REVIEW ARTICLE

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# Bioactive compounds from eight plant species traditionally used in Madagascar as medicines: A mini-review

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## ABSTRACT

The aim of this mini-review was to give an overview on our recent findings on some plant species ethno-medically used in the south of Madagascar. Based on ethno-pharmacological approach, we used the consistent *in vitro* model systems and modern phytochemical techniques for the scientific validation of the bioactivity of selected medicinal plants and their molecules. In this work, we reported 45 compounds identified from the essential oils of four aromatic plants (*Croton greveanus, C. borarium, C. geayi* and *Hazomalania voyronii*). This oil displayed bactericidal. Eight biologically active molecules were isolated and characterized from four medicinal plants (*Salacia leptoclada, Diospyros quercina, Eliea articulate* and *Cymbopogon pruinosus*) justifying their use in traditional medicine. These results show that the Malagasy plant species can serve as source of antibacterial, antiplasmodial, cytotoxic and vasodilator hits.

**Key words:** Ethno-pharmacology, medicinal and aromatic plants, bioactive compounds, infectious diseases, hypertension

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## 1. INTRODUCTION

The island of Madagascar, located in the Indian Ocean, presents all the characters of a small continent. Its flora is of an interest because of his diversity and its very great richness. The current Malagasy flora is marked by the persistence of kinds and very antiquated species belonging to only known families with the state of fossils on the other continents. Madagascar constitutes one of the most important biodiversity hotspots worldwide with more than 90% of its plant species being endemic. This rate of endemism is besides raised on all the taxonomic levels, eight families are regarded as being entirely endemic of the island.[1-5] Medicinal plants are a validated source for the discovery of new leads and standardized herbal medicines. The aim of this research program was to validate scientifically the ethno-medical use of eight plant species of Madagascar for their pharmaceutical application against tropical infectious pathologies (like malaria and bacterial diseases) and hypertension.

## 2. MATERIALS AND METHODS

Ethno-botanical surveys were conducted in the South of Madagascar (according to the convention on the biological diversity) and plant species were selected based on informant consensus factor among traditional healers.[6] The bioassay-guided fractionation of plant extracts was carried out by the combination of chromatography techniques (TLC and column chromatography) and *in vitro* bioassay using *P. falciparum* and P388 leukemia cell lines as models.[1,2] The structure of the biologically active pure compound was elucidated by 1D and 2D NMR spectroscopy and Mass spectrometry.[1,2,7,8] Essential oil (EO) extractions were done by hydro-distillation using a Clevenger-type apparatus while; their quantification and analysis were done by GC-FID and GC/MS.[3,9] The antimicrobial activity of the oil was assessed by both diffusion disc and micro-dilution tests.[10-14] *Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 25923, *Bacillus cereus* ATCC 10876, *Escherichia coli* ATCC 25922, *Salmonella typhii* ATCC 13311, *Pseudomonas aeruginosa* ATCC 27853 and *Enterobacter cloacae* ATCC 13047, etc. as model systems for validating the bioactivity of EO. The density functional theory studies were used for predicting the cytotoxicity of the isolated compound.

## 3. RESULTS AND DISCUSSION

### 3.1. Antibacterial activity

45 compounds were identified from the essential oils of four aromatic plants which displayed bactericidal activity:

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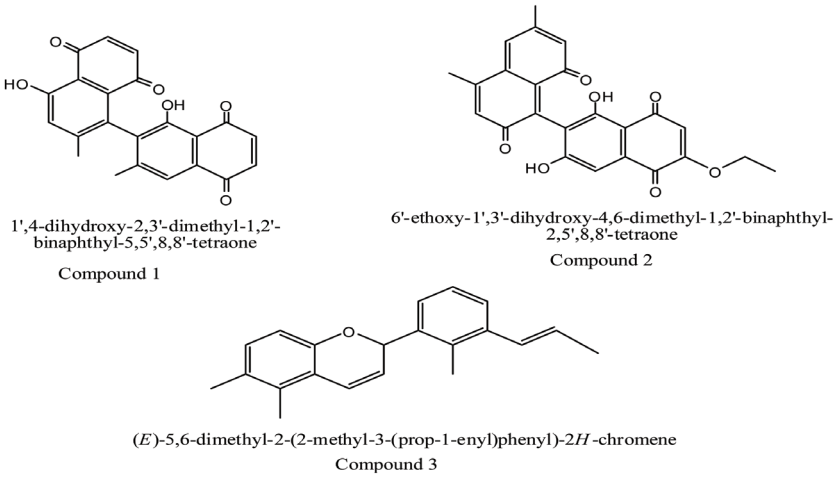


