



Review

Ethnobotanical, phytochemical, and pharmacological properties of *Cerbera manghas* L.

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In this review article, the ethnobotanical, phytochemical, and pharmacological properties of *Cerbera manghas* L. (Apocynaceae) are discussed. This plant has applications in traditional folk medicine as analgesic, anti-convulsant, a cardiostimulant and for hypotensive activity. Phytoconstituents of this plant are secondary metabolites like saponins, terpenoids, and alkaloids along with phenolic acids, flavonoids, cardiac glycosides, steroids, iridoids, lignans, and other compounds. The major phytochemical compounds are cardiac glycosides followed by terpenoids and phenolic acids. Again, the leaf has greater types and numbers of phytochemicals, followed by the fruit, seed, stem, and root. The plant also shows many pharmacological activities such as antioxidant, anticancer, anti-inflammatory, DNA damage protection, and antimicrobial. This review could help researchers in further investigations in these directions.

Keywords. Apocynaceae; *Cerbera manghas*; mangrove; ethnobotany; phytoconstituents; pharmacology

1. Introduction

Cerbera manghas (Family: Apocynaceae) is a poisonous plant and is common along the coasts of south Asia and Southeast Asia, northern Australia, and Polynesia. This mangrove species is classified as vulnerable (Ved *et al.* 2008) and is an endangered species in the Bhitarkanika National Park, Odisha, India (Upadhyay *et al.* 2008). This plant is widely used for greening as well as an ornamental plant. This plant fights infectious diseases. Swallowing any part of *Cerbera* tree, particularly the fruits, can cause nausea, vomiting, abdominal pain, and cramping (Scott and Thomas 2000). Deaths may occur following intentional self-poisoning with *C. manghas* plants (Eddleston and Persson 2003).

The taxonomic position of *C. manghas* L. is described by the IUCN (Yu and Qin 2019) and GBIF (GBIF database 2019). This species is also known by several vernacular names as it is distributed in the mangrove region of various parts of India (Ved *et al.* 2016). The details of taxonomic position and vernacular names are mentioned in

table 1. It is widely distributed from the islands of the Indian Ocean, tropical Asia, tropical Australia, the islands of the Pacific Ocean, and tropical Africa (Leeuwenberg 1999; Govaerts *et al.* 2003; Lemmens *et al.* 2006). It is indigenous to Southeast Asia, Australia, and also some islands of Polynesia (Scott and Thomas 2000).

C. manghas L. is a small tree which usually grows up to 20 m in height and up to 70 cm in diameter. The branches are thick and succulent. The stem has large lenticels and soft wood. The leaves are dark-green and arranged spirally. The fruits are nearly oval shape, turn bright red at maturity, single-seeded, and seedling with hypogeal germination (Lemmens *et al.* 2006). Vegetative propagation of this species takes place through stem-cuttings and air-layering by standard methods (Eganathan *et al.* 2000; Basak *et al.* 1995, 2000). This review article gives a critical description of the complete profile of the mangrove plant *C. manghas* L., mainly highlighting the various ethnobotanical uses, phytochemical constituents isolated, and pharmacological studies conducted on this plant.

Table 1. Taxonomical classification and Vernacular names of *Cerbera manghas* L.

Taxonomical Classification		Language	Vernacular names
Kingdom	Plantae	Sanskrit	Auddalakah, Svanamarah
Phylum	Tracheophytes	Hindi	Dabur, Pilikirbir, Sukanu
Class	Magnoliopsida	Tamil	Kadalma, Kadama, Kadamoth, Udalai, Utalai, Kottuma
Order	Gentianales	English	Beach milkwood, Grey milkwood, Sea mango
Family	Apocynaceae	Malayalam	Cattankaya, Chattankaya, Chaththankai, Pona, Ponna, Utalam
Genus	<i>Cerbera</i>	Marathi	Kharauro, Sukanu
		Kannada	Cande, Chande, Honde, Monde, Tende
Species	<i>manghas</i>	Odia	Paniambo

2. Ethnobotanical information

Cerberin of this mangrove species has been used as medicine in very small amounts to treat cardiac disorders (Barceloux *et al.* 2012). Traditionally, the fruit of *Cerbera* is used as to treat diseases, as analgesic, anti-convulsant, cardiotoxic, and hypotensive activity (Chang *et al.* 2000). Some of the allelochemicals from this sea mango are used in pest control in agriculture as termiticides (Tarmadi *et al.* 2014) and bactericides (Rajathi and Nambaru 2014). *C. manghas* is a medicinal plant which is traditionally known for cardiotoxic, analgesic, anti-inflammatory activity, etc. (Jeong *et al.* 2014).

