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Botany, traditional uses and pharmacological importance of *Karanjwa* (*Caesalpinia bonduc* (L.) Roxb.): A possible prophylactic AYUSH-unani single drug for the management of COVID-19

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Abstract

Karanjwa (*Caesalpinia bonduc* (L.) Roxb. Syn. *C. bonducella* (L.) Fleming) commonly known as a fever nut, is a flowering, straggling, and very thorny perennial shrub of Fabaceae, with a pantropical distribution. The species is well known for its medicinal and therapeutic values in Indian AYUSH-Ayurveda, Unani and Siddha systems of medicine. COVID-19 is an infectious disease caused by the recently discovered novel Coronavirus (SARS CoV-2). The most common symptoms of COVID-19 are fever, tiredness and dry cough. The Ministry of AYUSH, Government of India has issued the guidelines for qualified Unani practitioner to enhance the immunity and provide symptomatic relief in upper respiratory tract infection through prophylactic approach. One of the single drugs mentioned in the guidelines is *Karanjwa* (antipyretic, antimicrobial, anti-inflammatory and immuno modulator). In Unani, the plant parts; nuts and leaves are described as anti-inflammatory (Muha'lil-e-waram), anti-pyretic (*Musakkīn-e-alam*), blood purifier (*Musaffī-i-Dam*), anticonvulsant (*Dāfi 'i-Tashannuj*) and antiseptic (*Dāfi 'i-Ta'affun*) and used to treat various diseases, specifically seasonal fevers (*Hummā*), bronchial asthma (*Dīq al-Nafas*), bronchitis (*Su'al-o-Surfa*), ascites (*Istisqa' Ziqqi*), hydrocele (*Qarw Ma'i*) and pleurisy (*Dhat al-Janb*). The Seeds of *Karanjwa* contain a bitter substance named bonducin, bonducellin caesalpin sphytosterinin, citrulline and fatty acids. Seed coat as well as kernel's exhibits analgesic and anti-inflammatory activities. The purpose of this review paper is to compile the available information on and therapeutic uses of *Karanjwa* (*C. bonduc*) in context of Unani System of Medicine and to discuss the botany and importance of the plant on the basis of folk uses, pharmacological activities and chemical constituents. There is a possibility that the potential characteristics of *C. bonduc* may be utilized more efficiently through clinical trials and further research in the time of pandemic.

Keywords: AYUSH-Unani, Fevers (*Hummā*), *Caesalpinia bonduc*, Fever Nut, *Karanjwa*, Anti-inflammatory, Bronchial Asthma (*Dīq al-Nafas*)

Introduction

Karanjwa (*Caesalpinia bonduc* (L.) Roxb. Syn. *C. bonducella* (L.) Fleming), commonly known as a fever nut, is a flowering, straggling, and very thorny perennial shrub of Senna family (Fabaceae), with a pantropical distribution. The species is common all over India in coastal and other areas, especially the southern India, Mumbai and Bengal. The name of the species '*bonduc*' is derived from the Arabic word 'Bonduce' meaning a 'little ball' which indicates the globular shape of the seed. The seeds are grey coloured and resemble eyeballs, which explains the Sanskrit name 'Kubera' [1], meaning eyes of a Hindu God of wealth 'Kubera' [1]. Decoction of roasted kernels has been used in asthma [2, 3]. Paste prepared from kernel gives relief from boils and other such swellings [4]. Seeds of *Karanjwa* are claimed to be styptic, purgative and anthelmintic and cures inflammations; useful in colic, malaria, hydrocele, skin diseases and leprosy [2, 3, 5]. Pharmacological studies on *Karanjwa* seeds showed that the plant possess; anti-diarrhoeal, antiviral, antibacterial, antimicrobial, antifungal, antidiabetic, antitumor, antipyretic and analgesic, anti-filarial, anxiolytic, anti-inflammatory, antioxidant, immunomodulatory, and trypsin and chymotrypsin inhibitor properties [6]. Of different AYUSH systems, Ayurveda and Unani both have long, but different histories in the application of medicinal plants for therapeutic treatments. Unani System of Medicine (USM) is considered as one of the most ancient systems of medicine, originated in Greece and expanded itself to India as one of the recognized traditional system [7]. The drug *Karanjwa* is used in Ayurveda, Unani and Siddha (ASU) systems may have similar or different therapeutic applications, depend upon the use and processing of the drug. In Ayurveda, the plant is used to treat different diseases; tumours, cysts and cystic fibrosis [8].

