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Review Article

Cytotoxic bioactives of Combretaceae as a source of potential cancer therapeutics

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Abstract: Cancer is a major global health concern because of its uncontrolled cell proliferation resulting from genetic alterations and interactions with environmental factors. Rapid urbanization, pollution, unhealthy lifestyles and exposure to carcinogenic agents have significantly increased cancer incidence worldwide. Plant-derived bioactive compounds have gained considerable attention as alternative and complementary therapeutic agents due to their diverse pharmacological activities and relatively lower side effects. The family Combretaceae comprises numerous medicinally important species traditionally used in healthcare systems across different cultures. In India, plants such as *Terminalia chebula* (Haritaki) and *Terminalia bellirica* (Bahera) have long been used in household remedies for digestive disorders, infections and general health maintenance. Recent phytochemical investigations have identified several anti-cancer compounds including combretastatins, chebulagic acid, chebulinic acid, gallic acid, lupeol, arjunolic acid and ellagic acid from members of this family. These compounds exhibit anti-cancer activities through mechanisms such as induction of apoptosis, inhibition of angiogenesis, suppression of tumor growth and antioxidant action. Keeping the problems of carcinogenic agents in and around our environment and importance of plant species belonging to Combretaceae in treatment of cancer, an attempt has been made to gather the available literature on Combretaceae to be used as anti-cancer agent and is presented in this article. This review summarizes the ethnomedicinal significance, phytochemical constituents and anti-cancer potential of selected Combretaceae species while emphasizing their relevance in future drug discovery and therapeutic development.

Keywords: Cancer, carcinogens, *Combretum*, Combretaceae, cytotoxicity, *Terminalia*, therapeutics

Introduction

Cancer is one of the leading causes of mortality worldwide which arises due to abnormal cell growth caused by genetic mutations and disruptions in cellular regulatory mechanisms (Cooper, 2000). Mutations in oncogenes, tumor suppressor genes and DNA repair pathways, combined with environmental influences such as pollution, radiation, smoking, dietary habits and exposure to toxic chemicals, contribute significantly to cancer initiation and progression (Sandhu et al., 2024). Increasing industrialization and changing lifestyles have further accelerated the prevalence of different forms of cancer globally, creating an urgent need for safer and more effective therapeutic interventions. In recent years, increasing emphasis has been placed on natural products as sources of bioactive compounds with therapeutic value. Alongside medicinal applications, afforestation and conservation of medicinal plant diversity have become increasingly important because forest ecosystems serve as reservoirs of valuable phytochemical resources (Karjalainen et al., 2010). Sustainable management and preservation of medicinal plant species can support biodiversity conservation while ensuring long-term availability of pharmacologically important plants. The family Combretaceae consists of economically and medicinally important plant species distributed in tropical and subtropical regions (Zhang et al., 2019). Many members of this family (Plate 1) have been extensively used in traditional healthcare systems due to their antimicrobial, anti-inflammatory, antioxidant and therapeutic properties. In Indian households, traditional remedies involving *Terminalia chebula* (Haritaki/Harad) and *Terminalia bellirica* (Bahera) remain common practices. Haritaki is often used to relieve digestive disorders, stomach discomfort and constipation (Bulbul et al., 2022), whereas Bahera is widely employed for cough, throat infections and digestive ailments (Kumar and Khurana, 2018). Both species also constitute important components of the well-known Ayurvedic formulation Triphala (Peterson et al., 2017), reflecting their long-standing medicinal significance. Modern phytochemical studies have identified numerous secondary metabolites from Combretaceae species including tannins, flavonoids, phenolic acids, triterpenoids, lignans and stilbenoids (Rahate et al., 2019). Bioactive compounds such as combretastatins, gallic acid, chebulagic acid, lupeol, arjunolic acid and ellagic acid have demonstrated promising anti-cancer activities through diverse molecular mechanisms, including regulation of cell signaling pathways, inhibition of metastasis, induction of apoptosis and suppression of angiogenesis (Pelthadka et al., 2025). Therefore, understanding the therapeutic potential of these plants is of considerable importance. This review aims to compile available information regarding ethnomedicinal uses, phytochemical constituents with anti-cancer properties of selected Combretaceae species while highlighting their significance as potential sources of future anti-cancer therapeutics.

Methodology

The present review was conducted through a comprehensive assessment of available literature concerning the family Combretaceae. Relevant information was collected from major scientific databases, including Google Scholar, Scopus, PubMed, Web of Science and Plants of the World Online (POWO), to obtain updated taxonomic information as well as peer-reviewed articles, review studies, ethnobotanical reports and pharmacological investigations. Specific search terms such as

"cancer", "anti-cancer compounds", "secondary metabolites", "anti-proliferative activity", "ethnomedicinal applications" and "apoptosis" were employed to identify particular studies. Furthermore, regional floras, books and published reports documenting traditional medicinal knowledge and species distribution were also examined. Only studies providing authentic scientific evidence and validated ethnomedicinal information were considered for inclusion. The collected data were critically evaluated, synthesized and organized into relevant thematic sections to provide a coherent and systematic presentation of the findings. (Kumar, 2025; Sahu et al., 2026).

