Int. j. adv. multidisc. res. stud. 2025; 5(3):1395-1399

Received: 28-04-2025
Accepted: 08-06-2025

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Exploring the Potential of Mangrove as a Natural Agent in Ovarian Cancer Treatment: A Comprehensive Review

[1] **Sudhir Swati,** [2] **Nadaf Rubeen,** [3] **Ghagane Shridhar,** [4] **Huddar Vaishanavi,** [5] **Sayda Fareen**

[1, 2, 3, 4, 5] KAHER's Dr. Prabhakar Kore Basic Science Research Center, Jawaharlal Nehru Medical College, Belagavi - 590010, Karnataka, India

DOI: https://doi.org/10.62225/2583049X.2025.5.3.4463

Corresponding Author: **Nadaf Rubeen**

Abstract

Mangroves, resilient coastal plants, are known to produce bioactive compounds with significant anticancer effects. These compounds, which include various phytochemicals, hold promise in the treatment of ovarian cancer by inhibiting tumor cell proliferation and inducing apoptosis. Different mangrove species possess distinct chemical compositions, enhancing their ability to suppress tumor growth. By targeting key cancer pathways, they effectively reduce tumor proliferation and promote cell death. This review highlights the need for further research to better understand the specific mechanisms of action and therapeutic possibilities of these compounds in the treatment of various cancers.

Keywords: Mangroves, Ovarian Cancer, Anticancer Activity, Antioxidant Activity

1. Introduction

1.1 Mangroves

Mangroves are community of plants growing in both tropical and subtropical regions across the globe. Secondly, mangroves are found in coastal areas around the mounts of rivers with influences exerted by tidal currents. However, the pH tolerance limit to support the growth of mangroves is within the range of 6 to 7. Meanwhile, the temperature range for optimum functioning of the mangrove ecosystems ranges between 28°C-31°C. This temperature influences the rise of productivity of mangrove leaves. In the species *Rhizopora sp*., the optimum temperature of leaf productivity falls within a range of 28°C-31°C. While for *Avicennia sp*., this optimum temperature is about 18°C-20°C [1].

Mangroves are referred to as "soft structures" because they naturally provide a buffer against environmental threats. Their ability to reduce the impact of waves help limit the damage caused by major natural events like erosion, powerful storms, and tsunamis. For example, during the Super Typhoon Haiyan in 2013 and the Indian Ocean Tsunami in 2004, areas shielded by mangroves experienced less destruction compared to unprotected regions. This has led researchers to study how well mangroves reduce the impact of such natural disasters, focusing on their effectiveness in dampening waves and protecting coastlines [2].

Mangroves under arid conditions are some of the rarest and most extreme systems, dominated by temperature, radiation, precipitation, and salinity conditions. Under arid conditions, the mangroves develop into stunted forest made up of highly salt-resistant species, primarily those from the genus *Avicennia*. These might be of low productivity and have lower contents of carbon and nitrogen. However, there is still the prospect of stimulating restoration by carbon offsetting mechanisms. Better options are still needed in order for protection to extend to these mangroves and their restoration [3].

Mangroves are of much ecological significance and economic importance. Based on the coastal location, they are differentiated as deltaic, estuarine, lagoon, and fringe mangroves. Based on the functional type, mangroves are classified as fringe, riverine, basin, over-wash, scrub, and hammock mangroves. They are further differentiated as river-dominated, tide-dominated, and interior mangroves based on tidal range and sedimentation. In addition, there are also six general types of mangroves, namely: Large deltaic system; tidal plains; composite plains; fringing barriers with lagoons; drowned bedrock valleys; and coral coasts [4].

Mangroves fall into category of three different species of tropical wetland trees. They thrive in central and southern Florida's coastal region, generally along the shoreline of estuaries. Of the species discussed above, three are native to Florida and they are black mangrove *Avicennia germinans*, red mangrove *Rhizophora mangle*, and white mangrove *Laguncularia racemosa*. Additionally, mangrove plants are grouped into two major categories, namely true mangroves and mangrove associates. True mangrove plants are certainly confined on intertidal mangrove habitats, while the mangrove associates occur at the landward edge of mangrove ecosystems or in terrestrial marginal zones occasionally receiving higher tides [5].

