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Phytochemistry and pharmacology activities of *Detarium microcarpum* (Fabaceae) used in the treatment of parasitic diseases in Niger: A review

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Abstract

Among the many plants that have yet to be studied and that populate the rich African flora, an invaluable reservoir of bioactive molecules, is *Detarium microcarpum*, a tree of the Fabaceae family 8 to 12 m high, a species of the wooded savannahs and open forests of the Sudano-Sahelian zone of the African continent. This plant has long been used in traditional medicine to treat stomach aches, menstrual pain, dysenteric diarrhoea, dermatitis, meningitis, gonorrhoea, rheumatism, tuberculosis, smallpox, bilharzia, itching, gastric ulcers and diabetes. Phytochemical work on this plant reported about 40 secondary metabolites isolated mainly from extracts of trunk bark, leaves and fruits. The isolated compounds included carbohydrates, coumarins, flavonoids, sterols and terpenoids and other compounds. The crude extracts of the different organs and the compounds isolated from them showed a wide spectrum of pharmacological activities including antiviral, antioxidant, antibacterial, antiparasitic, antiinflammatory, antidiabetic, anthelmintic, larvicidal and molluscicidal activities. The aim of this review is to provide an update on the existing knowledge on the different organs of *Detarium microcarpum*.

Keywords: *Detarium microcarpum*, fabaceae, phytochemistry, pharmacology

1. Introduction

Intestinal parasitosis are widespread almost worldwide, with a high prevalence in many regions. Amoebiasis, ascariasis, hookworms are among the ten most common infestations in the world [1]. According to Crompton [2], one third of mankind is parasitized by worms. The number of worms parasitising humans is estimated to be at least 400 billion; this represents a considerable biomass and losses of proteins, vitamins, and various nutrients for the individuals concerned [3]. Parasite-related mortality is the leading cause of death among children aged 5-14 years in developing countries, ahead of the usual infectious diseases [4].

In many African countries, these parasitoses raise serious health and social problems leading to malabsorption, diarrhoea, blood spoliation, impaired work capacity and slowed growth [4-5].

In Niger, intestinal parasites, particularly those causing diarrhoeal diseases, are the third most common disease among the Nigerien population [6].

The fight against these intestinal parasitoses is now much easier than before, thanks to the discovery of effective drugs, the improvement and simplification of certain diagnostic methods and the progress made in the use of plants with medicinal properties. Thus, medicinal plants occupy an important place in the African pharmacopoeia [7]. They play a decisive role in the treatment of certain tropical diseases such as malaria, digestive disorders, jaundice, gonorrhoea, etc. [8]. The frequent use of these plants by traditional practitioners and the satisfactory results that follow in some cases have led some countries, mainly in Africa, to reflect further on the reevaluation of phytotherapy. Thus, the increase in interest has led Niger to rehabilitate traditional medicine, as shown by the government's adoption of Ordinance No. 97-002 of 10 January 1997 on pharmaceutical legislation [9]. These legislative and regulatory texts devote an important place to traditional medicine and pharmacopoeia through definitions and areas of intervention of this science that affect more than 80% of the population [10].

However, Ikhiri *et al.*, reported on the use of plants in traditional pharmacopoeia in Niger [8]. 186 medicinal species, among which *Detarium microcarpum* (Guill. & Perr.) has been identified in the treatment of intestinal parasitosis. *Detarium microcarpum* is a plant belonging to the fabaceae family that is widely used in traditional pharmacopoeia for the treatment of several human diseases in several regions of Africa [11].

In the literature, it is remarkable that all organs of *Detarium microcarpum* are used in traditional medicine in West Africa [12-15]. The diseases concerned are of various origins, but mainly concern bacterial or parasitic infections of the gastrointestinal sphere [16]. Previous chemical and pharmacological studies of *Detarium microcarpum* have shown that the extracts of the different organs and compounds isolated have interesting biological activities. These extracts and isolated compounds showed a wide spectrum of pharmacological activities including antiviral, antioxidant, antibacterial, antiparasitic, anti-inflammatory, antidiabetic, anthelmintic, larvicidal and molluscicidal activities. Based on the quality of the secondary metabolites present in *Detarium microcarpum* and its use in traditional medicine, it is necessary that an evaluation of its application in antiparasitic is undertaken.