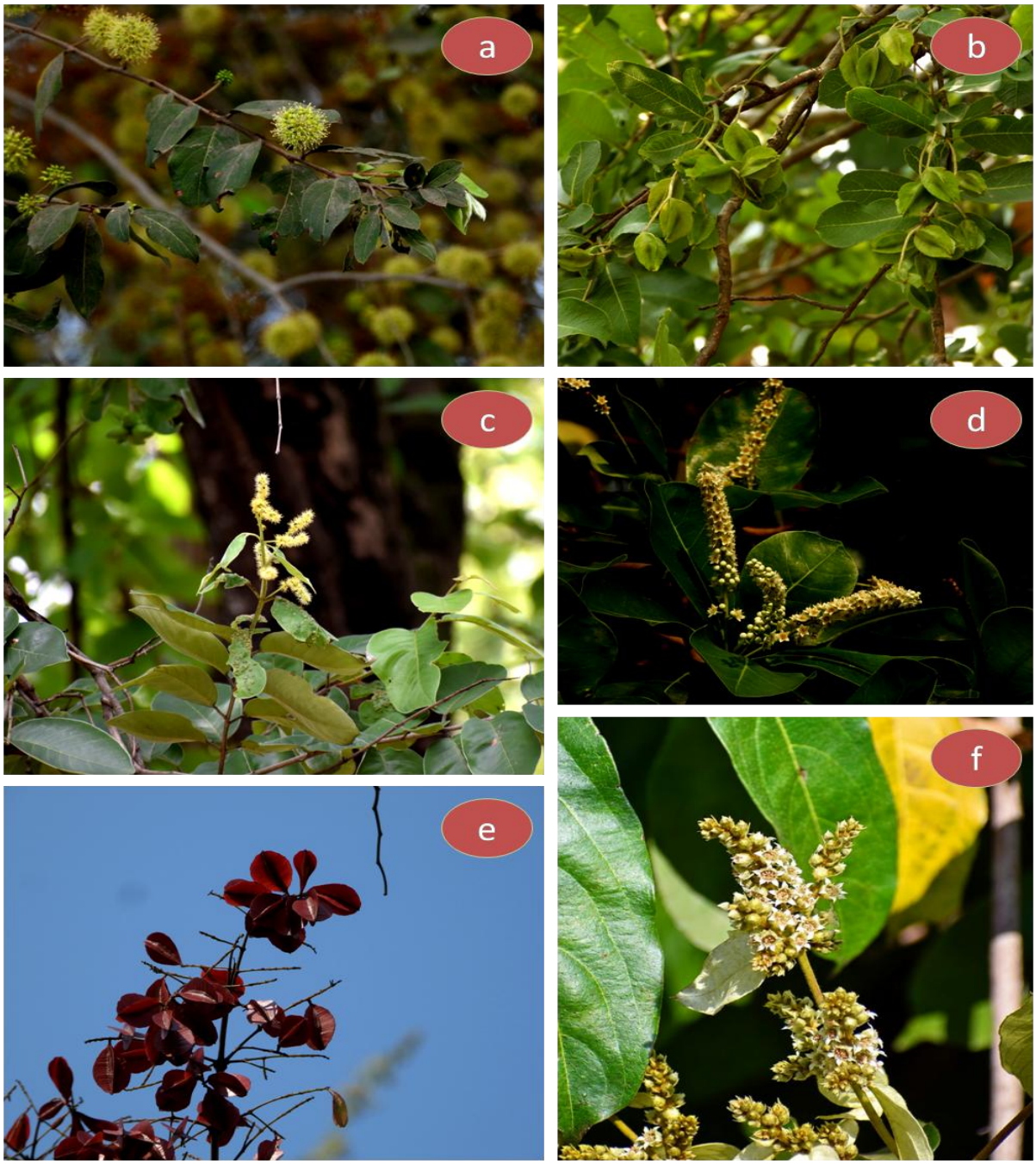

Plate 1: Plant species of Combretaceae family (a) *Terminalia pendula* var. *pendula*, (b) *Terminalia arjuna*, (c) *Terminalia chebula*, (d) *Terminalia catappa*, (e) *Combretum albidum* and (f) *Combretum roxburghii*

Combretaceae as a source of cytotoxic bioactive compounds

Family Combretaceae shows a strong relationship between traditional medicinal uses and the presence of bioactive compounds with anti-cancer potential. Many of these species contain secondary metabolites known for cytotoxic, antioxidant and antiproliferative activities. Species of *Combretum*, particularly *Combretum albidum* and *Combretum roxburghii*, contain combretastatins (Das et al., 2018), which inhibit tumor growth through disruption of microtubule formation. Different parts of the plants such as bark, leaves, fruits, roots, stems and seeds are traditionally used to treat infections, gastrointestinal disorders, respiratory ailments and inflammatory conditions (Rahate et al., 2019). Among them, two genuses *Combretum* and *Terminalia* shows broad spectrum activity. *Combretum indicum* contain compounds such as asiatic acid, oleanolic acid, gallic acid and lupeol, which are associated with apoptosis induction and inhibition of cancer progression (Forid et al., 2021). The genus *Terminalia* with species such as *Terminalia arjuna*, *Terminalia bellirica*, *Terminalia chebula* and *Terminalia elliptica* contain compounds like chebulagic acid, chebulinic acid, gallic acid, ellagitannins and luteolin (Pelthadka et al., 2025) which are renowned for their antioxidant and anti-cancer properties. The repeated occurrence of polyphenols, flavonoids, tannins and triterpenoid classes of bioactive compounds (Table 1) among these species showcase the potential of Combretaceae as a source of anti-cancer agents.