The leaves alleviate *Kapha* and *Vata*, are emmenagogue febrifuge and anthelmintic, and are useful in the treatment of fevers, splenomegaly, hepatomegaly, piles, intestinal worms, elephantiasis, amenorrhoea, dysmenorrhoea, and pharyngodynia^[9]. The Siddha healers of Malabar region traditionally use the leaves of *C. bonduc* for the treatment of psoriasis^[10]. *Karanjwa* is known to Unani System since ancient times. The Unani traditional scriptures and texts have various references to the use of this plant as an antipyretic, antimalarial, antimicrobial and antiseptic^[11, 12]. *Karanjwa* is useful in *Hummayat* (fevers) due to change of season (*mausam*) and the kernel of the seed is used in the cases of continued or intermittent fevers^[13]. The extract or powder of the kernel along with ginger, honey and salt give excellent stomachic effect to kids suffering from lactose intolerance^[14]. Paste prepared from kernel gives relief from boils and other such swellings^[4, 14]. COVID-19 is an infectious disease caused by the novel Coronavirus (SARS CoV-2). The most common symptoms of COVID-19 are fever, tiredness and dry cough. Unani Medicine recognizes the influence of surroundings and ecological conditions on the state of health of human beings^[15]. In Unani classical text the concept of epidemics is mentioned very clearly. The drugs in Unani System are used either singly or in combination. Unani medicine is one of the legitimately recognized traditional medicine systems of India. Considering the importance of the Unani System the Ministry of AYUSH, Government of India explored preventive, supportive and rehabilitative care of the patients, issued the guidelines^[15] for qualified Unani practitioner to enhance the immunity and to provide symptomatic relief in upper respiratory tract infection through prophylactic approach. Among all, one of the single drugs mentioned in these guidelines is *Karanjwa* (antipyretic, antimicrobial, anti-inflammatory and immuno modulator)^[15]. The present review attempts to provide the comprehensive information on *Karanjwa* (*C. bonduc*), its traditional uses in Unani Medicine, botany, pharmacology and important phytoconstituentsto explore current research prospects and a possible role in the preventive management of Covid-19 with Unani medicine.

2. Description

Caesalpinia bonduc (L.) Roxb.

2.1 Current Scientific Accepted Name *Caesalpinia bonduc*

2.2 Authority (L.) Roxb.

2.3 Synonyms

- *Caesalpinia bonducella* (L.) Fleming
- *Caesalpinia. Crista* Thun
- *Guilandinabonducella* L.
- *Guilandina bonduc* L.

2.4 Classical Names

- Ayurvedic: Kantakikaranjah, Kuberakshi, Latakaranja, Puti, Morata, Putikaranja
- Unani: Karanjawa
- Siddha: Kazharchikkaai

2.5 Vernaculars

- English: Bonduc Nut, Nicker Bean
- Hindi : Gachika, Gajga, Kanderi, Kantikaranja, Naktamala, Karanj
- Kannada: Gajaga, Heggajjiga, Kitta, SannaGajjuga
- Malayalam: Caretti, Kalanchik-Karu, Kalanci, Kulunje, Avil, Kalimarakam

- Marathi: Gajaga, Kanchaki, Karbath, Rahedo, Saagaragota
- Tamil : Cakarakoti, Carivacantam, Gech-Chakkay, Kaccakkay, Utarikkoti
- Telugu : Gachakaya, Thellagachha, Gutsakai, SukaJambuka, Yalaxhi
- Arabic : Akitmakit, HajraIlaqi, Hajra-ul-Aqaab, Hajra-ul-Masak, Hajra-ul-Nasara
- Persian: Ashak-e-Marium, Khayahe-i-Iblis, Khayahe-Iblis, Qana-e-Iblees

