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A BRIEF REVIEW ON CHEMICAL CONSTITUENTS AND PHARMACOLOGICAL PROPERTIES OF DAMMUL-AKHWAIN – *DRACAENA CINNABARI*

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Abstract

Dracaena cinnabari growing on the mountain ridges of Yemen's southern coast belongs to the family of Agavaceae or Asparagaceae. The tree produces a deep red resin containing valuable source of bioactive compounds belonging to the groups such as flavonoids, homoisoflavonoids, chalcones, sterols and terpenoids. The current review is based on relevant information on its chemical composition and pharmacological effects such as antimicrobial, anticancer, anti-diabetic, anti-inflammatory and analgesic activities. It has also been used in conventional medicine to treat gastric sores, dysentery and diarrhoea, along with haemostatic and anti-ulcer. It is primarily used as anti-haemorrhagic to avoid bleeding and facilitate wound healing when applied externally. Since not many activities have been reported, the plant can be used as a great source for further investigations and research studies in future.

Keywords: *Dracaena cinnabari, Dammul-akhwain, Traditional Uses, Herbal medicine & Dragon's blood Resin.*

INTRODUCTION

Medicinal herbs, which come in a range of forms, including liquid, are used to cure many ailments worldwide, and novel therapies are currently being found as a consequence of research on these plants [1, 2]. Natural compounds have long been utilized as a source of medicine and account for about half of the pharmaceuticals now in use [3]. Plants are frequently used as a source of medication in developed countries, where conventional medicine plays a significant part in health care [4]. Using a medicinal herb for disease therapy lacking sufficient clinical evidence to support efficacy and safety findings can be both toxic and ineffective [2]. Herbal medicines might produce various moderate to significant adverse effects due to the complex chemical compositions of medicinal plants. As a result, utilizing well-controlled and validated clinical toxicity tests or guidelines to assess medicinal plant protection is essential [5].

Dracaena cinnabari Balf.f. is a plant species native to the Island of Socotra that grows on the mountain slopes of Yemen's southern coast [6]. It belongs to the Agavaceae or Asparagaceae family and is called in Arabic and Yemen as 'Damm-ul-akhwain' or 'Cinnabar' [7, 8]. In the Old World tropics, the genus Dracaena comprises around 120 species found in wet and dry forests [9]. The tree's red gum is referred to as "Dragon's blood" [6]. *Dracaena cinnabari* Balf.f., unlike other monocot trees, contains secondary growth zones that resemble tree chains seen in dicot plant species [10]. It has a unique increase pattern termed "dracoid habitus" [11], that it shares with the other arboreous Dracaena species. It is a tall, single-trunked tree with smooth grey bark and a height of up to 10 meters. An umbrella-shaped crown is formed by the branches of sausage-shaped. On Socotra, populations DC trees do not regenerate significantly, and their age structure shows that trees are over matured. The DC tree's red "dragon's blood" resin oozes from fissures, branches and wounds in the bark. Its fruits are tiny fleshy berries with one to three seeds each. They change colour from green to black as they mature and finally to orange when fully matured. Birds (such as Onychognatus species) consume the fruit, which disperses the population. The seeds have a 4–5mm diameter and a weight of 68mg on an average. The dark red resin formed by the berries is called dragon's blood

[12]. Similar to monocotyledons, the plant develops from the point of the stem, with extended, firm leaves sprouting in thick rosettes which are present in the end. When it reaches maturity, it grows into an umbrella-tip crown with 60 centimetres in length and 3 centimetres in breath leaves. Stem along with its branches are robust and durable, branching is dichotomous, divides into two half on a regular basis [13].

Certain polyphenolic compounds have been discovered in the resin of *Dracaena cinnabari* Balf.f. such as flavones, homoisoflavans, bioflavonoids, chalcones [14], like cinnabarone [15], triflavonoids like damalachawin [16] and metacyclophanes like dracophane [17]. Besides, numerous sterols have also been reported such as campesterol, stigmasterol, sitosterol and stigmastanol [18].

