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ABSTRACT

Couroupita guianensis (L), also known as cannonball tree. *Couroupita guianensis* (*C. guianensis*) belongs to the family Lecythidaceae. It is a medicinal plant that exhibited potential antibacterial and anti-cancer activity in different experimental models. Based on recent studies the plant has been shown to have many phytochemicals such as terpenoids, saponins, alkaloids, amirins, tannins etc., which exhibit strong antioxidant activity that are essential to lead a healthy life. Furthermore, the medicinal and pharmacological usefulness of plants is expanding; plant extracts have huge potential in reducing inflammatory, depressive, neuropharmacological and other illnesses. Several *in vitro* studies reveal that phytochemicals are helpful to treat human diseases in which free radical generation plays a significant role and which needs more *in vivo* research. This review elevated some potential pharmacological importance of bioactive components and their biological activity based on *in vitro* studies. Also, studies showed that different phytochemicals were obtained by various solvent extractions that are capable of protecting against cancer and diabetes as well as shows wound healing activities and insecticidal activities. In this review we have summarized the research work done so far on *C. guianensis* to treat various ailments. Also, we have emphasized the future work need to be done.

Keywords: Couroupita guianensis, Phytochemistry, Pharmacology, Medicinal uses.

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INTRODUCTION

Medicinal plants are the backbone the traditional medicines since a decade.^[1] From the ancient time medicinal plants have been used in several ways as the good therapeutics in ayurveda sastra as they are the good source of antibiotics, antifungal and antiseptic components. The well-known plant cannonball tree belongs to Lecythidacae family. It is a fast-growing evergreen tree critically known as (C. guianensis).^[2] The tree is mostly found in Brazil, America, South Caribbean and India. In Hindu religion it is identified as sacred tree as the flower looks like the hood of sacred snake Naga which protect shiva Lingam.^[3] The tree grows up to 25 m in height and width is about 3 m long with large branches and it grows dark brown, large and round cannonball like fruits, hence it is also known as cannonball tree. The leaf is 10-20 cm long and 4-10 cm broad. The orangish pink flower is born on the trunk is about 8-12 cm in diameter. The pinkish orange colored corolla is long and large, round shaped spread



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over the small cap of pestle (Figure 1). Not only from the leaves and stem, but several compounds are also isolated from flowers, fruits and even from the bark. The fruit is about 15-20 cm long with a hard woody capsule and contains small seed in it.^[4,5] There are about 200-300 seeds are present in fruit and it reproduces through shelf and cross pollination by the vectors like bees and bat.^[6] The metabolites such as fatty acids, terpenoids, steroids etc. have been found which are rich in phytochemical activities. It has been observed that the alcoholic extract of the fruit is rich in saponin which is quietly used in treating cancers and lowering the cholesterol levels. The antioxidants obtained from the different parts of the plant are being widely used as neutralizing the free radicals and help to reduce stress conditions. Bioactive compounds are employed to serve as the key factor in order to have anti-cancerous and anti-inflammatory activities. The fruit pulp has been demonstrated to have antibacterial properties on wounds and diseased skin in animals. In South America, an extract from fresh green leaves were used to treat protozoan infections. Besides, it has been reported to have antithrombotic properties in wound treatments and stomach discomfort. The extracted volatile chemical from the cannonball flower has been demonstrated to have antifungal and antibacterial characteristics, making it useful for treating stomach diseases such as diarrhoea, scabies and piles etc.,^[4,7-9] The secondary metabolite alkaloids have an intense effect on anti-oxidant and anti-inflammatory activities.^[10]

MATERIALS AND METHODS

Literature search and study design

For the review we have taken the articles from google scholar, PubMed., research gate which are published between 1992 to 2024. The recent databases are escalated to review the functional activity of *Couroupita quianensis* plant. The different parts of plant compounds after which have been several phytoconstituents employed to treat different physiological disorders (Figure 2).

Inclusion criteria

The study includes the database from good and reputed scientific journals comprises with the primary and secondary metabolites with their structures, molecular targets and action of broad-spectrum diseases using *in vitro* and *in vivo* studies.

Exclusion criteria

The reports conclude with studies that are not appropriate or relevant for use in the study.