The seeds are used externally to treat scabies and itch, and hair tonic preparation. The bark is used for the treatment of dysuria and ringworm. The flowers are used to treat haemorrhoids. The roots, bark, latex, and leaves of *C. manghas* can be used as emetic and purgative. In Asia, the wood of this species is occasionally used for the preparation of interior trim, fruit cases, matches, shuttering, clogs, plain furniture, and carving, and also for charcoal (Fern 2014). *C. manghas*

is also used for the treatment of fever, malaria, pain, diabetes, gastrointestinal ailments, skin diseases, and ectoparasitic diseases (Wiar 2006).

3. Phytochemistry

The extract of *C. manghas* contains reducing sugars, tannins, steroids, alkaloids, glycosides, polyphenols, terpenoids, flavonoids, saponins, etc. (Hossain *et al.* 2013; Anwar *et al.* 2013; Xiaopo *et al.* 2010). *p*-Hydroxybenzaldehyde, benzamide, *n*-hexadecane acid monoglyceride, loliolide, β -sitosterol, cerberin, nerifolin, cerleside A, and daucosterol are the compounds present in the leaves of *C. manghas* (Chan *et al.* 2016; Zhang *et al.* 2010). Air-dried *C. manghas* leaves have 17 α -digitoxigenin and 17 α -tanghinigenin. Fresh leaves contain oleagenin glucosyl-thevetoside, digitoxigenin gentiotriosyl-thevetoside, glycosides, and glucosyl-thevetosides of digitoxigenin and tanghinigenin (Yamauchi *et al.* 1987).

The major phytochemical compounds of *C. manghas* are cardiac glycosides followed by terpenoids, phenolic acids, iridoids, flavonoids, steroids, lignans, and others. Seventeen terpenoids, 13 cardiac glycosides, 7 steroids, 7 iridoids, 5 flavonoids and 4 phenolic acids are only present in leaves. Also, 9 phenolic acids (only in fruits), 6 cardiac glycosides (only in seed), and 3 flavonoids (only in stem) are the other components of this species. Cerbinal (in all parts) and ursolic acid (in leaf and fruit) are the other terpenoids are present in *C. manghas*. *p*-Hydroxybenzaldehyde (in leaf and fruit) and vanillic acid (in fruit, stem, and root) are the other phenolic acids present in this species. Cerberin (leaf, fruit, and seed), 17 β -neriifolin (leaf, stem, root, and fruit) and 17 β -digitoxigenin- β -D-glucosyl-(1 \rightarrow 4)- α -Lthevetoside (stem and root) are the other cardiac glycosides present in *C. manghas*, while a few iridoid compounds are present in stem, bark, and root. Lignans are present in stem and root. Besides these, other compounds are also present in *C. manghas* (figure 1; table 2).

4. Pharmacological activities

4.1 Antioxidant activity

The extracts of *C. manghas* have antioxidant properties (Lee *et al.* 1998; Hossain *et al.* 2013). The antioxidants in *C. manghas* leaves can be due to the presence of phytoconstituents (Anwar *et al.* 2013). Phenolic