1.1 Botanic classification of *Detarium microcarpum*

According to the classification of Cronquist [17], *Detarium*

microcarpum Guill. & Perr. belongs to the class Magnoliopsida, subclass Rosidae, order Fabales, family Fabaceae, subfamily Caesalpinioideae, tribe Detarieae and genus *Detarium*. The family Fabaceae contains about 639 genera and at least 16,000 species. The subfamily Caesalpinioideae is found exclusively in tropical regions. This subfamily consists of trees, shrubs and very rarely herbs, and includes some 162 genera, 88 of which are found in Africa. Their leaves are pinnate or bipinnate, rarely simple or unifoliolate. The tribe Detarieae contains approximately 82 genera including *Detarium*. Despite its size, this tribe is little known, probably because a large proportion of its species are tropical trees, of which only a few are cultivated or even used. The genus *Detarium*, of African origin, is characterised by large, drupaceous, subdrupaceous, indehiscent, flattened and globose fruits with a hard epicarp and small hermaphroditic flowers, and has three species, which are *Detarium senegalense* J. F. Gmel., *D. microcarpum* Guill. & Perr. and *D. macrocarpum* Harms.

Table 1: Classification systématique du *D. macrocarpum*

| Kingdom | Plant |
|--------------|--|
| Branch | Tracheophyte |
| Class | Magnoliopsida |
| Sub-class | Rosidae |
| Order | Fabales |
| Family | Fabaceae |
| Sub-family | Caesalpinioideae |
| Tribe | <i>Detarieae</i> |
| Genus | <i>Detarium</i> |
| Species | <i>Microcarpum</i> |
| Name | <i>Detarium microcarpum</i> |
| Others names | Taura (Hausa); Fantu (Zarma); Takra (Tamachek) |

2. Morphological character and geographical distribution of *D. microcarpum*

2.1 Morphological character of *D. microcarpum*

Detarium microcarpum (Fig. 1) is an 8-12 m tall tree with scaly bark with a red, cracked edge on the lignified twigs and a yellow-green edge on the young shoots. The leaves are paripinnate or imparipinnate and have 6 to 8 leaflets, arranged

alternately or suboppositely. The leaves are rounded at the apex. The cream or creamy white flowers are grouped in axillary panicles 15-25 cm long and 6-10 mm wide, with 4 sepals and 10 stamens. The fruit is a flattened globose or subglobose drupe, 2.5 to 5 cm in diameter. The epicarp cracks at maturity, the greenish mesocarp is intertwined with fibres inserted on the core [11].



A

b

c

d

Fig 1: Photographs of *Detarium microcarpum* Guill. & Perr [16]. a) leaves; b) bark; c) fruits; d) inflorescence

2.2 Geographical distribution of *Detarium microcarpum* Guill. & Perr

Detarium microcarpum is a tree that grows from the driest to the wettest parts of Africa. It is found particularly in shrub to tree savannas, wooded savannas and open forests. It usually grows on sandy or lateritic soils.

The natural range covers the whole of arid sub-Saharan Africa from Senegal to Sudan. The species is found in Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Côte d'Ivoire, Gambia, Ghana, Guinea, Guinea Bissau, Mali, Niger, Nigeria, Senegal and Sudan [18].