2.6 Classification (Bentham and Hooker System)^[16]

Kingdom	:	Plantae– Plants
Division	:	Tracheophyta – Vascular plants
Class	:	Magnoliopsida– Dicotyledons
Order	:	Fabales
Family	:	Leguminosae (<i>nom. alt.</i> Fabaceae)
Subfamily	:	Caesalpinioideae
Genus	:	<i>Caesalpinia</i> L.
Species	:	<i>Caesalpinia bonduc</i> (L.) Rox



Fig 1A: Plant of *C. bonduc*; B. Long peduncled raceme with yellow flowers; C. Ovate-elliptical leaflet; D. Pods with sharp prickles; E. Seeds

2.7 Citations^[16]

Caesalpinia bonduc (L.)Roxb. Fl. Ind. 2: 362. 1832. emend Dandy & Exell in J. Bot. 76: 175. 1938; Saldanha & Nicolson, Fl. Hassan 871.1978. *Guilandina bonducella* (L.) Flem. Asiat. Res 11: 159.1810. *nom. illeg.*: FBI 2: 254. 1878. *Caesalpinia crista* auct, Gamble 1: 393. 1919.

2.8 Habitat

Common hedges, scrub forests, open areas, in plains and sacred groves

2.9 Habit

Large straggling very thorny perennial shrubs ((Fig 1.A),

2.10 Stem

Stem grey-downy, armed with hooked and straight hard yellow prickles.

2.11 Leaves

Leaves are bipinnate, 15–22 cm long; pinnae 4–6 pairs, prickled; leaflets 7-9 pairs, ovate – elliptic (Fig 1.C),, 1.5-3.5 x 1-2 cm, glabrous above, pubescent below, base truncate, rotund, margin entire, apex obtuse, mucronate, petiole ca. 1 mm; stipules foliaceous.

2.12 Inflorescence

Long peduncled terminal and axillary racemes (Fig 1.B).

2.13 Flowers

Flowers 1.2 cm across, pale yellow (Fig 1B), in terminal and supra axillary spicate racemes, calyx tube campanulate, to 5 mm, gibbous at base, sepals 5 unequal, oblong-obovate, 4.5–5 x 1 mm; tomentose: petals 5. oblanceolate upper one smaller, 5 x 2 mm; laterals 5-6 x 1.5 -2.5 mm, apex obtuse, marked with yellow color: stamens 10, declinate, alternate, 5 long, to 5 mm, 5 short, to 4 mm, filaments attenuate, base glandular - villous, to 3 mm, ovary stipitate, globose, to 3 mm; style short to 2 mm, pubescent.

2.14 Fruit

Pods oblong-obovoid, somewhat flattened, 5-7 x 2.5-4.5 cm, brick colour, densely clothed with sharp prickles (Fig 1.D), apex beaked to 1 cm, dehiscent.

2.15 Seed

Seeds 1 or 2, subglobose, to 3 x 6 mm, oblong, smooth, polished, lead coloured (Fig 1E)
Flowering: August-October; Fruiting. December-April

2.16 Distribution

This species is globally distributed in the Pantropics. Within India, it is found wild throughout the plains and in the deltaic regions of the western, eastern and southern India and reaching up to an altitude of 850 m. in the Himalayas. It is also cultivated as a hedge plant

3. Description in Unani Classical Texts ^[12, 13]**3.1 Mizāj (temperament)**

Unani scholars have identified its temperament but differed in opinion related to its temperament ^[13]

- Hot and Dry in First Degree
- Cold and Dry in First Degree
- Hot and Dry in Third Degree (only few Physician accepted)

3.2 Part Used

- Seed nut / Seed Kernel/Leaves

3.3 Dose

- 3-5 g

3.4 Muzir (Adverse/Toxic Effect)

- Nausea, Dryness

3.6 Musleh (Corrective)

- Mirchsiyah (*Piper nigrum*) is used to remove its adverse effects.