1.2 The Potential Antioxidant and Anticancer Properties of Mangroves

Mangroves, the unique coastal ecosystems found in tropical and subtropical regions, are home to several plant species that have long been utilized for their medicinal properties. These plants are known for producing a variety of bioactive compounds that exhibit a range of biological activities, particularly in the areas of antioxidant and anticancer effects. Due to the harsh environmental conditions in which they grow, mangrove plants have developed remarkable mechanisms to survive, including the production of secondary metabolites that are thought to play a role in their defense against oxidative stress and disease. Recent research has increasingly focused on understanding how these compounds may contribute to human health, particularly in the prevention and treatment of cancer [6, 7].

1.3 Antioxidant Properties

One of the key therapeutic properties of mangrove plants is their potent antioxidant activity. Antioxidants are substances that can neutralize free radicals which are highly reactive molecules that contribute to oxidative stress, a condition that can damage cellular structures, including DNA, proteins, and lipids. Oxidative stress has been implicated in the development of numerous diseases, including cancer. Mangrove species, such as *Avicennia marina*, *Rhizophora mucronata*, and *Bruguiera gymnorhiza*, produce a variety of polyphenolic compounds, flavonoids, tannins, and terpenoids, all of which have demonstrated to have antioxidant properties. These compounds work by scavenging free radicals, preventing cellular damage, and reducing the overall burden of oxidative stress. The antioxidant activity of mangrove derived compounds have shown to protect cells from oxidative damage, enhance the body's defense mechanisms, and support the repair of damaged DNA. This makes them promising candidates for prevention of cancer, as oxidative stress is a key factor in the initiation and progression of tumorigenesis. Additionally, antioxidants play an important role in reducing inflammation, which is often associated with cancer development [8].

1.4 Anticancer Properties

The anticancer properties of mangroves have also assembled significant interest in recent years. Several mangrove species produce bioactive compounds that have shown promising activity against a range of cancer types, including ovarian, breast, liver, and colon cancers. The anticancer effects of mangroves are primarily attributed to their ability to inhibit cancer cell growth, induce apoptosis (programmed cell death), and prevent the spread of cancer through metastasis [9].

Mangrove derived compounds such as flavonoids, alkaloids, and tannins possess cytotoxic properties that selectively target cancer cells while leaving normal cells unharmed. One of the most studied compounds, luteolin, found in *Avicennia marina*, has been shown to inhibit the growth of ovarian cancer cells by suppressing cell proliferation and inducing apoptosis. Additionally, flavonoids in mangroves have been found to modulate various signaling pathways involved in cancer progression, such as the PI3K/Akt/mTOR pathway, which is essential for tumor cell survival, migration, and resistance to chemotherapy [10].

In addition to their ability to induce cell death, mangrove compounds also interfere with the formation of new blood vessels (angiogenesis) that tumors require for growth and metastasis. By inhibiting angiogenesis, these compounds can limit the nutrient supply to growing tumors, thereby restricting their ability to proliferate. Furthermore, the antioxidant effects of mangrove compounds contribute to their anticancer potential by protecting healthy cells from damage while enhancing the efficacy of chemotherapeutic agents [11].

1.5 Medicinal and Ecological Importance of Mangrove

The toxic effects of bioactive compounds extracted from the mangrove plants are helpful as raw materials for anti-cancer drugs. Mangrove plants contain a wealth of bioactive compounds with various biological activities as compared to many plants and marine animals [12].

