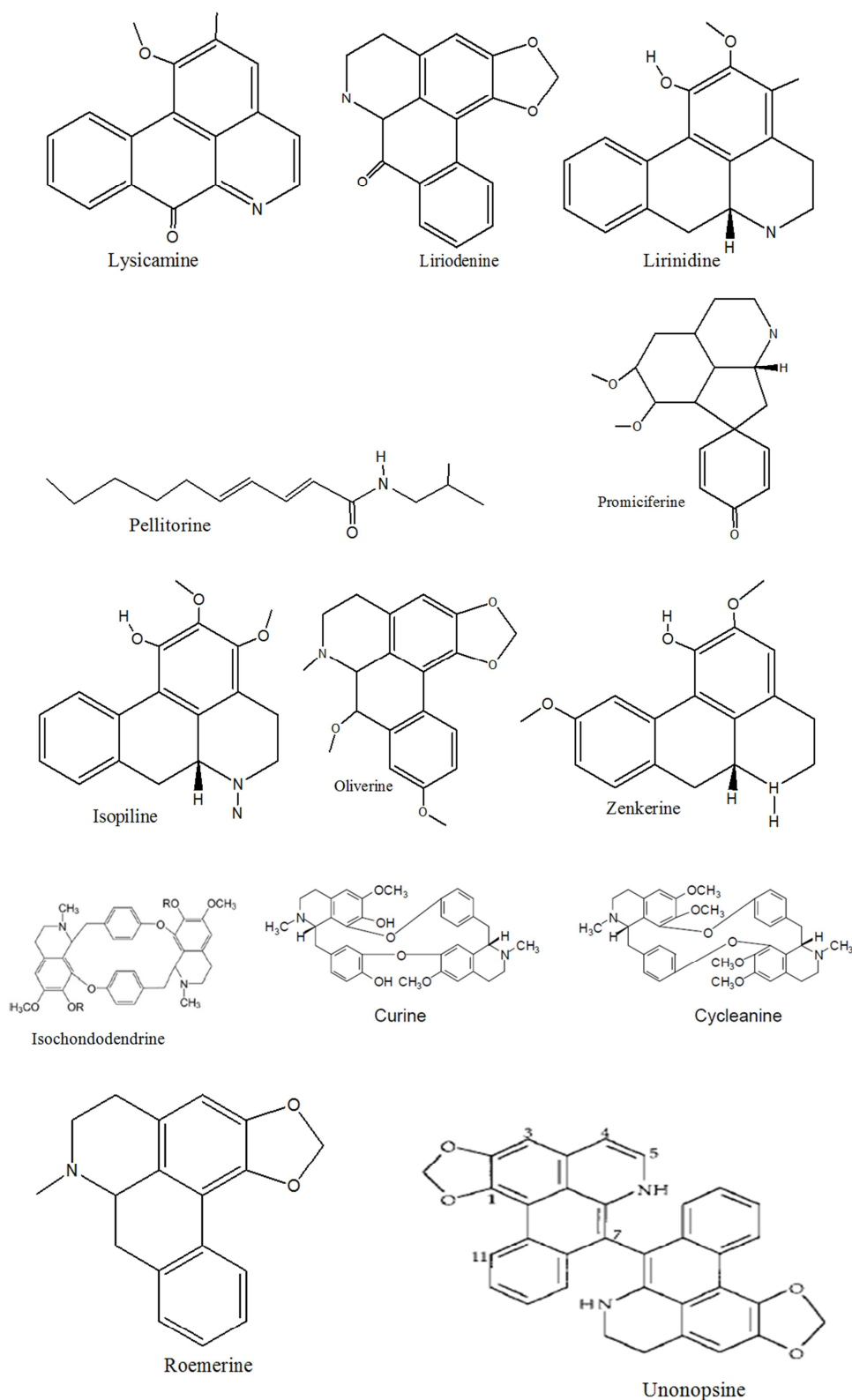


Figure 2. Different chemical structures of active compounds isolated from *Isolona* genus Engl. & Diels.

### 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  $8.00 \mu\text{g.mL}^{-1}$  [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 K1 strain of *P. falciparum*. Among them, the aqueous extracts from *Quassia africana* root bark and stem bark were the most active ones ( $IC_{50} < 1.5 \text{ mg.mL}^{-1}$ ). The 7 other extracts ( $5 \text{ mg.mL}^{-1} < IC_{50} < 15 \text{ mg.mL}^{-1}$ ) included *A. cordifolia* leaves, *Enantia chlorantha* stem bark, *Harungana madagascariensis* stem bark, *Isolona hexaloba* root bark, *Ocimum gratissimum* leaves, *Piptadeniastrum africanum* stem bark, *Psidium guajava* leaves and *Triclisia dictyophylla* 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, reducing 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 anthelmintic activity. Plant species from *Annona* genus are also good drug candidates for external use like wound healing medicines.

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