3.7 Badal (Substitute)

- *Berg-e-Karanjwa* (Leaves of *C. bonduc*)

3.8 Afa'al (Pharmacological Actions in Unani medicine)

As per the Unani classical text ^[12, 13, 17, 18] *Karanjwa* is;

- Anti-inflammatory (*Muha; lil-e-waram*)
- Anti-pyretic (*Musakkīn-e-alam*)
- Blood Purifier (*Musaffī-i-Dam*)
- Anticonvulsant (*Dāfi 'i-Tashannuj*)
- Antiseptic (*Dāfi 'i-Ta'affun*)
- Carminative (*Kasir-i-Riyāh*)
- Fluid Absorbent (*Jādhīb Ruṭūubat*)

- Dessicant (*Mujaffif*)
- Antiasthmatic (*Dāfi 'i-Zeequnnafas*)
- Demulcent (*Mulattif*)
- Diuretic (*Mudirr-i-Bawl*)
- Difficulty in micturition (*Ushr-i-Bawl*)
- Expectorant (*Munaffis*)

3.9 Istem'al (Therapeutic Indications in Unani medicine)

^[12, 13, 17, 18]

- Bronchial Asthma (*D īq al-Nafas*)
- Bronchitis (*Su 'al-o-Surfa*)
- Orchitis (*Waram- al-Khusyatayn*)
- Ascites (*Istisqa' Ziqqi*)
- Hydrocele (*QarwMa'i*)
- Seasonal Fever (*Hummā*)
- Pleurisy (*Dhat al-Janb*)
- Stomatitis (*Qula*)

Leaf of *Karanjwa* is useful in *Hummayat* (fevers) due to season (*mausam*) and predominance of morbid phlegm, blood and black bile (*Fasad-e-Balgham, Dam and Sauda*) ^[12, 13]. A poultice made up of powder and oil is useful to treat acne and pimples. The seed-kernel, burnt in any oil, is applied to infected wounds and cutaneous affections. Vaidyas suggested that the seasonal fever goes away by taking powder made by grinding the equal amounts of *Karnajwa* and black pepper (8-10 g) twice a day ^[12, 13].

In Unani system of medicine, a prescription, *Habbe Karanjwa*, is given as an antiperiodic in the fourth-day fever. *Karanjwa* leaves, pounded with *Piper nigrum* are given in diseases due to vitiated blood. *Karanjwa* is also used in various other conditions such as; bronchial asthma, bronchitis, fever, hydrocele, joint pain, and pleurisy ^[12, 13, 17].

4. Folk-medicinal Uses

In folk medicine, the plant juice is given for two weeks after meals to cure intermittent fever. The ointment made from the seed-kernels is applied to hydrocele. As an infusion, they are prescribed in haemorrhages. *Karanjwa* mixed with honey or castor oil is given as an anthelmintic. Mostly, grounded and roasted seeds are given internally ^[19, 20]. Seeds and root bark are very useful in simple, continued, and intermittent fevers, asthma, and colic. Seeds are febrifuge and antiperiodic; they are also valuable for dispersing swelling, restraining haemorrhage, and keeping off infectious diseases ^[1, 2, 19, 20]. Tender leaves are efficacious in liver disorders. Oil expressed from them is useful in convulsions and nervous complaints. Doses - Seed powder- 1 to 2 g; root powder- 1 to 2 g; leaf infusion - 12 to 20ml. The young leaves are applied to affected areas for the treatment of infections, gargle for sore throat, elephantiasis and smallpox, disorders of the liver and for expelling intestinal worms ^[3, 4, 19, 20].

The seeds are astringent and have been used to control contagious diseases, treat inflammation, colic, hydrocele, skin diseases and leprosy. The seed sprouts have been used for tumours. The root bark is used to treat fever, intestinal worms, tumours, amenorrhoea, cough and for removing the placenta after childbirth ^[1, 3, 4, 20]. An analysis of the literature on ethnobotanical data available (Table 2.) on *C. bonduc* (*Karanjwa*) seed, followed by leaf and root (Fig. 2), mostly in crude powder form (53%) followed by paste (33%). However, nearly 7% used *Karanjwa* as decoction and infusion (Fig. 3). Most of the workers reported its ethnomedicinal uses as antipyretic (maximum), followed by treatment of hydrocele

and diabetes. Other reports include the disease conditions including; pneumonia, piles, asthma, skin disorders, cough and arthritis (Fig 4.).