It has been used in conventional medicine to cure stomach sores, diarrhoea and dysentery [19] and is utilized as a haemostatic, anti-ulcer, antispasmodic, analgesic, anticancer, antiviral, antimicrobial, anti-inflammatory, wound healing, and antioxidant [1, 20, 23]. The resin from *Dracaena cinnabari* Balf f. was used in Socotra to dye wool, glue pottery, purify breath, and embellish pottery and homes and even as a lipstick. It is generally used for different skin or mucosal disorders and can minimize bleeding and improve wound healing when administered externally [24-26]. It is also used in ceremonial magic and alchemy due to the belief that it is dragon's blood.

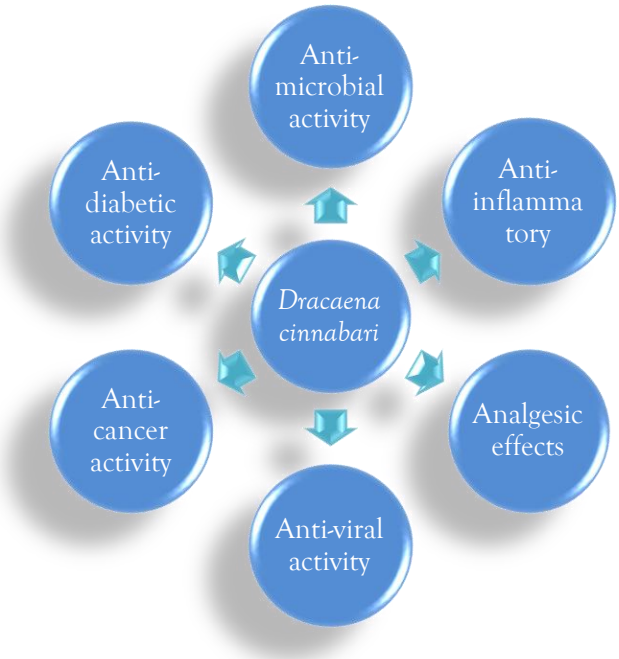


Fig.1 Pharmacology Activity of *Dracaena cinnabari* Balf.f.

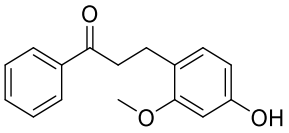
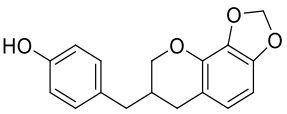
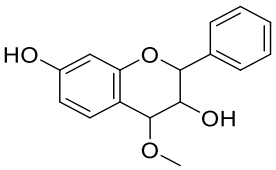
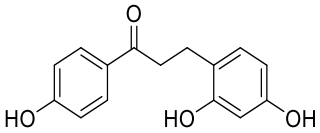
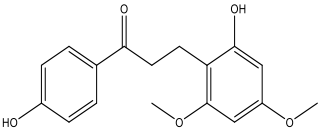
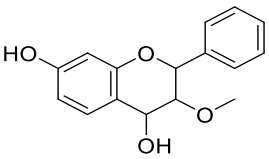
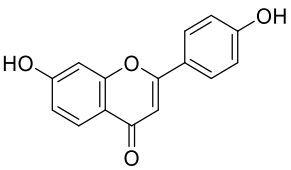
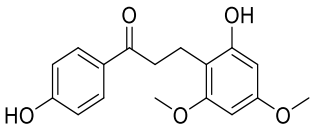
CHEMISTRY

The Numerous flavonoids, chalcone polymers, stilbenes, sterol saponins and chalcones have also been discovered in the blood of the dragon *D. cinnabari* Balf.f [1]. In all, twenty terpenoid chemicals, twelve sesquiterpenes and including eight monoterpenes, are found in the resins of *Dracaena cinnabari* Balf.f. Out of the 20 terpenoids, 13 of them are volatile in nature, which includes 5 monoterpenes, camphene, namely α-thujene, β-pinene, α-pinene, δ-2-carene, and 8 sesquiterpenes, γ-elemene, namely (−)-isodauca-6, 9-diene, 5-diene, trans-muurola-3, γ-himachelene, γ-humulene, ω-amorphene, ε- and α-muurolene [27].