Mangroves are salt-tolerant plants that grow mainly in brackish water in an intertidal zone between land and ocean. As these are salt-tolerant, they are known as halophytes and can easily be adapted to any unfavorable environmental condition like flood and cyclone due to their root systems. These plants have a unique salt filtration system with complex root structures in order to manage salt water inclusion along with extreme wave action. These plants make an adjustment to the low oxygen conditions of water logged mud, but most of them are likely to flourish on the upper water layer of the intertidal zone. The mangroves contain special kinds of roots known as "Pneumatophores" and "Rhizophores," which help in respiration because mangroves grow on anaerobic soils. The submerged habitat of their root provides nourishment to juvenile species of various kinds, whether it might be a fish or the environment. Physically, they maintain a balance between aquatic and terrestrial communities and help protect coastal areas against environmental hazards. Since the beginning of human civilization, different parts of the mangrove plants are used by human beings for medicinal purposes. The plants are most valuable for their bioactive compounds like antimicrobial and antioxidant compounds. Over 200 biologically active metabolites have been identified from mangroves found in tropical and subtropical regions. These include alkaloids, flavonoid, steroids, saponins, tannins, and phenols. Most of these compounds have important medicinal properties with a wide range of applications. The medicines extracted from the different parts of the mangrove plants were mainly used to treat malaria, dysentery, elephantiasis, ulcers, leprosy, TB, and skin diseases. As mangrove plants are a huge source of plant secondary metabolites, they help them to stand in different types of unfavorable environment conditions. These secondary metabolites play a key role in different types of defense and survival mechanisms. Medicinal properties of mangrove plants, having therapeutic ability, are used for the treatment of arthritis, asthma, diabetes, inflammation, and rheumatism. Mangrove plants can produce substances having different types of biological activities like antioxidant, hepatoprotective mosquito larvicidal, antibacterial, antifungal, antiviral, anti-diarrhoeal, anti-feedant, insecticidal, and cytotoxic activity [13].

India ranks as the third richest country in the world for mangrove biodiversity, following Indonesia and Australia. With a total mangrove cover of 49,921sq.km, India accounts for approximately 3.2% of world's mangrove forests. Globally, mangrove flora includes about 81 species across 30 genera and 17 families. In India, 46 true mangrove species are recorded, encompassing 22 genera and 14 families, with 42 species and four natural hybrids making India's mangrove ecosystem the most diverse in terms of floristic variety worldwide. On India's east cost, mangroves constitute around 57% of the cover, containing 88% of the species diversity, while the Andaman and Nicobar Islands (ANI) hold 30% of the cover and represent 62% of the mangrove species on the west coast. Together, the Sundarbans and Gujarat account for 66% of India's mangrove forests, with 43% and 23% of the cover, respectively. Notably, ANI(Andaman and Nicobar Islands) ranks as India's third largest mangrove forest, holding 13% of the national cover. Mangroves create a unique ecological environment and are also valuable sources of bioactive compounds. Various parts of mangrove plants have been traditionally used in folk medicine to treat conditions like leprosy, ulcers, tuberculosis, elephantiasis, malaria, and dysentery. Mangrove compounds exhibit several beneficial biological properties, such as anti-oxidant, hepatoprotective, anti-microbial, anti-diarrheal, anti-feedant, insecticidal, and cytotoxic activities. The key bioactive compounds derived from mangroves include polyphenols, flavonoids, alkaloids, carotenoids, tannins, saponins, steroids, amino acids, carbohydrates, proteins, vitamins, terpenes, and glycosides [14].

Mangrove plants, particularly from the *Rhizophora* genus, hold promising therapeutic potential for various diseases, including cancer, due to their rich phytochemical content found in fruits, seeds, leaves, and roots. The cytotoxic activity of mangrove plants is attributed to active compounds such as phenolics, flavonoids, tannins, and terpenoids. Among the different plant parts, the fruit extract of *Rhizophora* shows the strongest cytotoxic activity against cancer cells based on cytotoxicity tests [15].

Fig 1: (a) Geography of Mangrove plant sample; (b) *Rhizophora mangle. L* (Mangrove plant); (c) Leaves sample

2. Ovarian Cancer

2.1 Epidemiology of Ovarian cancer

Ovarian cancer ranks as the eighth most frequently diagnosed cancer in women worldwide, representing approximately 3.7% of cancer case and 4.7% of deaths from cancer in 2020. Up until the early 2000s, northern Europe and North America had the highest age-standardized incidence rates. However, these rates have been decreasing in these regions, while they are on the rise in parts of Eastern Europe and Asia [16].