Primary and Secondary Metabolites

Plants secrete primary and secondary metabolites known as phytochemicals which help in cell proliferation and growth of plants, have the antibiotic and a disease resistance activity respectively. There are several quantitative phytochemical tests that have been performed in order to search for new compounds from the different parts of the plant. The plant is rich is high medicinal value as nearly all the parts of the plant contain useful phytochemicals (Figure 3).^[11] The flowers contain high amount of stigmasterol, alkaloids and phenolic compounds. Alkaloids works as anti-inflammatory, cardioprotective agents as well as anesthetics.^[12-14] Extraction of dry fruit yields quinazoline and isatin and colored compound indigo that is shown to have anti-HIV and analgesic effects. There are several research have been done to prove the presence of alpha-sitosterol, amirin, steroids, terpenoids and hydrocarbons. The dyes such as indigo and indirubin are characterized as Tetripenoid esters of fatty acids. [15,16] Campesterol is isolated from the extracts of young leaves of C. guianensis. It functions as a dietary supplement as emulsifier and stabilizer in various food industries. Also, it helps to increase the shelf life of the foods including texture. Moreover, it has been identified as an antioxidant to protect the food from spoilage. Volatile compounds like saponins and glycosides are extracted from the alcoholic extraction of stem which serves as the treatment for heart failure by inhibiting Na⁺/K⁺ATPase activity in cardiac patients. [17-19]

Phytochemical Activities

Compounds like stigmasterol and alkaloids help in diabetic patients to reduce fasting glucose and serum insulin level, hence can be used as food supplement for the patients in hyperglycemic condition. It helps in expression and translocation of GLUT 4 activity in diabetes type 2 mellitus.^[15] Alkaloids are merely used in clinical purposes as the constituent of morphine, nicotine and ephedrine. Alkaloids also exhibit antiviral and anti-metastatic activities both in in vivo and in vitro. Another secondary metabolite named statin is used in medicine in order to reduce the blood cholesterol by lowering low density lipoprotein in blood that gives a protection against liver cancer.^[20] Both a and β amirin provides an effective panacea in complication of liver diseases mainly in liver cirrhosis.^[21] Quinazoline is the biologically active compound which acts upon broad spectrum microbes. 12-dioxoindolo [2,1-b] quinazoline is a derivative of quinazoline that is extracted from fruit of C. guianensis. It shows the anti-cancerous effect by inhibiting EGFR and tubulin polymerase to continue polymerization. Furthermore, it inhibits DNA repair enzyme. Studies proved the effectiveness of terpenoids in cancer and parasitic infections as a good therapeutic effect. Volatile compounds like methanol work as raw material for industrial purposes in flavoring, spices and cosmetics. Saponin acts as treating clinical conditions like hypercholesterolemia by decreasing the blood lipids as well as blood glucose response. Glycoside, the secondary metabolites obtained from the bark, widely used in pharmacological industries as its effectiveness in curing atrial arrhythmia.^[22] To identify the antioxidant property several experiments scavenging have been conducted to recognize the free radical activity. Quercetin and myricetin were found to have most anti-radical activity through 2 2-Diphenyl-1-Picrylhydrazyl (DPPH) assay. Therefore, about ten molecules showed radical scavenging activity including Quercetin and Myricetin molecules. Many individual compounds are isolated from C. guianensis such as stigmasterol, alkaloids, statin, amyrins, terpenoids etc. and their pharmacological activity was evaluated (Table 1).

Pharmacological Activity

C. guianensis is a plant with multiple medicinal values such as antimicrobials, anti-oxidant, anti-cancer, anti-nociceptive, anti-ulcer, antihelminthic, anti-fertility and anti-fungal properties. The pharmacological activities (Figure 4) of plant extract were discussed in detail in the below sections.

Antimicrobial activity

Methanolic and aqueous extract of *C. guianensis* was discovered to have both antifungal and anti-bacterial activity. Recent studies demonstrated remarkable antibacterial effect against common pathogenic bacteria such as *S. typhi, E. coli* and *S. aureus in vitro* conditions. The maximum activity was observed against *S. typhi*. Minakshi et.al reported the alcoholic extract also effective against



Figure 1: Representation of Couroupita guianensis plant with Fruits and flower.