Certain compounds belong to the category of flavonoids, homoisoflavonoids and chalcones, namely quercetin, galangin, chrysin, 7-hydroxy flavone, 7-hydroxy-3 (2-methoxy-4-hydroxybenzyl) chromane, 7,8-methylenedioxy-3 (4- hydroxy benzyl) chromane, 7-acetoxy-3 (4-acetoxybenzyl) chromane, 7-hydroxy-3 (4-hydroxybenzyl) chromane, 4,6-dihydroxychalcone, 4,4,6-trihydroxy-2- methoxychalcone, 2-hydroxychalcone and 1-phenyl-3 (2-methoxy-5-hydroxyphenyl) propan-1-ol are also present in the resin of the plant [28].

Besides this, β-caryophyllene is present as a single volatile component in *Dracaena cinnabari* Balf.f. resin, which is soluble in n-hexane extract [29]. Certain other compounds have been reported such as dracidione [30], damalachawin [16], dracophane [17] and cinnabarone [15].

Table1: Chemical composition of *Dracaena cinnabari* Balf.f.

Sl. No	Category	Compound name	Structure	Bioactivity	Reference
1.	Flavonoid	i. 4-hydroxy-2-methoxydihydrochalcone		Antioxidant property	[31]
		ii. 3-(4 Hydroxybenzyl)-7,8methylendioxychroman		Antioxidant property	[31, 32, 33]
		iii. Cinnabarone (2S)-7,3'-Dihydroxy-4'-methoxyflavan;		Antioxidant property	[15]
		iv. Damalachawin 2,4,4'-Trihydroxydihydrochalcone.		Antitumor property, chemoprotective activity.	[16] [33, 34]
		v. Dracophane: 2,4'-Dihydroxy-4,6-dimethoxydihydrochalcone;		Antitumor property, chemoprotective activity.	[1, 34]
		vi. (±)-7,4'-Dihydroxy-3'methoxyflavan.		Antioxidant property, Anticancer property, Antimicrobial property and Neuro protechtive.	[31, 37, 38]
		vii. 7,4'-Dihydroxyflavone		Antioxidant property, Anticancer property, Anti-inflammatory property.	[36]
2.	Sesquiterpene	Dracophane: 2,4'Dihydroxy-4,6 dimethoxydihydro halcone		Cytotoxic effects	[31, 36]

TRADITIONAL USES

D. cinnabari Balf.f. resin from Socotra is widely recognized as a conventional medicine with a lengthy history [26] For centuries, it has been traded as a medication and as a colorant ingredient for use in artworks, as evidenced by its discovery in specific artworks in a German museum [25]. Yemeni folks have long been utilizing this resin for wound healing, fevers, diarrhoea, haemorrhage, sore throat, dysentery, gastric ailments, oral cavity ulcers [1]. It is also used to treat blood clots (menses).

Fig 2: Images of (a) *D. cinnabari* tree (b) Dragon's blood resin (c) Powder of Dragon's blood (d) Dragon's blood extracted solution.

PHARMACOLOGICAL PROPERTIES

Antimicrobial activity:

At a dosage of 50 mg/ml, the ethanolic extract of *Dracaena cinnabari* Balf.f. inhibits Gram +ve (Staphylococcus saprophyticus) and Gram -ve (Pseudomonas aeruginosa, Proteus vulgaris, Klebsiella pneumonia and Escherichia coli.) microbes with zones ranging from 7 mm to 14 mm as seen in the study conducted by Altwair et al [8].