In 2018, GLOBOCAN reported 295,414 cases of ovarian cancer, representing 3.4% of all cancer cases among women. The Age Standardized Rate (ASR) for ovarian cancer was estimated at 6.6 that year. Incidence rates of epithelial ovarian cancer differ across age and racial groups, with higher rates found in more developed countries. About 30% of global cases occurred in European nations. In 2012, the countries with highest incidence rates were China (14.60% of cases), India (11.33%), and the United States (81.8%). In U.S alone, 22,240 cases were identified. Among Asian countries, Singapore, Kazakhstan, and Brunei had the highest standardized incidence rates. In 2018, ovarian cancer was responsible for 184,799 deaths, representing 4.4% of all cancer-related fatalities among women. According to GLOBOCAN 2018, the age-standardized mortality rate (ASR) for ovarian cancer stood at 3.9. While cancer incidence is higher in countries with a high Human Development Index (HDI), and a decline in mortality rates has also been observed. India has the highest mortality rate in Asia, but Europe and North America have seen a reduction, particularly among younger populations. African women face a high mortality-to-incidence ratio, reflecting limited access to appropriate treatments. High-grade serous carcinoma accounts for two-thirds of ovarian cancer deaths [17].

An estimated 133,818 new patients with serous cancer, 35,712 with mucinous cancer, 29,319 with endometrioid cancer, and 17,894 with clear cell cancer were diagnosed in the year 2020. Variations among different regions were also seen in most histological subtypes of ovarian cancer. Serous and mucinous carcinomas had a high rate of incidence in Eastern Europe; by contrast, endometrioid carcinomas were highest in Northern Africa and clear cell carcinomas were highest in Eastern Asia [18].

OC is responsible for approximately 239,000 new cases and 152,000 deaths worldwide each year. The highest incidence rates, at 11.4 per 100,000 for new cases and 6.0 per 100,000 for deaths, are observed in Eastern and Central Europe. Although China has a lower incidence rate of 4.1 per 100,000, its large population results in about 52,100 new cases and 22,500 deaths in 2015. In comparison, the United States saw an estimated 21,290 new cases and 14,180 deaths in the same year. A woman's lifetime probability of developing ovarian cancer is 1 in 75, with a 1 in 100 chance of dying from the disease. Most cases are diagnosed at a late stage, when the 5-year survival rate is just 29%. Only a small fraction of cases (15%) are diagnosed early, a stage 1, where the 5-year survival rate is significantly higher, at 92%. Globally, the 5-year survival rate for ovarian cancer typically ranges between 30% and 40%, and there has been little improvement (2%-4%) in these numbers since 1995 [19].

The prevalence rates of ovarian cancer have very prominent differences around the world. Jyoti *et al*. conducted a retrospective analysis of patients treated for ovarian cancer (OC) at a leading cancer center in North India between January 2014 and December 2018. This study represents the first comprehensive report from Himachal Pradesh, providing an in-depth evaluation of treatment patterns and outcomes in those patients. Ovarian cancer constituted 2.49% out of a total of 11,470 cancer cases registered during the study period. A similar prevalence was noted in a separate retrospective study by Meena *et al*., which reported a 2.94% incidence of ovarian cancer over a nine-year span (2010–2018) at a single institution in North India [20].

Western Europe and Northern America have the highest prevalence; Southern and Eastern Europe and South America have intermediate prevalence, and the Middle East and Asia have the lowest. Typically, in countries with highest and lowest prevalence for ovarian cancer may be explained by racial reproductive, socioeconomic, and cultural differences. Several factors may account for higher prevalence in developed as compared to further developing countries. First: It might be due to significant increase in life anticipation in developed countries. Second: Due to significant reduction in fertility rate, or decrease in family size, in contrast with some developing countries where large families still exist and women still have motivation for a higher numbers of pregnancies. Further, women of developed countries are less likely to practice lactation, which was found to be protective against ovarian cancer and its protective effect can last for almost three decades after lactation. Thirdly, in developed countries, westernized lifestyle has a major impact on increasing most types of cancers including ovarian cancer. Additionally, increased in daily consumption of fatty diet and dense caloric food, typical to most developed countries is also linked with almost all types of cancers [21].

2.2 Diagnosis

Ovarian cancer is a heterogeneous disease, comprising different subtypes each with distinct prognosis. Patients harbouring type I tumors tend to be diagnosed at an early stage and usually have an excellent long-term prognosis. In contrast, patients with aggressive type II tumors are generally diagnosed at advanced stages and have poor survival rates. CA125 is a high molecular weight glycoprotein and has been the major ovarian cancer biomarker for approximately four decades. However screening for ovarian cancer at stages I and II using CA125 have yielded limited hope of early diagnosis [22].