3. Traditional use of *Detarium microcarpum*

Table 2: Traditionals uses of the various organs of the *D. microcarpum*

| Plant part | Extraction mode | Activity | Country of origin | References |
|------------|-------------------------|--|-------------------|------------|
| Fruits | consumption | Aspect nutritionnel | Mali | [16] |
| fruits | decoction | Nutritional aspect; meningitis | Burkina Fasso | [19] |
| Leaves | | Scabies | | |
| Stem bark | | Antihemorrhoidal antibleorrhagic. | | |
| Root bark | | Scabies; stomach ache; syphilis; dysenteric diarrhoea | | |
| Seeds | | Dermatoses. | Mali | [11] |
| fruits | consumption | Meningitis; malaria; diarrhoea | Niger | |
| | | syphilis and diarrhoea | | |
| Leaves | decoction | Stomach ache, malaria and diarrhoea, chest pain, mental disorders and kwashiorkor, tooth decay | Mali | |
| | | Anti-diarrhéique et anti-asthénique | Niger | [20] |
| Root bark | Decoction/maceration | Headaches and stomach aches; diarrhoea, rheumatism, tuberculosis, smallpox, bilharzia, itching, paralysis and stomach ulcers. | Mali | [11] |
| Stem bark | decoction | Stomach aches, headaches in children, malaria and measles. | | |
| Fruit | unspecified | texture and flavour, but also for their chemical and nutritional properties | Nigeria | [21] |
| Leaves | unspecified | | | |
| Stem bark | unspecified | | | |
| Leaves | infusions ou décoctions | Diuretic and astringent; rheumatism, venereal diseases, urogenital infections, haemorrhoids, caries, stomach ache, intestinal worms and diarrhoea, dysentery | Mali | [18] |
| Root bark | | | | |
| Stem bark | | Headaches, sore throats, backaches and painful periods. | | |
| Fruits | Unspecified | Tuberculosis, meningitis, childhood itching and diarrhoea, snake bites, and swelling of the arms and legs | Nigeria | [22] |
| Leaves | Unspecified | | | |
| Stem bark | Unspecified | | | |
| Root bark | unspecified | | | |

4. Phytochemistry and pharmacology

Considering the medicinal importance of this tree in West Africa, several phytochemical and pharmacological studies were conducted on the different organs of *D. microcarpum*.

4.1 Carbohydrates

L-quinio-1,5-lactone (1), D-(-)-bornesitol (2), D-pinitol (3), myo-inositol (4), sucrose, D-glucose and D-fructose were isolated from the trunk bark [12]. In fact, D-pinitol and its derivatives are known for their beneficial effect in cases of insulin resistance, such as diabetes and its complications: obesity, hyperlipidemia, atherosclerosis, hypertension, etc... It

has also shown anthelmintic and larvicidal properties on *Aedes aegypti* and *Culex quinquefasciatus* [23], as well as an anti-inflammatory activity in rats, in cases of acute and subacute inflammation [24].

As for myo-inositol, it is a compound that is vital to many biological processes, both in humans and animals. Among other things, it is essential for the growth of rodents. In humans, this compound is partly provided endogenously. In terms of therapeutic activities observed for this compound, it has a positive effect on depression, panic attacks and obsessive-compulsive disorders [16].

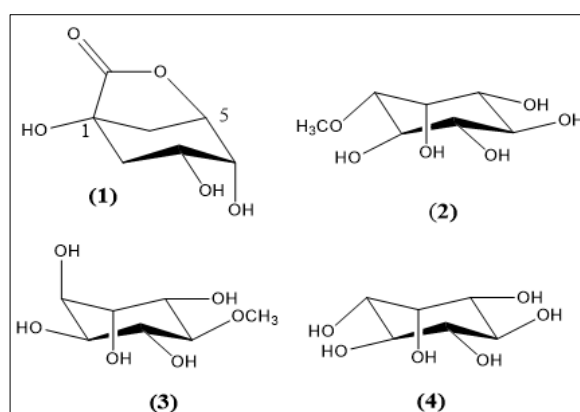


Fig 2: Chemical structures of compounds 1–4

4.2 Phenolic compound

Coumarin (5) [20] and melilotoside (6) [25] were isolated from the trunk bark. Methyl gallate (7) was isolated from fruits [26]. Coumarin has anti-edematous properties. It was indicated in cases of lymphedema of the upper limb after radiosurgical treatment of breast cancer. The number of cases of hepatitis attributable to this molecule led to the withdrawal of the

corresponding drug in 1996 in France and then in other European countries [16].

Concerning coumarin derivatives, some of them have pharmacological activities, mainly anticoagulant. The best known are dicoumarol and esculoside, both venotonic and vasculoprotective [27-28]. Melilotoside (6), has demonstrated *in vitro* antimicrobial activities against *Entamoeba histolytica* and *Giardia lamblia* [29].