**Figure 1** Structure of three cytotoxic compounds isolated from ***Diospyros quercina***

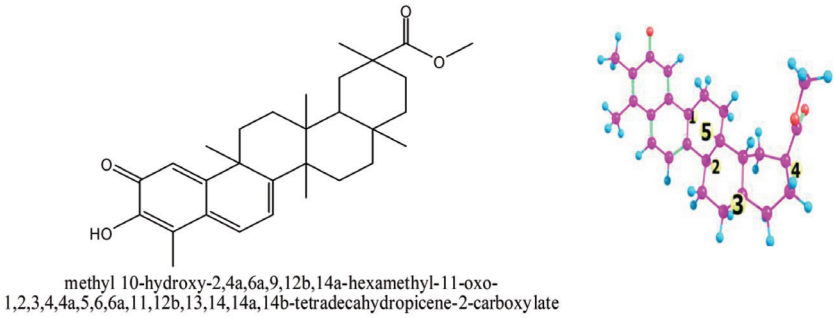


**Figure 2** Structure of antiplasmodial compound isolated from ***Salacia leptoclada*** and it most stable DFT stereoisomer

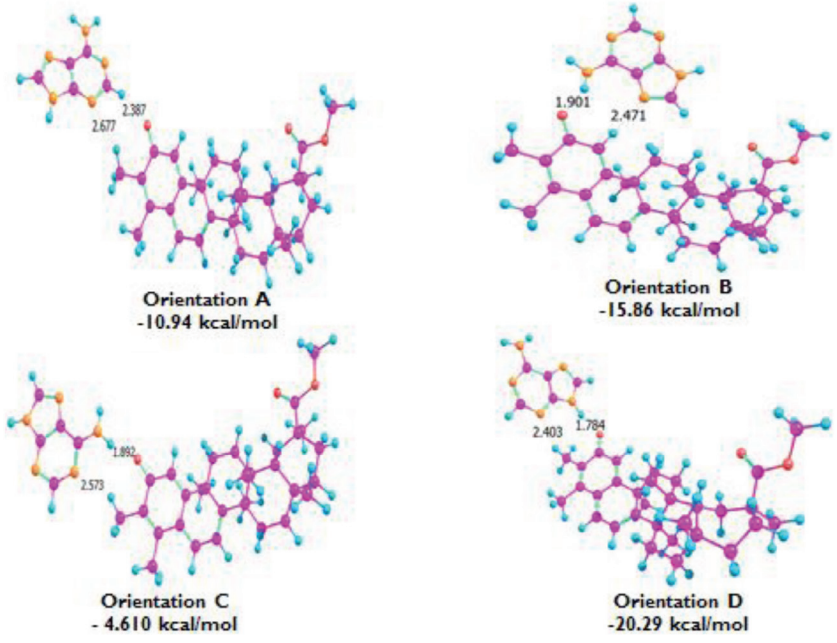


**Figure 3** Molecular modeling of different complexes bioactive compound carbonyl group with adenine in different orientations (A-D)

- ***Hazomalania voyronii***
  (-) Spathunelol (42.3%), Eucalyptol (22.0%), Limonene (10.3%), Borneol (10.2%), Myrtenal (2.0%), Perrylaldehyde (1.3%) and α-pinene (1.4%). The essential oil from *H. voyronii* displayed also vasorelaxant activity.[3]
- ***Croton greveanus***
  1,8 cineol (40.40%), linalol (23.81%) and α- terpineol (8.2%), sabinen transhydrate (10.17%), sabinen (6.87%) and finally terpinen-4-ol (1.52%).[9]
- ***Croton borarium***
  β-phellandren (39.72%), α-terpineol (25.121%), and camphene (13.74%), α- pinene (10.70%). The minor compounds where terpinen-4-ol (1.71%), germacren-D (6.68%), α-copaen (4.71%), sabinen (3.63%), β-pinen (2.46%), limonene (2.31%), β- caryophylen (2.18%), α-hulemen (1.76%), p-cymen (1.051%), γ-terpinen (1.29%), β-myrcen (1.22%) and epoxy-caryophyllen (1.092%).[9]
- ***Croton geayi***
  β-pinene (28.74%), limonene (22.92%) and secondarily by eucalyptol (10.42%), α-terpineol (8.2%), transhydrate of sabinen (5.67%), β-Phellandren (7.47%), β- caryophylen (4.80%), α-pinene (4.32%), trans-nerolidol (3.88%), β-myrcen (3.06%), germacren-D (2.56%), cis-nerolidol (2.50), aromadren (2.35%), fenchol (2.04%), sabinen and terpinen-4-ol (1.05%), caryophyllen oxide (1.09%).[9]