2.3 Treatment

Primary cytoreductive surgery (PCS) accompanied by platinum-based chemotherapy remains the standard approach for treating patients with advanced stage epithelial ovarian cancer (EOC). For those with bulky stage III or IV disease, where achieving complete cytoreduction (RO) is unlikely, or for individuals considered unfit for surgery, neoadjuvant chemotherapy may be an alternative. For stage IV patients, cytoreductive surgery may be attempted, with 30% achieving optimal tumor reduction successfully [23].

Although, conventional treatments of ovarian cancer usually lead to drug resistance, adverse reactions, and long term complications. Exosomes represents a great potential either as a putative therapeutic marker of cancer or as an efficient, fast, safe vehicle of antitumor drug delivery in ovarian cancer immunotherapy. It is exosome based immunotherapies that could be administered to the body in order to stimulate the immune responses in destroying the tumor [24].

2.4 Management

Research indicates that physical activity plays a key role in health outcomes of women with ovarian cancer. Supporting women in maintaining or becoming physically active especially through exercise interventions during or after treatment can significantly enhance their quality of life. Future research should focus on targeted interventions that address the unique challenges of the disease, ensuring that these scientific insights lead to tangible improvements in ovarian cancer. Physical activity is an advantage to the women diagnosed with ovarian cancer, particularly through structured, intentional, and specific exercise programs. Moreover, the noticed decrease in their physical activity levels following diagnosis suggests that there is potential for improvement. However, due to the variations in disease stage at diagnosis, common treatments, side effects associated with treatment, and prognosis compared to other more prevalent cancers, there is still much to discover about the advantages of physical activity and exercise for this particular group [25].

Research suggests that consuming green leafy vegetables, allium vegetables, fiber, flavonoid rich food, green tea, broccoli, fruits, fish, low fat dairy products, etc may reduce the risk of ovarian cancer in women. However diets high in total fat, saturated fat, cholesterol, cheese, wines, etc could increase the risk [26].

3. Conclusion and Future Research

The growing body of evidence supporting the antioxidant and anticancer properties of mangroves underscores their potential as a source of novel therapeutic agents. While much progress has been made in understanding the bioactive compounds derived from mangroves species, further research is needed to fully elucidate their mechanisms of action and to identify the most effective compounds for clinical application. Further studies should focus on the isolation and characterization of these compounds, as well as their interactions with cancer-related pathways. Clinical trials and preclinical studies will be essential to determine the efficacy and safety of mangrove based therapies for cancer prevention and treatment.

In conclusion, mangroves offer a promising avenue for the development of natural and sustainable treatments for cancer, particularly ovarian cancer, by combining their potent antioxidant properties with anticancer effects. As research in this area progresses, mangroves could play a pivotal role in the fight against cancer, providing new hope for patients worldwide.

4. References

1. Riska JA, Syukur A, Zulkifli L. Association between Mangrove Types and Some Mangrove Crab Species in West Lombok Sheet Mangrove Ecosystem. Jurnal Penelitian Pendidikan IPA. 2023; 9(7):5610-5619.
2. Kamil EA, Takaijudin H, Hashim AM. Mangroves as coastal bio-shield: A review of mangroves performance in wave attenuation. Civil Engineering Journal. 2021; 7(11):1964-1981.