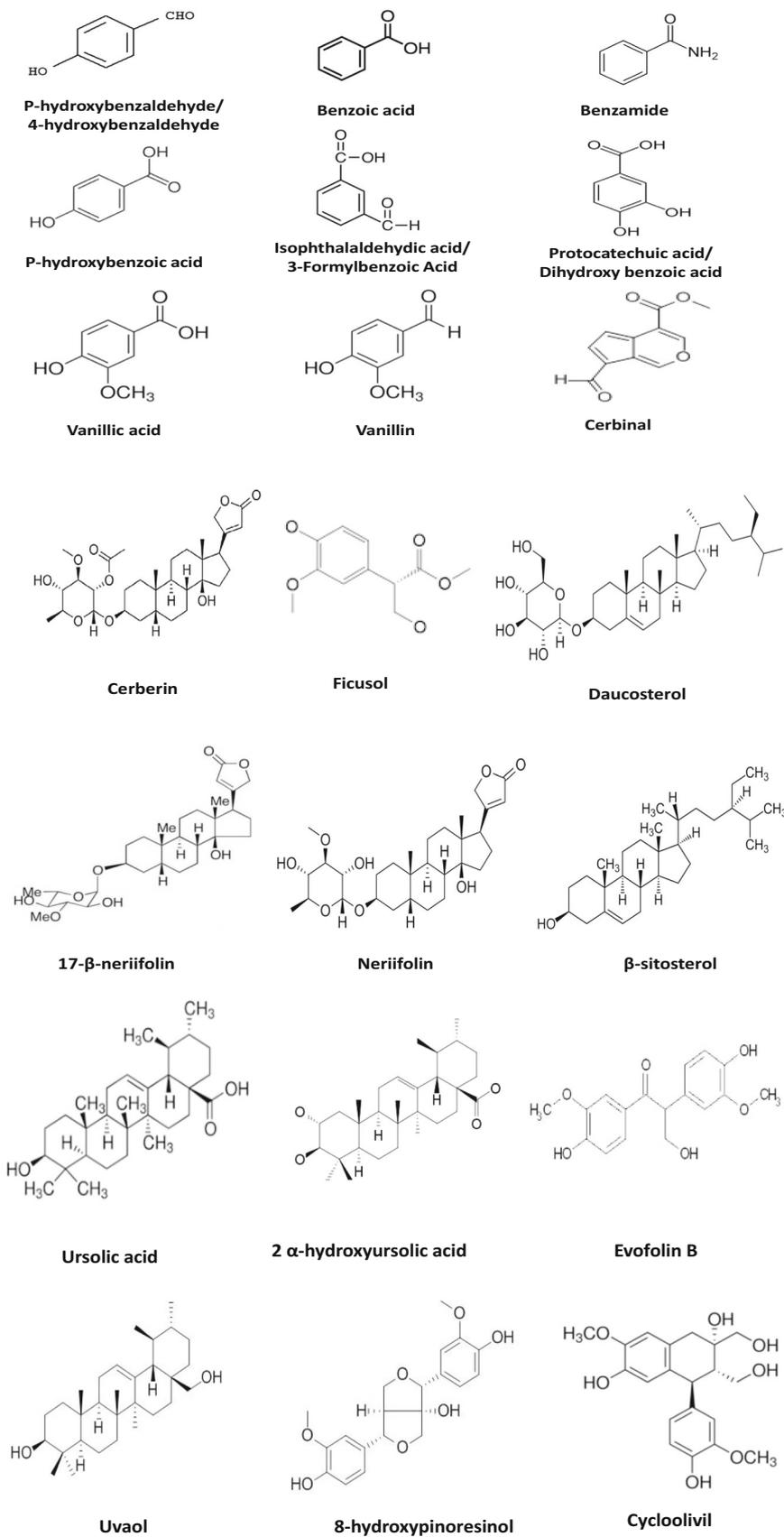


Figure 1. Chemical structures of some phytoconstituents present in *Cerbera manghas* L.

Table 2. Phytoconstituents isolated from *Cerbera manghas* L.