Gupta et al. evaluated the in vitro antimicrobial activity of resin of the Dragon's blood produced from *D. cinnabari* Balf.f. The resin extract was produced using three solvents (petroleum ether, dichloromethane and methanol) depending on its polarity and the dichloromethane resin extract demonstrated the maximum activity due to its high phenolic content, against nine distinct bacterial strains with MIC values against test microorganisms ranged from 0.156 to 1.25 mg/ml [21].

The antimicrobial property of *D. cinnabari* Balf.f. resin extract was investigated by Ansari et al. on antibiotic multi-resistant human pathogens as well as poly-microbial cultures. He reported that the *Dracaena cinnabari* Balf.f. ethanolic extract has substantial antimicrobial property against Gram -ve and Gram +ve pathogens of human, being most sensitive against Staphylococcus aureus and least sensitive against Aspergillus nidulans with an MIC value of 1.25 µg/mL (w/v) against Escherichia coli ATCC 10402, Staphylococcus aureus ATCC 29212 and Klebsiella pneumonia ATCC 10031,and of 2.5 µg/mL (w/v) for microbes (Pseudomonas aeruginosa ATCC 2785, Candida albicans ATCC 10231 and Salmonella typhimurum ATCC 3311) [39].

In another study conducted by Mothana et al. the antimicrobial property of several medicinal plants from the island of Socotra, including *Dracaena cinnabari* Balf.f., against both Gram -ve and Gram +ve bacteria, including species used in the technique of agar diffusion. He discovered that both methanolic and chloroform extracts of *Dracaena cinnabari* Balf.f. is active against species such as Micrococcus flavus (SBUG16), Staphylococcus aureus (ATCC 6538), Escherichia coli (ATCC 11229) and Bacillus subtilis (ATCC 6059) [22].

Anti-inflammatory and analgesic effects:

In animal model of acute pain and inflammation *D. cinnabari* Balf.f. exhibited that the plant ethanolic extract has an analgesic potential of 56.93 percent at 50mg/kg and of 67.79 percent at 150mg/kg as compared to aspirin (standard) of 44.11 percent at 200 mg/kg body wt., as well as a noteworthy reduction in inflammation during a period of 3 hr. The data indicates that the plant exhibits peripheral analgesic as well as anti-inflammatory activity and does not show any impact centrally [40].

In another study of Gupta et al. it was revealed that the methanolic extract of *D. cinnabari* Balf.f. resin and that 4'-hydroxy-7,8-methylenedioxyhomoisoflavan (MHF) one of its components, inhibited nitrite, tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6) generation in the lipopolysaccharide-stimulated mouse macrophage cell line RAW 264.7 with a rise in concentrations. He validated the activity further by observing a decrease in the rat's hind paw edema [41].

Antiviral activity:

On the island of Socotra, researchers assessed the anti-hepatitis B viral activity of native medicinal plants. This work showed that ten indigenous plants from Yemen contain anti-hepatitis-B virus (HBV) property. The methanolic extracts of the plant comprising *Dracaena cinnabari* Balf.f. was initially evaluated for cytotoxic activity to HepG2. cells and cytotoxic concentration (CC50) values were resolved. The anti-HBV potential was evaluated by suppressing HBeAg and HBsAg formation in the culture supernatant and determining their therapeutic index (TI) and half-maximum inhibitory concentration (IC_{50}). The IC_{50} value of *D. cinnabari* Balf. f. was found to be 20.93 μg/ml, proving an effective antiviral property [23].