3. Adame MF, Reef R, Santini NS, Najera E, Turschwell MP, Hayes MA, *et al*. Mangroves in arid regions: Ecology, threats, and opportunities. Estuarine, Coastal and Shelf Science. 2021; 248:106796.
4. Kathiresan K. Mangroves: Types and importance. Mangroves: Ecology, biodiversity and management, 2021, 1-31.
5. Chowdhury R, Bhuia MS, Al Hasan MS, Hossain Snigdha S, Afrin S, Büsselberg D, *et al*. Anticancer potential of phytochemicals derived from mangrove plants: Comprehensive mechanistic insights. Food Science & Nutrition. 2024; 12(9):6174-6205.
6. Yu B, Zeng W, Zhou Y, Li N, Liang Z. Characterization and Bioactive Metabolite Profiling of Streptomyces sp. Y009: A Mangrove-Derived Actinomycetia with Anticancer and Antioxidant Potential. Microorganisms. 2024; 12(11):2300.
7. Rahmawati SI, Izzati FN, Harmoko R, Bayu A, Hadiani I, Yusmur A, *et al*. Evaluation of phytochemical, antioxidant and anticancer activities of Indonesian mangroves herbal tea. InBIO Web of Conferences 2024 (Vol. 112, p. 06005). EDP Sciences.
8. Sivaperumal P, Kamala K, Sangeetha VL, Ganapathy DM, Kumar GJ. Antioxidant potential from true mangroves and their associated marine organisms. InMarine Antioxidants 2023 Jan 1 (pp. 233-240). Academic Press.
9. Chan HT, Wong SK, Chan EW. Diversity and Conservation of Mangrove and Associate Species with Anticancer Properties: An Overview.
10. Cerri F, Giustra M, Anadol Y, Tomaino G, Galli P, Labra M, *et al*. Natural products from mangroves: an overview of the anticancer potential of Avicennia marina. Pharmaceutics. 2022; 14(12):2793.
11. Singaraj R, Manikkam R. Determination of Anticancer Property of Mangrove Microbiome. In Mangrove Microbiome: Diversity and Bioprospecting 2025 Mar 13 (pp. 405-424). Singapore: Springer Nature Singapore.
12. Nugroho RY, Hendri M, Putri WA, Agussalim A. Phytochemical profile and toxicity of extracts from the leaf of Avicennia marina (Forssk.) Vierh. collected in mangrove areas affected by port activities. South African Journal of Botany. 2022; 150:903-919.
13. Das SK, Das B, Jena AB, Pradhan C, Sahoo G, Dandapat J. Therapeutic potential and ethnopharmacology of dominant mangroves of Bhitarkanika National Park, Odisha, India. Chemistry & Biodiversity. 2022; 19(3):e202100857.
14. Parthiban A, Sivasankar R, Sachithanandam V, Khan SA, Jayshree A, Murugan K, *et al*. An integrative review on bioactive compounds from Indian mangroves for future drug discovery. South African Journal of Botany. 2022; 149:899-915.
15. Saroyo H, Saputri NF. Cytotoxicity of mangrove leaves (rhizophora) ethanolic extract on cancer cells. Journal of Nutraceuticals and Herbal Medicine. 2021; 4(1):43-52.
16. Webb PM, Jordan SJ. Global epidemiology of epithelial ovarian cancer. Nature Reviews Clinical Oncology. 2024; 21(5):389-400.
17. Momenimovahed Z, Tiznobaik A, Taheri S, Salehiniya H. Ovarian cancer in the world: Epidemiology and risk factors. International Journal of Women's Health, 2019, 287-99.
18. Wang M, Bi Y, Jin Y, Zheng ZJ. Global incidence of ovarian cancer according to histologic subtype: A population-based cancer registry study. JCO Global Oncology. 2024; 10:e2300393.
19. Reid BM, Permuth JB, Sellers TA. Epidemiology of ovarian cancer: A review. Cancer biology & medicine. 2017; 14(1):9-32.
20. Sharma J, Gupta M, Thakur V, Fotedar V, Vats S. Assessment of clinical epidemiology, treatment patterns, and survival outcomes in epithelial ovarian cancer: A retrospective analysis from a tertiary cancer centre in North India. International Journal of Reproduction, Contraception, Obstetrics and Gynecology.; 13(6):1500.
21. Ali AT, Al-Ani O, Al-Ani F. Epidemiology and risk factors for ovarian cancer. Menopause Review/Przegląd Menopauzalny. 2023; 22(2):93-104.
22. Charkhchi P, Cybulski C, Gronwald J, Wong FO, Narod SA, Akbari MR. CA125 and ovarian cancer: A comprehensive review. Cancers. 2020; 12(12):3730.
23. Kuroki L, Guntupalli SR. Treatment of epithelial ovarian cancer. Bmj. 2020; 371.
24. Gong X, Chi H, Strohmer DF, Teichmann AT, Xia Z, Wang Q. Exosomes: A potential tool for immunotherapy of ovarian cancer. Frontiers in Immunology. 2023; 13:1089410.
25. Jones TL, Sandler CX, Spence RR, Hayes SC. Physical activity and exercise in women with ovarian cancer: A systematic review. Gynecologic Oncology. 2020; 158(3):803-811.
26. Khodavandi A, Alizadeh F, Razis AF. Association between dietary intake and risk of ovarian cancer: A systematic review and meta-analysis. European Journal of Nutrition. 2021; 60:1707-1736.