Chemical compound/ Component (parts of tree)	References
<i>Terpenoids</i>	
Uvaol (leaf)	Zhang <i>et al.</i> (2011)
(23Z)-9, 19-cycloart-25-ene-3 β ,24-diol (leaf)	Zhang <i>et al.</i> (2011)
Euphorbol (leaf)	Zhang <i>et al.</i> (2011)
2 α -hydroxyursolic acid (leaf)	Zhang <i>et al.</i> (2011)
3-O-acetyl ursolic acid (leaf)	Zhang <i>et al.</i> (2011)
Blumenol A (leaf)	Chan <i>et al.</i> (2016)
Cerberidol-3 (leaf)	Chan <i>et al.</i> (2016)
10-bis- <i>O</i> - β -D allopyranoside (leaf)	Chan <i>et al.</i> (2016)
Cerberidol (leaf)	Chan <i>et al.</i> (2016)
Cerberidol-3- <i>O</i> - β -D allopyranoside (leaf)	Chan <i>et al.</i> (2016)
Cyclocerberidol (leaf)	Chan <i>et al.</i> (2016)
Cyclocerberidol-3- <i>O</i> - β -D allopyranoside (leaf)	Chan <i>et al.</i> (2016)
Cyclocerberidol-3- <i>O</i> - β -D glucoside (leaf)	Chan <i>et al.</i> (2016)
Euscaphins AB (leaf)	Chan <i>et al.</i> (2016)
Epoxyerberidol (leaf)	Chan <i>et al.</i> (2016)
Epoxyerberidol-3- <i>O</i> - β -D allopyranoside (leaf)	Chan <i>et al.</i> (2016)
Epoxyerberidol-3- <i>O</i> - β -D glucoside (leaf)	Chan <i>et al.</i> (2016)
Cerbinal (leaf, stem, bark, fruit, root)	Chan <i>et al.</i> (2016), Yan (2010), Cao <i>et al.</i> (2013)
Ursolic acid (leaf, fruit)	Zhang <i>et al.</i> (2011), Chan <i>et al.</i> (2016), Cao <i>et al.</i> (2013)
<i>Phenolic acids</i>	
Succinic acid (leaf)	Chan <i>et al.</i> (2016)
m-carboxyphenylacetic acid (leaf)	Chan <i>et al.</i> (2016)
p-hydroxycinnamic acid (leaf)	Chan <i>et al.</i> (2016)
Isophthalic acid (leaf)	Chan <i>et al.</i> (2016)
Benzoic acid (fruit)	Chan <i>et al.</i> (2016), Cao <i>et al.</i> (2013)
Vanillic acid (fruit, stem, root)	Chan <i>et al.</i> (2016), Yan (2010), Cao <i>et al.</i> (2013)
Vanillin (fruit)	Chan <i>et al.</i> (2016), Cao <i>et al.</i> (2013)
p-hydroxybenzaldehyde (leaf, fruit)	Xiaopo <i>et al.</i> (2010), Chan <i>et al.</i> (2016), Zhang <i>et al.</i> (2010), Cao <i>et al.</i> (2013)
Isophthalaldehydic acid (fruit)	Chan <i>et al.</i> (2016), Cao <i>et al.</i> (2013)
β -hydroxypropiovanillone (fruit)	Chan <i>et al.</i> (2016), Cao <i>et al.</i> (2013)
Ficusol (fruit)	Chan <i>et al.</i> (2016), Cao <i>et al.</i> (2013)
Evofofolin B (fruit)	Chan <i>et al.</i> (2016), Cao <i>et al.</i> (2013)

Table 2. (continued)

Chemical compound/ Component (parts of tree)	References
3, 4'-dihydroxypropiofenone (fruit)	Chan <i>et al.</i> (2016), Cao <i>et al.</i> (2013)
p-hydroxybenzoic acid (fruit)	Chan <i>et al.</i> (2016), Cao <i>et al.</i> (2013)
Protocatechuic acid (fruit)	Chan <i>et al.</i> (2016), Cao <i>et al.</i> (2013)
<i>Flavonoids</i>	
Clitorin (leaf)	Chan <i>et al.</i> (2016)
Manghaslin (leaf)	Chan <i>et al.</i> (2016)
Nicotiflorin (leaf)	Chan <i>et al.</i> (2016)
Rutin (leaf)	Chan <i>et al.</i> (2016)
3-O-(2-Rhamnosyl-rutinosyl)-7-O- β -glucosylquercetin (leaf)	Chan <i>et al.</i> (2016)
Aromamadedrin (stem)	Chan <i>et al.</i> (2016)
(+)-Dihydroquercetin (stem)	Chan <i>et al.</i> (2016)
Naringenine (stem)	Chan <i>et al.</i> (2016)
Naringenine-7-glucoside (stem)	Chan <i>et al.</i> (2016)
<i>Cardiac glycosides</i>	
17 α -Tanghinigenin (leaf)	Yamauchi <i>et al.</i> (1987), Chan <i>et al.</i> (2016)
17 β -Tanghinigenin (leaf)	Chan <i>et al.</i> (2016)
17 α -Solanoside (leaf)	Chan <i>et al.</i> (2016)
17 β -Solanoside (leaf)	Chan <i>et al.</i> (2016)
Neriifolin (leaf)	Xiaopo <i>et al.</i> (2010), Zhang <i>et al.</i> (2010), Chan <i>et al.</i> (2016)
17 α -neriifolin (leaf)	Chan <i>et al.</i> (2016)
17 α -Cerdollaside (leaf)	Chan <i>et al.</i> (2016)
17 β -Cerdollaside (leaf)	Chan <i>et al.</i> (2016)
Cerleaside A (leaf)	Xiaopo <i>et al.</i> (2010), Zhang <i>et al.</i> (2010), Chan <i>et al.</i> (2016)
Cerleaside B (leaf)	Chan <i>et al.</i> (2016)
Deacetyltanghinin (leaf)	Chan <i>et al.</i> (2016)
17 α -Deacetyltanghinin (leaf)	Chan <i>et al.</i> (2016)
17 β -Deacetyltanghinin (leaf)	Chan <i>et al.</i> (2016)
17 β -neriifolin (leaf, stem, root, fruit)	Yan (2010), Cao <i>et al.</i> (2013), Chan <i>et al.</i> (2016)
Tanghinin (seed)	Chan <i>et al.</i> (2016)
Thevetin B (seed)	Chan <i>et al.</i> (2016)
2'-O-Acetyl cerleaside A (seed)	Chan <i>et al.</i> (2016)
2'-O-Acetyl thevetin B (seed)	Chan <i>et al.</i> (2016)
7,8-Dehydrocerberin (seed)	Chan <i>et al.</i> (2016)
Deacetyltanghinin (seed)	Chan <i>et al.</i> (2016)
Cerberin (leaf, fruit, seed)	Xiaopo <i>et al.</i> (2010), Zhang <i>et al.</i> (2010), Cao <i>et al.</i> (2013), Chan <i>et al.</i> (2016)
17 β -Digitoxigenin- β -D-glucosyl-(1 \rightarrow 4)- α -Lthevetoside (stem, root)	Yan (2010)