### 3.2. Antiplasmodial and cytotoxic activities

An antiplasmodial compound belonging to the chemical family of quinones methides was isolated from ***Salacia leptoclada*** with a therapeutic index of 0.788.[2] Three cytotoxic compounds [Isodiospyrin, 6'ethoxy-1', 3'- dihydroxy-4, 6-dimethyl-1,2'-binaphthyl-2,5', 8, 8'tetraones, (E)-5,6-dimethyl-2-(2-methyl-3-(prop- 1-enyl) Phenyl)-2H-Chromene] were also isolated from the root bark of ***Diospyros quercina***.[1]

The density functional theory studies on molecular structure and reactivity of quinone methide pentacyclic triterpenoid derivative isolated from *Salacia leptoclada* confirmed the cytotoxicity of this compound through it interaction with adenine (as revealed by the energy value of optimized geometry of complex with adenine in orientation D, figure 3).[15] This result indicates that DNA (Deoxyribonucleic acid) could be a putative target of such bioactive compound which could be act as DNA replication inhibitor (inhibition mammal cells or cancerous cells division).

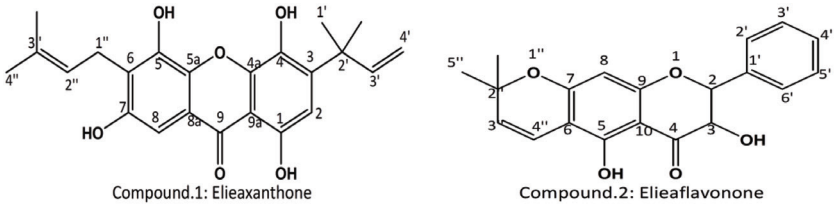


**Figure 4** Structure of new molecules isolated from ***Eliea articulata***

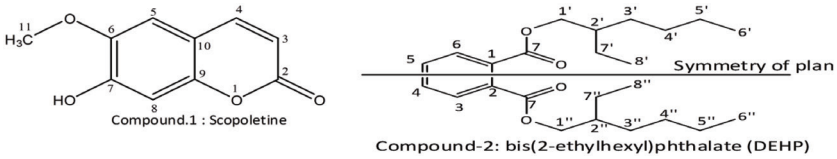


**Figure 5** Structure of vasodilator active molecules isolated from ***Cymbopogon pruinosus***

Obviously, the intake of medicinal plants is life-long in endemic areas. Although acute toxicity rarely is missed by traditional healers and chronic toxicological risks pass unrecognized. The results of cytotoxicity test revealed that it would be too dangerous, if the plants are ingested daily for a long period of time.

- ***Eliea articulata***
  In the south of Madagascar, the root bark decoction of *Eliea articulata* Cambess is used by the local communities to treat fever and incurable wounds. From the root bark of this plant species, we isolated and characterized two new compounds typical of Xanthone and flavonone named *Elieaxanthone* (compound 1) and *Elieaflavonone* (compound 2).[8]

### 3.3. Vasorelaxant activity

The aerial part of *Cymbopogon pruinosus* is widely used in the Southern part of Madagascar for the treatment of hypertension. Bioassay-guided fractionation of this plant led to the isolation and structural characterization of two bioactive pure compounds: Scopoletin and Bis(2-ethyl hexyl) phthalate (DEHP). The vasorelaxant effect of *Cymbopogon pruinosus* extract and it bioactive compounds were found to be partially endothelium dependent, mediated by nitric oxide.[7]

The role of plant species as sources of the pharmacologically active compounds is well documented. They constitute a pivotal pipeline for pharmaceutical discovery. These phytochemical constituents are protective, disease preventing plant substances. Over the time, the animal kingdom developed anti-parasitic behaviors through plant-animal co-evolution relationships in which some animal phylum like human primates utilize the chemical defenses of plants to protect themselves from their own parasites or to solve health problem.[14]

## CONCLUSION

The studied plant species contain compounds of pharmaceutical relevance, evidencing their potential for drug discovery. Chemical modification of these lead compounds could generate a library of useful bioactive molecules. The development of standardized phytomedicines for the control of hypertension, malaria and bacterial infections is therefore a feasible goal.

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