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PHYTOCHEMICAL COMPOSITION AND PHARMACOLOGICAL APPLICATIONS OF HERBAL PLANTS: A COMPREHENSIVE EXPLORATION OF THEIR ANTIMICROBIAL, ANTI-INFLAMMATORY, AND ANTIOXIDANT PROPERTIES IN BONE CANCER

Geetha Balasubramani[1*], Prince Wilfred J.[2] and Paul Pradeep J.[3]

[1*]PhD Research Scholar, Department of Biomedical Engineering, Sathyabama Institute of Science and Technology, Chennai.
[2]B.Sc. - Department of Physics, Loyola College, Chennai.
[3]Founder & CEO, Medcuore Medical Solutions Private Limited, Chennai.

***Corresponding Author: Geetha Balasubramani**
PhD Research Scholar, Department of Biomedical Engineering, Sathyabama Institute of Science and Technology, Chennai.

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ABSTRACT
Bone cancer presents a significant therapeutic challenge in oncology, requiring new, effective treatment strategies. Phytotherapy offers potential alternatives due to its bioactive compounds that may reduce side effects compared to conventional cancer treatments. This review compares the phytochemical profiles, anti-cancer, and anti-inflammatory properties of three medicinal plants: *Blepharis maderaspatensis* (Elumpu Otti), *Centella asiatica* (Vallarai), and *Calotropis procera* (Vellarukku), to explore their efficacy against bone cancer. A comprehensive analysis of the in vitro and in vivo effects of these plants on cancer cells was conducted, focusing on their mechanisms of action, such as apoptosis induction and angiogenesis inhibition. The review also evaluates the synergistic potential of combining these herbs with conventional therapies. The review demonstrates that *Blepharis maderaspatensis*, *Centella asiatica*, and *Calotropis procera* possess significant anti-cancer and anti-inflammatory properties. They exhibit mechanisms such as inducing apoptosis and inhibiting angiogenesis in cancer cells, suggesting their potential in bone cancer treatment with minimal toxicity. The findings indicate that these plants offer promising complementary options for bone cancer therapy. Their bioactive compounds could provide safer, effective alternatives or adjuncts to conventional treatments, warranting further in-depth research into their synergistic effects.

KEYWORDS: Bone cancer, phytotherapy, Blepharis maderaspatensis, Centella asiatica, Calotropis procera, anti-cancer, anti-inflammatory, apoptosis, angiogenesis.

1. INTRODUCTION

In the rapid increase of the cases in cancer, especially bone cancer, the treatment has become hard, brutal and increases side-effects. Cancer is because of the rapid multiplication of cells with the inability to control or stop the spread, forming tumors of malignant cells with the potential of being metastatic. It poses severe therapeutic challenges due to its aggressive nature. Traditional treatment modalities such as surgery, radiation therapy, and chemotherapy have significantly improved survival rates over the past few decades. However, these treatments often come with severe side effects, highlighting the urgent need for more effective and less toxic therapeutic strategies. Every year, more than 10 million people are diagnosed with cancer. Osteosarcoma is also a very prominent cancer-causing fatality. Because of the serious and often terminal nature of the cancer, patients are a vulnerable population and may have a large financial and psychological investment in herbal therapies. As of 2024, the American Cancer Society estimates that 3,970 new cases are diagnosed and record about 2,050 deaths (Cancer.org, n.d.) The National Cancer Institute also confirmed these statistics. India has been conventional towards traditional medicine and ethnopharmacology for practice (Joshi DY, et al., 2021). The Indian systems of medicine include Ayurveda, Homeopathy, Siddha, and Unani which are the most ancient restorative practices, known to the world and derive greater formulations from plants and plant extracts (Verma, A.K, et al., 2007). The value and importance of traditional knowledge are now being increasingly acknowledged worldwide Herbal medicine, with its far-stretched ancient and valued history of use in traditional healing systems, has attained attention and interest as a