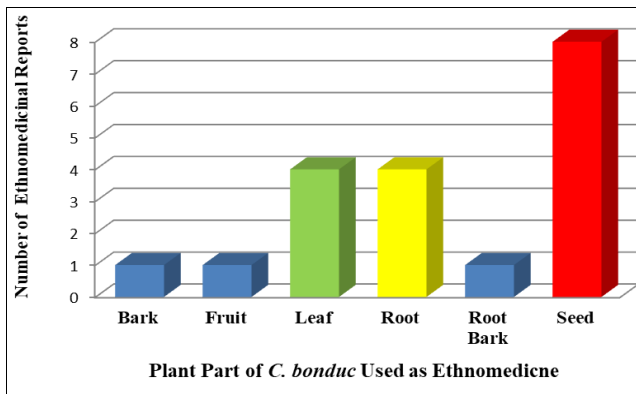


Fig 2: Part of *Karanjwa* (*C. bonduc*) plant used as ethno-medicine

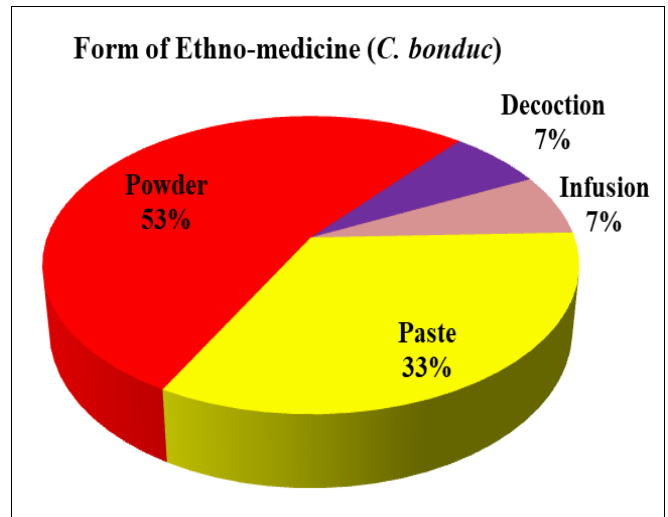


Fig 3: Form of ethnomedicine – *Karanjwa* (*C. bonduc*)

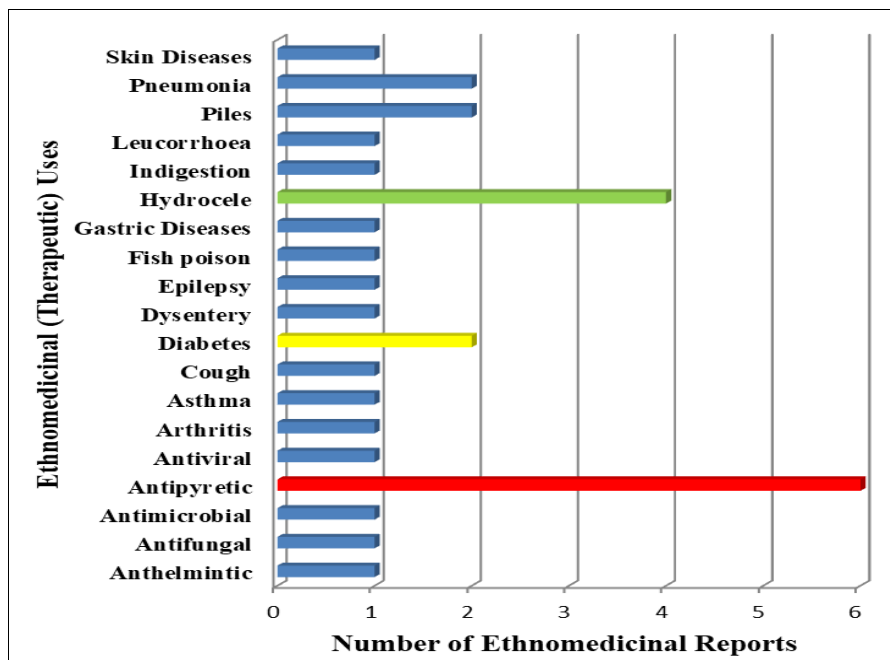


Fig 4: Ethnomedicinal uses of *Karanjwa* (*C. bonduc*) in different disease conditions