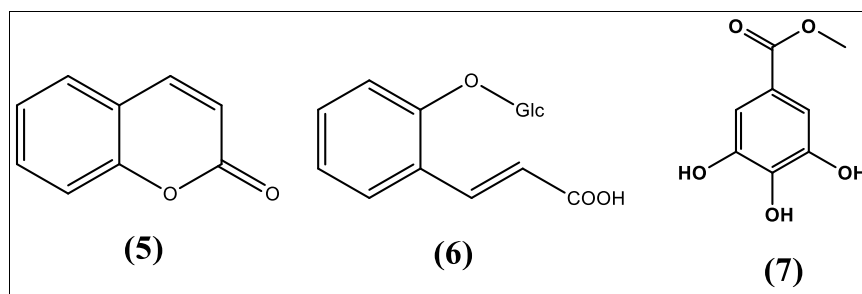


Fig 3: Chemical structures of compounds 5–7

4.3 Flavonoids

Catechin (8), epicatechin (9), catechin-7-O-galloylester (10) and epicatechin-3-O-galloylester (11) were isolated from the trunk bark [25], while kaempferol-3-O- β -glucopyranoside (12) was isolated from leaves [30], luteolin (13) and epicatechin were isolated from fruits [26]. Catechin, being one of the basic

structures of flavan-3-ol, is found in many plant species. It is also the basic structure giving rise to catechic tannins. Like most flavonoids, it has antioxidant properties [28]. The anti-HIV-1 activity of compounds (8) to (11) was evaluated on a cell line infected with the HIV-1III_B strain, and compound (11) showed a strong toxicity [31].

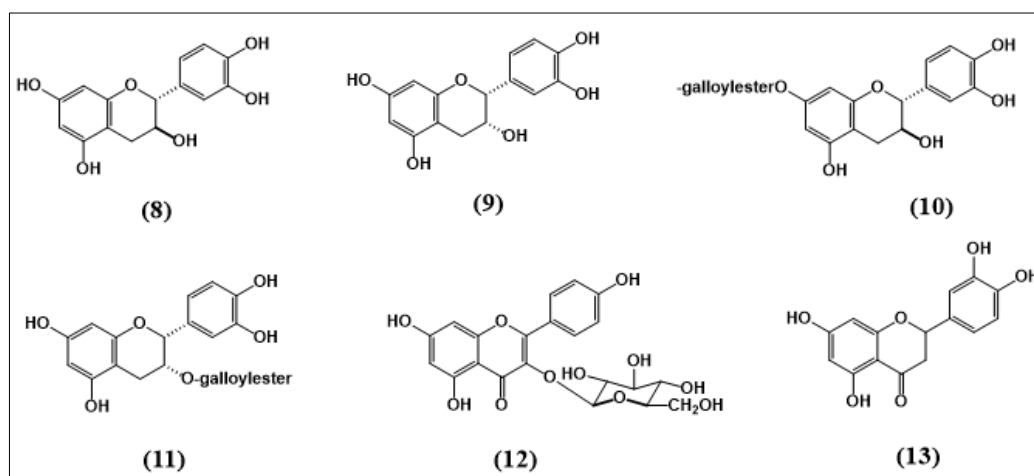


Fig 4: Chemical structures of compounds 8–13

4.4 Steroids

The β -sitosterol (14), campesterol (15), stigmasterol (16), sitosterol-3- β -O-[6'-O-palmitoyl-2',3',4'-O-triacetyl- β -D-glucopyranoside] (17), were isolated from the trunk bark of

D. microcarpum [32] and β -sitosterol from 3-O- β -D-glucopyranoside (18) was isolated from fruits [26]. β -sitosterol, campesterol, and stigmasterol are the three sterols most frequently found in the unsaponifiable matter of an oil [28].