source of potential anticancer and anti-inflammatory agents (Kumar Ganesan and Baojun Xu, 2017). Phytochemicals that are the bioactive compounds found in plants show promising anticancer properties in various phytochemical and pharmacological studies. These compounds can target multiple pathways involved in cancer progression, including apoptosis (programmed cell death), angiogenesis (formation of new blood vessels), and metastasis. Some well-known anticancer phytochemicals include curcumin (from turmeric), epigallocatechin gallate (from green tea), resveratrol (from grapes), and quercetin (found in many fruits and vegetables). Traditional medicine systems, such as Ayurveda, Traditional Chinese Medicine (TCM), and various indigenous healing practices, have utilized herbal plants for centuries to treat a wide range of ailments, including cancer. These systems often employ a holistic approach, focusing not only on the disease itself but also on the overall well-being of the patient. In the context of bone cancer, several herbs have been traditionally used for their potential to strengthen bones, reduce inflammation, and inhibit tumor growth.

Scientific Classification

Centella asiatica (Family: Apiaceae) is a herb known as Gotu Kola, widely used for its wound healing and cognitive-enhancing properties. Blepharis maderaspatensis (Family: Acanthaceae) is a lesser-known plant with anti-inflammatory benefits, traditionally used in Indian medicine. Calotropis procera (Family: Apocynaceae), or Sodom Apple, contains potent compounds with notable anticancer and wound healing effects but requires careful handling due to its toxicity. The following tables show the scientific Classification of the herbal plants which are mentioned above.

Table 1: Blepharis maderaspatensis.

Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Asterids
Order	Lamiales
Family	Acanthaceae
Genus	Blepharis
Species	B. Maderaspatensis

Table 2: Centella asiatica.

Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Asterids
Order	Apiales
Family	Apiaceae
Genus	Centella
Species	C. asiatica

Table 3: Calotropis procera.

Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Asterids
Order	Gentianales
Family	Apocynaceae
Genus	Calotropis
Species	C.procera

2. Bone Cancer and its Types

Bone cancer is the growth of mass cells in a bone or in its region. It is irrespective of all ages and affects all. It may be considered as a rare-type of cancer but still the fatality and the growth in the number of patients proves it a treat and a serious issue in the field and medicine. Bone cancer affects the surrounding region, the lymph nodes, the tissues, the organ and all the other areas. The treatment for bone cancer is very much similar to other cancer treatments such as surgery, medication, radiation and chemotherapy. Based on the affecting region and age, they are classified into various categories and the stages of cancer are based on the TNM system with four stages. The treatment for bone cancer is based on the

stage of the cancer that is detected in the patient by various diagnoses. Early detection and treatment can help to reduce the side effects of cancer. Regular check-ups and monitoring can also help to detect any changes in the cancer. This rare malignant tumor originates from primitive mesenchymal cells. Multiple types are prevalent, with osteosarcoma, chondrosarcoma and Ewing sarcoma being the most prevalent and common of all. These cancer types vary in demographic locations, biological behavior and imaging appearance. The bone cancer is aggressive because of the metastasis nature. The cancer cells that are formed in other regions of the body aggregate and migrate to the bone and cause cancer in the bones, these weaken the bone and furthermore break them when the virulent nature increases. Surgical excision remains the mainstay of curative treatment, with chemotherapy and radiotherapy used in conjunction. Osteosarcoma, a type of bone cancer, is a high malignant grade tumor. The tumor cells produce osteoid in the region of the bone. This type is the most common non hematopoietic bone malignancy. This is also most common after myeloma that affects the bone. In medical field this type is further called with certain names such as osteogenic sarcoma, osteosarcoma of the jaw bones, conventional osteosarcoma, chondroblastic osteosarcoma, osteoblastic osteosarcoma. Chondrosarcoma is a type of cancer that originates in the cartilage cells of the bone. It is most commonly found in the pelvis, ribs, and long bones of the arms and legs. This cancer typically affects adults aged 40 to 70 years and is often slow-growing, but more aggressive variants can occur (Gelderblom et al., 2017). Symptoms include persistent pain, swelling, and restricted joint movement due to tumor growth. It often presents as a large mass on imaging studies (Grimer et al., 2018). Chondrosarcomas are resistant to conventional chemotherapy and radiation, making surgical resection the primary treatment. Complete removal of the tumor is crucial, as incomplete excision can lead to recurrence (Dorfman & Czerniak, 2017). Advanced and high-grade chondrosarcomas may metastasize to the lungs, making the prognosis poor if not detected early (Fletcher et al., 2020). Ewing's Sarcoma is a highly aggressive bone cancer that typically affects children, adolescents, and young adults, with a peak incidence between 10 to 20 years of age. It usually arises in the long bones, such as the femur, pelvis, and ribs, and is characterized by a small round blue-cell tumor on biopsy (Balamuth & Womer, 2010). Common symptoms include localized pain, swelling, and sometimes fever. Because of its rapid growth, Ewing's Sarcoma can quickly spread to the lungs, bone marrow, and other bones (Miser et al., 2012). The standard treatment involves a combination of chemotherapy, radiation therapy, and surgical resection. Multi-modal therapy has significantly improved survival rates, especially in localized cases (Jurgens et al., 2013). Despite advances in treatment, the prognosis for patients with metastatic Ewing's Sarcoma remains poor, with a five-year survival rate of less than 30% (Leavey & Collier, 2008).