Table 2: Ethnomedicinal uses of *Karanjwa* (*Caesalpinia bonduc*)

S. No	Part Used	Ethnomedicine (Form)	Ethnomedicinal (Therapeutic) Uses	References
1	Seed	Paste	Leucorrhoea, hydrocele	[21]
2	Leaf, Bark, Root, Seed	Powder	Antimicrobial, anti-fungal, anti-viral, Piles, Antipyretic	[22]
3	Seed	Powder	Vomiting, Hydrocele	[23]
4	Seeds	Powder and Paste	Pain Indigestion, Dysentery, Piles, Worms, Cough, Diabetes, Skin Diseases	[24]
5	Leaf	Paste	Hydrocele	[25]
6	Seed	Paste	Fever	[26]
7	Root	Powder	Asthma	[27]
8	Seed	Decoction	Arthritis, Resettlement of disturbed joints and bones specially after trauma,	[28]
9	Root	Powder	Fish Poison	[29]
10	Seeds, Leaves	Powder	Fever, Diabetics	[30]
11	Seeds, Leaves	Paste	Fever, Hydrocele	[31]
12	Root	Infusion	Malaria	[32]
13	Root Bark	Powder	Epilepsy	[33]
14	Fruit	Powder	Pneumonia, Gastric Troubles	

5. Pharmacological Evidence/ Experimental studies

A number of studies showed that *C. bonduc* plant possessed broad pharmacological properties including; anti-

inflammatory, antioxidant, anticancer, antihyperuricemic hepatoprotective, antibacterial activity, and anti-fungal (Table 3).

Table 3: Pharmacological studies on *Caesalpinia bonduc*

S. No.	Activity	Part/ extract/	Experimental Studies/Cell Lines/ Animal Model/ microorganism
1	Antidiabetic	Alcoholic Extract- Seed Polyphenol Extract	Alloxan Induced Diabetic Male Albino Rats [34] Different doses of extract to hyperglycemic rats restored blood and serum glucose, insulin, reduced oxidative stress in pancreatic β cells by restoring free radical scavenging potential [35]
		Seed and shell Extract	<i>in-vitro</i> [36]
		Seed Extract	Showed a significant Antidiabetic activity in alloxan induced hyperglycemia in rats [37]
		Aqueous and Ethanolic Extracts -Seeds	Significant blood sugar lowering effecting both type 1 and 2 diabetes mellitus in Long Evans rats [38]
2	Anti-inflammatory Antipyretic and Analgesic	Seed Oil	The oil exhibited anti-inflammatory activity in experimental rats in a paw edema test induced by carrageenan [39].
		Ethanolic extract of whole seeds	In experimental albino rats [39]
		Ethanolic extract (70%) of seed kernel	Exhibited marked antipyretic activity against Brewer's yeast- induced pyrexia in rats, significant central analgesic activity and peripheral analgesic effect in both mice and rats In adult albino rats or mice [40]
		Flower extract	Reduced pyrexia in adult mice in carrageenan-induced inflammation, cotton pellet induced chronic granulomatous inflammation and autacoids-induced inflammation [41]
3	Antibacterial and Cytotoxic activities	Methanolic Seed extract	Inhibited growth of Gram-positive and Gram-negative bacteria by the diffusion method and exhibited a similar activity of the standard antibacterial kanamycin [42]
		Methanol extract and fractions of leaves	The extracts showed different zones of inhibition against four gram-positive and five gram-negative bacteria [43]
		Methanolic leaf and Bark extracts	Gram positive and Gram negative bacteria [44]
4	Anti-cancer	Phytochemicals from young twigs and leaves	<i>In silico</i> interaction between phytochemicals and cancer target proteins (TK, VEGF, and MMP) compared with their respective drug inhibitors [45]
5	Anticonvulsive	Petroleum Ether	Exhibited activities in convulsions models [46]
6	Antioxidant	Ethanolic extract	<i>in vitro</i> -showed a high free radical-scavenging activity [47]
		Chloroform Extract	Exhibited <i>in vitro</i> radical scavenging effect [48]
7	Anti-filarial	crude extract or fractions of the seed kernel	Exhibited gradual fall in microfilariae count in <i>L. sigmodontis</i> -cotton rat model [49]
8	Anti-malarial	Aqueous, cold alcoholic and hot alcoholic extracts	Exhibited inhibition in growth of <i>Plasmodium falciparum</i> [50]
		Root Extract	Exhibited dose-dependent suppression of parasite growth <i>in vivo</i> in mice [51]
9	Anti-Tumour	Methanol extract	Exhibited significant antitumor activity in Ehrlich ascites carcinoma (EAC)-bearing Swiss albino mice [52]
10	Immunomodulatory	Ethanolic Seed Extract	<i>in vivo</i> experiments- sheep red blood cell and rats [53]
		Aqueous Seed extract	<i>in vivo</i> , cell mediated and humoral components of the immune system in rats [54]