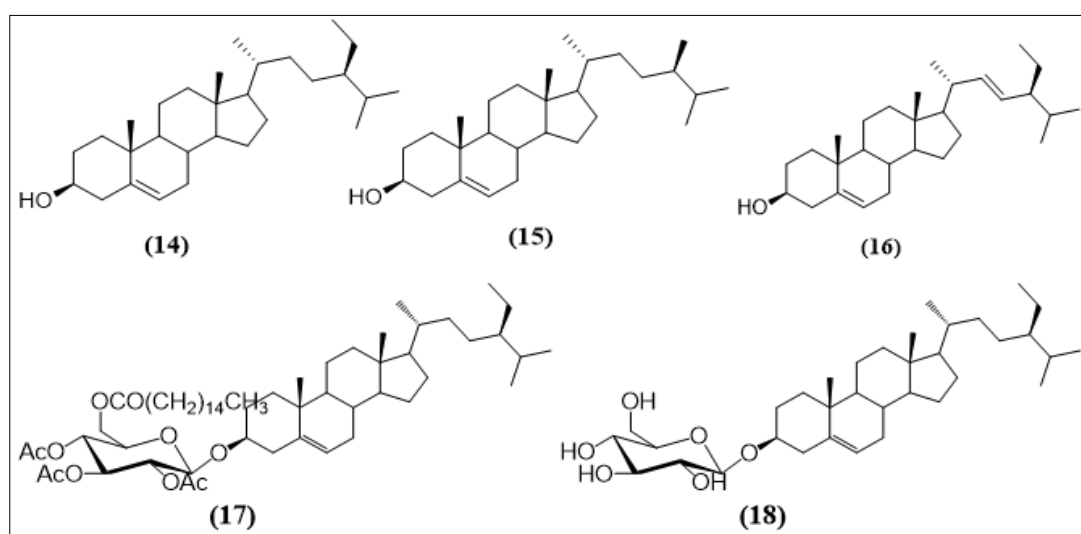


Fig 5: Chemical structures of compounds 14–18

4.5 Terpenoids

Compound (19) [33] a diterpene of the clerodane type and compound (20) [20] a diastereomer of this molecule were isolated from the trunk bark. Compounds (19) 2-oxo-

kolavenic acid, (21) kolavenic acid, (22) 2-pentenoic acid and (23) ent-4(18), 13*E*-clerodien-15-oic acid are four clerodane-type diterpenes isolated from leaves [30].

Compound (24) copalic acid, a labdane-type diterpene was isolated from trunk bark [20].

Compounds (25) 1-naphthalene acetic acid-7-oxo-1,2,3,4,4a,7,8,8a-octahydro-1,2,4a,5-tetramethyl and (26) 1-naphthalene acetic acid-5-carboxy-1,2,3,4,4a,7,8,8a-octahydro-1, 2, 4a-trimethyl, two tetranorditerpenes were isolated from trunk bark [33].

The compounds (27) 3, 4-epoxyclerodan-13E-en- oic acid; (28) 5R,8R-(2-oxokolavenic acid); (19) 2-oxo-kolavenic acid; (29) 3,4-dihydroxyclerodan-13E-en-15- oic acid; (30) 3,4-dihydroxyclerodan-13Z-en-15- oic acid and (24) copalic acid were isolated by bioguided fractionation and subsequently

identified as diterpenes from fruits [16]. Compounds (27)-(28) are clerodane, while compound (29) is labdane. Compound (19) was identified as 2-oxo-3-en-5 β , 10 α -trans-17 β , 20 β -ent-clerod-13E-en-15-oic acid, previously isolated from the leaves and bark of *D. microcarpum* [30, 33]. X-ray diffraction analysis of the crystals of compound (29) showed that it is a diastereomer of compound (30). It differs from (30) by a cis junction between the rings, and a trans relationship between the CH₃-17 and CH₃-20 methyl groups. Thus, this compound is referred to as 2-oxo-3-en-5 β , 10 β -cis-17 β ,20 α -ent-clerod-13E-en-15-oic acid; it has a novel relative configuration.