Table 2. (continued)

Chemical compound/ Component (parts of tree)	References
<i>Steroids</i>	
Bornesitol (leaf)	Chan <i>et al.</i> (2016)
β -sitosterol (leaf)	Zhang <i>et al.</i> (2010), Chan <i>et al.</i> (2016)
Daucosterol (leaf)	Xiaopo <i>et al.</i> (2010), Zhang <i>et al.</i> (2010), Chan <i>et al.</i> (2016)
3 α ,12 β - Dihydroxy-pregname-16- en-20- one (leaf)	Chan <i>et al.</i> (2016)
3 β ,12 β - Dihydroxy-pregname-16- en-20- one (leaf)	Chan <i>et al.</i> (2016)
12 β - Hydroxy-5 α -pregname-16- en-3,20- dione (leaf)	Chan <i>et al.</i> (2016)
12 β - Hydroxy-pregname-4,16- diene-3,20- dione (leaf)	Chan <i>et al.</i> (2016)
<i>Iridoids</i>	
10- <i>O</i> - Benzoyltheveside (leaf)	Chan <i>et al.</i> (2016)
10- <i>O</i> - Benzoyltheviridoside (leaf)	Chan <i>et al.</i> (2016)
10-Carboxyloganin (leaf)	Chan <i>et al.</i> (2016)
10-Dehydrogeniposie (leaf)	Chan <i>et al.</i> (2016)
Loganin (leaf)	Chan <i>et al.</i> (2016)
Theveside (leaf)	Chan <i>et al.</i> (2016)
Theviridoside (leaf)	Chan <i>et al.</i> (2016)
Cerberic acid A, B (bark)	Chan <i>et al.</i> (2016)
Cerberinic acid (bark)	Chan <i>et al.</i> (2016)
Coniferaldehyde (stem, root)	Yan (2010)
<i>Lignans</i>	
Cerbera lignin A-I (stem)	Chan <i>et al.</i> (2016)
Cerbera lignin J-N (stem)	Chan <i>et al.</i> (2016)
(-)-Cycloolivil (stem, root)	Chan <i>et al.</i> (2016), Yan (2010)
(+) – Cycloolivil (stem)	Chan <i>et al.</i> (2016)
(-)-Olivil (stem, root)	Chan <i>et al.</i> (2016), Yan (2010)
Olivil 4- <i>O</i> - β - D glucose (stem)	Chan <i>et al.</i> (2016)
Olivil 4'- <i>O</i> - β - D glucose (stem)	Chan <i>et al.</i> (2016)
<i>Others</i>	
17 α -digitoxigenin (leaf)	Yamauchi <i>et al.</i> (1987)
Oleagenin glucosyl-thevetoside (leaf)	Yamauchi <i>et al.</i> (1987)
Digitoxigenin gentiotriosyl-thevetoside (leaf)	Yamauchi <i>et al.</i> (1987)
Benzamide (leaf)	Zhang <i>et al.</i> (2010)
Loliolide (leaf)	Xiaopo <i>et al.</i> (2010), Zhang <i>et al.</i> (2010)
n-hexadecane acid monoglyceride (leaf)	Zhang <i>et al.</i> (2010)

Table 2. (continued)

Chemical compound/ Component (parts of tree)	References
8-Hydroxypinoresinol (stem, root)	Yan (2010)
1,3-bis(<i>m</i> -carboxylphenyl)-propan-2-one (bark)	Zhang <i>et al.</i> (2009)
2-(<i>m</i> -carboxylphenyl)- 3-(<i>m</i> -carboxylbenzyl) succinic acid (bark)	Zhang <i>et al.</i> (2009)

contents, flavonoid contents, etc., are the phytoconstituents present in *C. manghas* that determine its antioxidant activity (Maharana *et al.* 2015, 2020; lawsipo *et al.* 2017).