6. Phytoconstituents

The main phytochemicals of *C. bonduc* seeds are; bonducin (a bitter substance), phytosterin in, fatty acids, caesalpins (α , β , γ , δ and ψ), the new constituents; diterpine caesalpin, homoisoflavone- bonducellin and citrulline, and different fatty acids [55]. Cassanefurano diterpene with good antimalarial activity against MDR K1 strain of *P. falciparum*,

and many cassane diterpenoids [56] have been reported from the seed kernel [57]. Pipataline isolated from bark [58]. Cassane diterpenes, including caesaldekalin A, were isolated from roots [59]. Cytotoxic flavonoids have been isolated from young twigs and leaves [60]. The phytoconstituents are summarized in Table 4.

Table 4: Major Chemical constituents of *C. bonduc* (Karanjwa)

S. No.	<i>C. bonduc</i> Plant Part(s)	Name of the Chemical Constituents	References
1.	Seed Seed Kernel	Bonducin- A bitter substance Phytosterinin Fatty acids, Caesalpins (α , β , γ , δ and ψ), Bonducellin (Homois of lavone) Citrulline Cassanediterpenes, Neocaesalpins C, D Bondenolide Neocaesalpin P, Neocaesalpin H Cordylane A, CaesalpininB Bonducellpin E,	[55, 61]
		Caesalpinolide A Caesalpinolide C, D and E	[56]
		Cassane Diterpinoids	[57]
		Cassane Furanoditerpene	
2.	Bark	Caesaldekalin J Pipataline	[58]
3.	Young Twigs Leaves	Cytotoxic Flavonoids	[60]
4.	Roots	Caesaldekalin A	[59]

7. Conclusion

Karanjwa (*C. bonduc*; Syn. *C. bonducella*), fever nut, is a very important Unani medicinal plant, which is mentioned in classical texts in-detail for its various actions and therapeutic values especially as analgesic and anti-inflammatory uses. *Karanjwa* is also recorded in other traditional systems, like Ayurveda and Siddha. It has been widely used as a traditional ethno-medicine to treat fever, hydrocele, diabetes, and other disease conditions by tribal communities. The current review deliberated the uses of *Karanjwa* available in classical Unani texts and other literature. Furthermore, current pharmacological actions and a reasonable amount of phytochemical and ethnobotanical data endorse it to be a promising prophylactic medicinal plant which could be utilized judiciously through new modern techniques and target specific clinical trials to find out a possible approach in the preventive management of Covid-19 especially with Unani medicines. However, to be clinically useful, more scientific data are needed.

8. Acknowledgements

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9. Note (Disclaimer)

This review paper is based on the data and literature available in public domain and not intended to claim any specific prevention, management or cure for COVID-19.

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