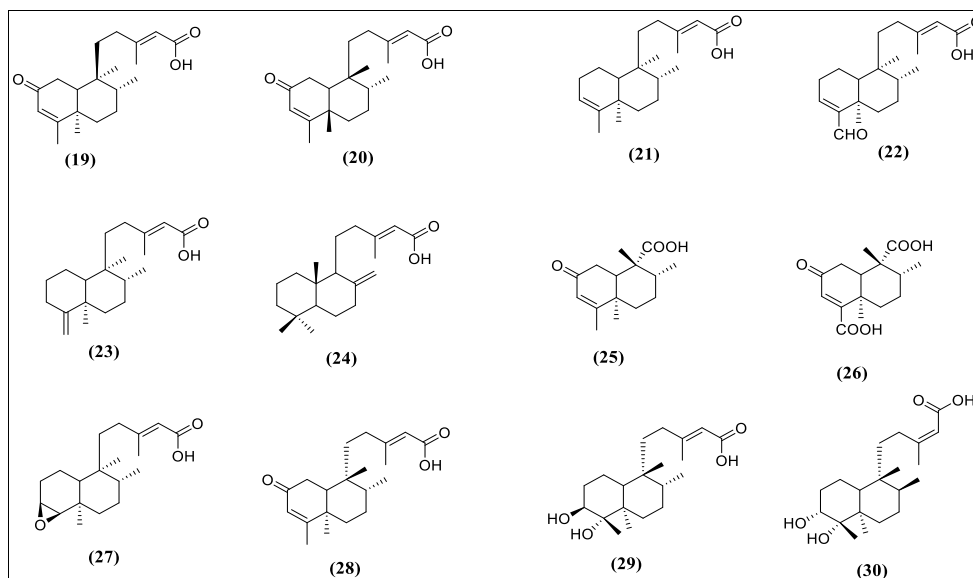


Fig 6: Chemical structures of compounds 19–30

Lupeol (31), lup-20(29)-en-2 α ,3 β -diol (32) are two pentacyclic triterpenes of the lupane series isolated from trunk bark [32], lupeol and betulinic acid (33) were isolated from fruits [26]. Lupeol is a compound frequently produced by plants, and has different pharmacological activities: cytostatic, antioxidant and anti-inflammatory [34].

Microcarposide (34), a diglucosilated isovaleronitrile isolated from fruits has shown antimicrobial activities against *salmonella typhi* [26].

Rhinocerotinoic acid (35) has been isolated from root barks and shows activities against *Salmonella typhi* and *Salmonella enteritidis* [35].

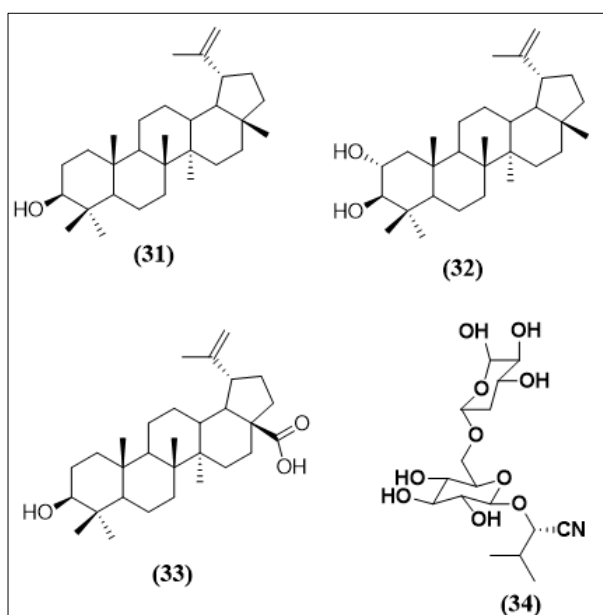


Fig 7: Chemical structures of compounds 31–34

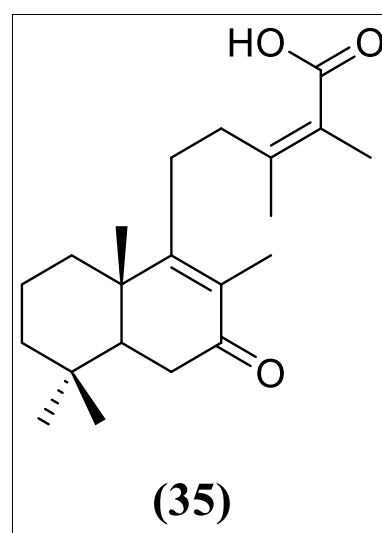


Fig 8: Chemical structure of compound 35.

The seed oil had low biogenic and oxidative fastness; a desired property in oils for consumption, industrial purposes and pharmaceutical applications [36]. The seed kernel is dark brown and more or less fatty and edible. Nutritionally, the seed that is used as a traditional soup thickener containing lipids, carbohydrates, proteins, crude fiber and the essential elements Na, K, Mg, Ca, S, P and Fe [12, 32].

Saponins, phytates and cyanides are presumed to be present as anti-nutrients in *D. microcarpum* seeds [37]. The defatted seeds produce gum, which has been used as a bioadhesive agent in the formulation of mucoadhesives and sustained release tablets [36]. The gum content of the seeds was high; Linoleic acid was the predominant fatty acid [38].

The aqueous extract of *D. microcarpum* seeds possesses broad spectrum antimicrobial activity against clinical isolates of *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Salmonella paratyphi* and *Candida albicans* [39]. Inhibition of growth of the pathogenic fungus (*Cledosporium eucumerinum*) by *D. microcarpum* pulp extract has been reported by Cavin [16].