Table 1: Diversity of ethnomedicinal uses and anti-cancer compounds among selected species of Combretaceae

Plant species	Common name (s)	Ethnomedicinal use(s)	Anti-cancer bioactive compound(s)	Source(s)
Combretum albidum G.Don (plate 1e)	Buffalo Calf	Stem, seed oil and roots are used in eye problems.	Combretastatins	Das et al., (2018); Sharma et al., (2021)
Combretum indicum (L.) DeFilipps	Rangoon Creeper	Seeds are used for diarrhea and fever.	Asiatic acid, Arjunolic acid, Oleanolic acid, Gallic acid and Lupeol	Forid et al., (2021)
Combretum roxburghii Spreng. (plate 1f)	White Combretum	Leaf paste is useful in skin infections.	Combretastatins	Das et al., (2018); Pelthadka et al., (2025)
Getonia floribunda Roxb.	Paper Flower Climber	Leaves are used for intestinal worms.	Pachypodol, Calycopterones, 4′-hydroxy-6,7,8,3′-tetramethoxyflavonol, calyflorenones A and B	Suttaratrungse et al., 92015); Bharat et al., (2019); Thavare et al., (2025)

Terminalia anogeissiana Gere & Boatwr.	Axlewood	Bark decoction is used as a remedy for cough.	Ellagic Acid, Lupeol, Stigmasterol, Vitexin and Phytol.	Patil and Gaikwad, (2011); Hassan et al., (2024)
Terminalia arjuna (Roxb. ex DC.) Wight & Arn. (plate 1b)	Arjun	Leaf and bark juice is used against ear infections.	Arjunin, Casuarinin, Luteolin, Arjunic acid and Arjunolic acid	Pawar and Bhutani, (2005); Pelthadka et al., (2025)
Terminalia bellirica (Gaertn.) Roxb.	Beleric Myrobalan, Bahera	Fruits are used in treating constipation and parasitic infection.	Punicalagin, Terchebin, Ellagitannins, Chebulinic acid and Gallic acid.	Gupta et al., (2020); Pelthadka et al., (2025)
Terminalia catappa L. (plate 1d)	Indian Almond	Bark is used in dysentery.	Punicalagin, Rutin and Catechin,	Shanehbandi et al., (2021); Warnasih et al., (2024)
Terminalia chebula Retz. (plate 1c)	Black Myrobalan, Haritaki, Harad	Fruits are used in stomach pain.	Chebulagic Acid, Chebulinic Acid, Gallic Acid and Corilagin	Kumar et al., (2014); Pelthadka et al., (2025)
Terminalia elliptica Willd.	Indian Laurel	Brak is used in bronchitis.	Chebulagic Acid and Chebulinic Acid	Shreevatsa et al., (2024); Kumar et al., (2026)
Terminalia pendula var. *pendula* (plate 1a)	Button Tree	Bark is used in treatment of anaemia and dysentery.	Anolignan C and (-)-secoisolariciresinol	Rimando et al., (1994); Hossain et al., (2026)

Future aspects

Comprehensive investigation of the anti-cancer potential of Combretaceae species through advanced pharmacological and molecular studies should be the goal of future research. Although many bioactive compounds have been identified, several species remain underexplored regarding their mechanisms of action, toxicity profiles and clinical efficacy. *In vivo* studies and clinical trials are necessary to validate therapeutic claims and establish safety standards for medicinal use. Biotechnological approaches such as metabolomic profiling, molecular docking and nanotechnology-

based drug delivery systems may improve the efficacy and targeted delivery of plant-derived compounds. Furthermore, sustainable afforestation and conservation programs should be promoted to preserve medicinal plant diversity and ensure continuous availability of valuable species for future research and drug development.

Conclusion

Family Combretaceae represents an important source of medicinal plants with significant ethnopharmacological value and promising anti-cancer potential. Traditional medicinal practices, particularly the use of Haritaki and Bahera in Indian households, indicate the long-standing therapeutic relevance of these species. The presence of diverse bioactive compounds such as combretastatins, chebulagic acid, gallic acid, lupeol and arjunolic acid shows their potential in cancer prevention and treatment. Continued integration of traditional knowledge with modern scientific approaches may facilitate the discovery of novel plant-derived anti-cancer agents and contribute to the development of safer and more effective therapeutic strategies.

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