3. Phytochemistry & Pharmacological Properties

Blepharis maderaspatensis (Family: Acanthaceae) is a traditional medicinal plant used extensively in Indian folk medicine for its diverse therapeutic properties. Phytochemical studies have revealed that the plant contains significant amounts of flavonoids (quercetin, kaempferol), phenolic acids (gallic acid, caffeic acid), alkaloids, saponins, and terpenoids, contributing to its bioactivity (Kumar et al., 2021). The antioxidant activity of the plant is attributed to its flavonoid content, which demonstrates strong free radical scavenging effects (Sharma & Gupta, 2019). Its antimicrobial properties have been reported against a wide range of pathogens, including Staphylococcus aureus and Candida albicans (Patel et al., 2020).

Table 4: Phytochemical Constituents of Blepharis maderaspatensis.

Phytochemical Class	Specific Compounds	Reported Activity
Flavonoids	Quercetin, Kaempferol	Antioxidant, Anti-inflammatory
Phenolic Acids	Gallic Acid, Caffeic Acid	Antimicrobial, Anti-cancer
Alkaloids	Blepharin	Analgesic, Antibacterial
Saponins	Triterpenoids	Hepatoprotective, Immunomodulatory
Terpenoids	Essential Oils	Anti-inflammatory, Antiviral

Additionally, the anti-inflammatory effects of the plant are linked to the presence of terpenoids and phenolic compounds, which modulate pro-inflammatory cytokines (Raj et al., 2018). Hepatoprotective activity has also been observed, suggesting potential use in liver health supplements (Singh & Verma, 2020). Preliminary antidiabetic studies indicate blood glucose-lowering effects, highlighting its potential as an adjunct therapy for diabetes management (Khan et al., 2022). Overall, Blepharis maderaspatensis exhibits promising pharmaceutical applications, warranting further research for clinical validation and formulation development (Rao & Mehta, 2021). Centella asiatica (Gotu Kola) has gained attention in recent years for its potential benefits in bone health and regeneration. The key bioactive compounds in Centella asiatica, particularly triterpenoids like asiaticoside and madecassoside, are known for their anti-inflammatory and antioxidant properties, which play a vital role in promoting bone healing and regeneration (Jiang et al., 2021).

Table 5: Phytochemical Constituents of Centella asiatica.

Phytochemical Class	Specific Compounds	Pharmacological Activity
Triterpenoids	Asiaticoside, Madecassoside, Asiatic Acid	Wound healing, Anti-inflammatory, Antioxidant
Flavonoids	Quercetin, Kaempferol, Rutin	Antioxidant, Neuroprotective, Anti-inflammatory
Phenolic Acids	Caffeic Acid, Chlorogenic Acid, Rosmarinic Acid	Antioxidant, Antimicrobial, Anti-diabetic
Volatile Oils	α-Pinene, β-Caryophyllene, Myrcene	Anti-inflammatory, Antioxidant, Antimicrobial
Sterols	β-Sitosterol	Cholesterol-lowering, Anti-inflammatory
Tannins	Gallic Acid	Astringent, Wound healing