Anticancer activity:

Apoptosis-inducing as well as cytotoxic properties of *Dracaena cinnabari* Balf.f. on human oral squamous cell carcinoma (OSCC) was reported by Alabsi et al. and was observed to be more evident in H400 cells. It was discovered that the sub-fractions of *D. cinnabari* Balf.f. resin (DCc 15 and DCd 16) displayed the highest cytotoxicity against H400 cells, therefore inhibiting them in a time-dependent way and was mainly accomplished through apoptosis. Externalization of the phospholipid phosphatidylserine was identified utilizing the Annexin V/4', 6-diamidino-2-phenylindole (DAPI) fluorescence double staining technique, which was investigated using the mitochondrial membrane potential (MMP) assay, caspase activities and cytochrome co-enzyme-linked immunosorbent, caspase properties, which revealed depolarization of MMP and concomitant, significant activation of caspases 3/7 and 9 along with S phase arrest [42].

Methanolic extract of *D. cinnabari* Balf.f was used to investigate the apoptosis induction potential in the carcinoma cell H103, a squamous cell line of tongue, as well as the chemo protective effect of the herb extract against carcinogenesis of tongue by (4NQO) in rats. In a time-dose dependent way, DCBME was cytotoxic to H103 cells, but had no cytotoxic property on normal cell line. In H103 cells, it produced cell morphological alterations, a substantial decrease in cell migration, S and G2/M-phase cell cycle arrest and triggered death through the intrinsic pathway. It can be concluded that the methanolic extract of *Dracaena cinnabari* Balf.f. can be used as a potent anticancer in the treatment of squamous cell carcinoma of tongue [43].

The polarographic behaviour of three homoisoflavonoids and four flavonoids isolated from Dragon's blood in an aprotic solution was studied by Vachalkova et al. and thereby determined the potential carcinogenicity tg α values, which indicated that most of the compounds possess either no or minimal carcinogenic effect, but structural modification in simple flavonoid structure possesses potential carcinogenic effect [14].

Antidiabetic activity:

Dracaena cinnabari Balf.f. resin ethanolic extract (DCBR) was tested for its anti-diabetic properties in Alloxan-induced diabetes and exhibits action in a time and dose-dependent way. On comparison with the untreated group, treatment of an ethanolic extract of resin at two dosages (100 and 300 mg/kg) leads to a substantial drop in FBG levels and revival of the damaged pancreatic cells in Alloxan-induced diabetic SD rats [44].

Helal et al. reported that dracidione, a newer C-linked chalcone-dihydrochalcone dimer isolated from *D. cinnabari* Balf.f. ethyl acetate extract showed considerable α-glucosidase inhibitory action with IC50 1/4 40.27 mg/ml [30].

TOXICITY

Acute oral toxicity indicated that the *Dracaena cinnabari* Balf.f. extract might be well tolerated up to a dosage of 2000mg/kg and at the dose of 1500mg/kg, the sub-acute test revealed no indication of any treatment-related alterations of the animals utilized in the study [45].

CONCLUSION

Dracaena cinnabari Balf.f. is a wild indigenous plant from island of Socotra, all of the locals utilizing it for a variety of illnesses. The resin has been used for both medicinal as well as non-medicinal purposes. This plant has been reported to have anti-microbial, analgesic, anti-inflammatory, anti-oxidant anti-cancer and anti-diabetic properties. Since the resin offers considerable potential, further investigation should be done for future studies of various compounds present, which seem to have better therapeutic effects regions.

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Conflict of Interest

There is no conflict of interest on the part of the authors.

Abbreviations

DC: *Dracaena cinnabari* Balf.f;
MHF: Methylenedioxyhomoisoflavan;
IL-6: Interleukin-6;
CC50: Cytotoxic Concentration;
TI: Therapeutic Index;
DAPI: 4', 6-diamidino-2-phenylindole; MMP:
Mitochondrial membrane potential;
DCBME: *Dracaena cinnabari* Balf.f methanolic extract;
4NQO: 4-nitroquinolone-1-oxide;
DCBR: *Dracaena cinnabari* Balf.f resin;
FBG: Fasting Blood Glucose;
MIC: Minima Inhibitory Concentration;
TNF-α: Tumor necrosis factor-α;
HBV: Hepatitis B Virus;
IC50: Inhibitory Concentration;
OSCC: Oral squamous cell carcinoma;

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