Studies conducted by Ablassé *et al.*, showed that the ethanolic extract of *D. microcarpum* fruit pulp showed no genotoxic effect but a DNA protective effect against cyclophosphamide induced damage in a dose dependent manner. The observed genoprotective effect was related to the anti-oxidant molecules of the fruit having hydroxyl radical (generated by cyclophosphamide metabolism) as well as peroxy and alkoxy radicals from lipid peroxidation [15].

The studies conducted by Alassane, involved 290 patients aged 6 to 16 years carrying intestinal parasites (*E. coli*, *E. histolytica*, *Giardia intestinalis* and *Trichomonas intestinalis*), they were divided equally into two groups, one of which received treatment with *Detarium microcarpum* and the other with Metronidazole at the usual dosage with clinical and parasitological controls at D2, D4 and D7. The clinical results showed a partial improvement of the symptomatology at D4 and a cure of all the patients at D7 with an excellent tolerance. Parasitological results showed a high sensitivity of most of the parasites with a cure at D7 of 91.13% of the subjects treated with *Detarium microcarpum* and 91.72% with Metronidazole. According to him, *Detarium microcarpum* had very interesting amoebicidal and flagellidal properties that justified its traditional use [40].

The trunk bark of *D. microcarpum* has an inhibitory potential against alpha-glucosidase and alpha-amylase with the methanolic extract of *D. microcarpum* [41]. Extracts with ethyl acetate, butanol and the aqueous fractions of the methanolic extract of *D. microcarpum* trunk bark also showed strong inhibitory potentials against alpha-amylase and alpha-glucosidase. These extracts and its fractions inhibit alpha-glucosidase more strongly than they inhibit alpha-amylase [41]. The methanol extract of *D. microcarpum* roots and its fraction significantly reduced blood glucose levels in alloxan-diabetic rats without producing hypoglycemia, an effect attributed to the abundant flavonoids present in the extract [36]. The crude alkaloids of the methanolic extract of *D. microcarpum* trunk bark were found to be highly active against *E. coli*, *P. aeruginosa*, *Streptococcus aureus*, *Staphylococcus aureus* and these showed that the alkaloids of this plant could be used as broad-spectrum antibiotics against the diseases caused by the tested microbes [42]. Similarly, ethanol extract of *D. microcarpum* trunk bark showed antimicrobial action against some pathogenic organisms such as *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Citrobacter freunditis* *Staphylococcus aureus*, *Streptococcus pyrogenes* and *Listeria monocytogenes* [32, 43].

Flavones present in the methanol extract of *D. microcarpum* have activity to strongly inhibit HIV-1 and HIV-2 [44]. Antiviral activity of the fractions of *D. microcarpum* trunk bark methanol extract was reported using the 7 Replicon assay. The active fraction MTH-1700 selectively inhibited hepatitis C virus (HCV) [45].

Similarly, the trunk bark extract of *D. microcarpum* showed significant molluscicidal activity against *Lymnaea natalensis* [44].

Cavin. (2007) showed that clerodane-type diterpenes isolated from *D. microcarpum* fruits inhibited the growth of the plant pathogen *Cladosporium cucumerinum* and the enzyme acetylcholinesterase (AChE). One of the compounds (2-oxokolavenic acid) was ten times more potent than galanthamine, a clinically useful drug for Alzheimer's disease. Inhibition of AChE is currently the most effective approach to managing the symptoms of Alzheimer's disease.

Phytochemical screening of *D. microcarpum* organs showed high levels in total polyphenols, total flavonoids and total tannins for leaves, trunk and root bark [46]. These have shown strong antioxidant activities [47].

Iful (2008) reported that *D. microcarpum* leaf extract reduced mortality in animals treated with *Echis carinatus* venom (carpet meat). The study also revealed that the extract relaxed the isolated rabbit jejunum and contracted the rat frenulum nerve muscle [48].

5. Conclusion

We have tried to review the existing knowledge on the different organs of *Detarium microcarpum*. Despite the fact that a wide range of its traditional uses is known and that several extracts of its different organs and pure compounds have indicated various biological activities, there are few in-depth studies on antiparasitic activities.

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