4.2 Anticancer activity

Cardiac glycoside (Neriifolin) from *C. manghas* reduced viability of HepG2 cells, induced S and G2/M phase arrests of the cell cycle, and stimulated apoptosis of HepG2 cells. Neriifolin can be considered for the treatment of hepatocellular carcinoma (Zhao *et al.* 2011). Cardiac glycoside (Tanghinigenin) is found in the seed of *C. manghas*. This compound can reduce the viability of human promyelocytic leukemia HL-60 cells and can efficiently induce apoptosis in HL-60 cells (Wanga *et al.* 2010). Cardenolides present in the roots of *C. manghas* have antiproliferative properties against a human colon cancer cell line (Col2) and the Ishikawa cell line (Chang *et al.* 2000). New cytotoxic Cardenolides glycosides (7, 8-sehydrocerberin, deacetyltanghinin, and tanghinin) of *C. manghas* seed also have antiproliferative properties against oral human epidermoid carcinoma (KB), human breast cancer cell (BC), and human small cells lung cancer (NCI-H187) (Cheenpracha *et al.* 2004). Cerberin compound has potential anti-carcinogenic properties (Kour 2014; Liu *et al.* 2008). *Apocynaceae* family species contains cardioactive glycosides, as in *C. manghas* (Sakushima *et al.* 1976). Cardiac glycoside, i.e., β -D-glucosyl-(1-4)- α -L-thevetosides of 17 β -digitoxigenin (GHSC-73) of *C. manghas* seed can reduce the viability of human hepatocellular carcinoma HepG2 cells (Feng *et al.* 2012).

4.3 Anti-inflammatory activity

Methanolic extracts of *C. manghas* have anti-inflammatory actions on LPS-stimulated macrophages. These actions are mediated by targeting c-Jun N-terminal

kinase (JNK) in the AP-1 signalling pathway (Yi *et al.* 2016). Inhibition of Syk/Src and the NF- κ B pathway by kaempferol could play a key role in the anti-inflammatory pharmacological action of *C. manghas* (Jeong *et al.* 2014).

4.4 DNA damage protective activity

GHSC-74, i.e., 2'-epi-2'-O-Acetylthevetin B (cardiac glycoside), present in seeds of *C. manghas* inhibit human hepatocellular carcinoma HepG2 cells by inducing S and G2 phase arrest of the cell cycle and by triggering apoptosis (Feng *et al.* 2010).

4.5 Antimicrobial activity

Plants from the genus *Cerbera* have potential antifungal properties (Iqbal *et al.* 2017; Susilo *et al.* 2019). Water extract of *C. manghas* leaf has the effect of killing fungi like *Aspergillus* species and *Penicillium* species (Sukmawati 2016). Water extract of *C. manghas* leaves are effective against many bacteria (Rajathi and Nambaru 2014). Both butanol and hexane extract of *C. manghas* leaves have antibacterial activity against *Klebsiella pneumoniae*. Butanol leaf extract is more powerful than the Hexane leaf extract of *C. manghas* (Musdja *et al.* 2018).

Ethanollic extracts of *C. manghas* are effective against vesicular stomatitis (VSV) viruses (Ali *et al.* 1996). Both ethyl acetate and dichloromethane extracts of *C. manghas* leaf have antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*. Dichloromethane leaf extract has a little stronger antibacterial activity than the ethyl acetate leaf extract in *C. manghas* (Musdja *et al.* 2019).

5. Conclusion

Several *in vitro* studies reported that *C. manghas* has therapeutic potential which includes antioxidant, antimicrobial, anti-inflammatory, analgesic, anti-cancer, and DNA damage protection activities. The maximum numbers of compounds present in this species are cardiac glycosides followed by terpenoids, phenolic acids, iridoids, flavonoids, steroids, and lignans. The majority types of compounds are present in the leaf followed by fruits or seed, stem, and root. This review highlighted several

ethnobotanical, pharmacological, and phytochemical properties of *C. manghas*.

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