Asiaticoside has been shown to enhance osteoblast differentiation and stimulate collagen synthesis, contributing to improved bone matrix formation and increased bone density (Kim et al., 2016). The anti-inflammatory effects of the plant also help reduce bone loss and mitigate conditions such as osteoporosis by decreasing the activity of osteoclasts (bone-resorbing cells) (Cheng et al., 2013). Additionally, the flavonoids and phenolic acids present in Centella asiatica help in reducing oxidative stress, which is crucial for maintaining bone health and preventing bone degeneration (Pittella et al., 2009). Animal studies have shown that supplementation with Centella asiatica extracts can accelerate fracture healing and enhance bone mineralization, making it a promising herbal remedy for bone-related disorders (Lee et al., 2018). Calotropis procera (Family: Apocynaceae), commonly known as Sodom Apple or "Erukku," is a traditional medicinal plant used for its anti-inflammatory, analgesic, and antimicrobial properties. The phytochemical profile of Calotropis procera includes alkaloids (calotropin, calactin), flavonoids (quercetin, kaempferol), and terpenoids (β-amyrin, lupeol), which contribute to its bioactivity (Kumar et al., 2015).

Table 6: Phytochemical Constituents and Pharmacological Activities of Calotropis procera.

Phytochemical Class	Specific Compounds	Pharmacological Activities
Alkaloids	Calotropin, Calactin, Uscharin	Analgesic, Anti-inflammatory, Anticancer
Flavonoids	Quercetin, Kaempferol, Rutin	Antioxidant, Anti-inflammatory, Antimicrobial
Terpenoids	β-Amyrin, Lupeol, Taraxasterol	Anti-inflammatory, Hepatoprotective, Antimicrobial
Cardiac Glycosides	Calotropin, Uscharidin	Cytotoxic, Cardioprotective, Anticancer
Latex Proteins	Calotropain	Wound healing, Anti-inflammatory, Proteolytic
Phenolic Compounds	Caffeic Acid, Ferulic Acid	Antioxidant, Anti-inflammatory
Sterols	β-Sitosterol	Anti-inflammatory, Cholesterol-lowering

The plant's latex contains proteolytic enzymes like calotropain, known for their wound healing and anti-inflammatory effects (Choudhary et al., 2014). Triterpenoids and cardiac glycosides such as calotropin exhibit strong cytotoxic and anticancer properties, showing promise in cancer therapy (Singh et al., 2017). Calotropis procera also demonstrates antimicrobial activity against pathogens like Staphylococcus aureus and Candida albicans, attributed to its flavonoid and alkaloid content (Patel et al., 2018). Despite its medicinal potential, the plant's toxic components, especially cardiac glycosides, require cautious use to avoid poisoning (Ali et al., 2020). The plant holds potential for future drug development, but further research is needed for standardization and safe application.

4. CONCLUSION

In conclusion, Centella asiatica, Blepharis maderaspatensis, and Calotropis procera exhibit diverse and promising properties for bone health and bone cancer treatment. Centella asiatica stands out for its role in promoting bone healing and regeneration, aided by its triterpenoids (asiaticoside, madecassoside), which stimulate collagen synthesis and enhance osteoblast activity. These effects, combined with its anti-inflammatory and antioxidant properties, suggest potential applications in treating osteoporosis and bone injuries. Blepharis maderaspatensis, while less researched, shows promise in supporting bone health through its strong anti-inflammatory and antioxidant effects, which could help reduce bone resorption and inflammation. Calotropis procera, on the other hand, is particularly notable for its anticancer potential against bone malignancies like osteosarcoma. The plant's bioactive compounds, including cardiac glycosides and proteolytic enzymes, have demonstrated significant cytotoxic effects, inducing apoptosis in cancer cells and promoting bone repair. Overall, these plants offer valuable natural compounds that could be developed into effective therapies for bone-related conditions, but further clinical research is essential to fully understand their mechanisms and ensure safe usage.

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