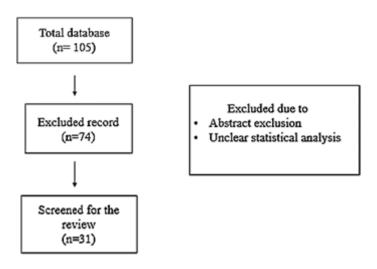


Figure 2: Systematic selection of databases for the study of current review.

skin pathogens like Candida albicans and Micrococcus sp. Whereas chloroform extract of fruits showed antifungal and antimicrobial activity at low concentration of extract than ethanolic extract.^[23,24] Compared to rifampicin the chloroform extract of the fruit shows low activity against *Mycobacterium tuberculosis*, though it has given in a high concentration. Also, this compound shows effective antibacterial activity against both the gram positive and gram-negative bacteria at a low dosage. For example, most of the gram-positive bacteria such as Bacillus sp., E. aerogenes etc., and gram-negative bacteria like P. aeruginosa and S. flexneri the alcoholic extract of the fruit was shown to have highly effective.^[23] Moreover, in other clinical study the extract showed moderate activity against pathogenic fungi. For instance, most of the HIV affected people commonly found pathogenic fungi is C. albicans. that causes candidiasis in most of the patients. Also, that leads to stress conditions to the person as well as compromised immune disorders. The fruit extract has been observed to show moderate inhibiting activity on the growth of the fungi against pathogenic bacteria.[25,26]

Antibiofilm properties

Chloroform extract is reported to have antibiofilm activity against Pseudomonas sp. This confers the inter species communication in similar and different genera of lower organisms like prokaryotes and eukaryotic cells. Polyphenols present in chloroform extract interferes in bacterial signaling pathways which are highly resistant to conventional antimicrobials.[27] The chloroform extract at low concentration inhibits 52% of zone of inhibition in biofilm formation. The ions present in the bacterial cell surface and CSH plays crucial role in biofilm formation. Many gram positive and gram-negative bacteria cause biofilm associated disease such as gingivitis, streptococcal and other bacterial infections. But the plant extract appreciatively inhibits the growth of those pathogenic bacteria as well as shows anti-biofilm activity. Bacteria exhibits strong antibiotic resistance capacity due to their complex cell wall and due to presence of some adhesion compound like lipoteichoic acid. The bioactive compound present in the fruit extract such as phenolic compounds and

sterols interferes with those adhesion compounds to release and stop producing the biofilm around them.^[28-30]

Wound healing activity

The ethanolic extract of fruit helps to treat wounds, scar etc. That repairs injuries to skin and soft tissues. The compound shown to up-regulate the immunity system by responding the process of wound healing with DAMPs (Damage Associated Molecular Patters) and MAMPs (Microbes Associated Molecular Patterns).^[31,32] In Wistar albino rat model, the crude extract of fruit pulp was given in order to check the stimulating process of wound healing. It has observed that, the wound area has been cured

 Table 1: Molecular targets of different compounds of Couroupita guianensis.

SI. No.	compounds	Pharmacological activities
1.	Stigmasterol	Regulates GLUT2 activity in diabetes mellitus.
2.	Alkaloids	Maintain fasting glucose level and serum insulin level in hyperglycemia.
3.	Statin	Regulates LDL.
4.	Amirin	Protect against liver diseases.
5.	Quinazoline	Inhibits EGFR and tubulin polymerase activity.
6.	Terpenoids	Protect against parasitic infections.
7.	Saponin	Therapeutics against hypercholesterolemia.
8.	Glycoside	Protect against atrial arrhythimia.
9.	Quercetin	Antioxidant effects.
10.	Myricetin	Free radical scavenging activity.

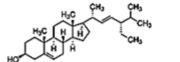
about 89% in just 15 days and also helps in formation of collagen by increasing the amount of hydroxyproline. Furthermore, the ethanolic extract of plant was shown to modulate VEGF and TGF at genetic level in healing process.^[30,33]

Anti-inflammatory effect

Ethanolic extract of *C. guianensis* fruit shows anti-inflammatory effect. High dose of extract prevents migration of white blood cells into peritoneal cavity. It inhibits other cell migration as well as cytokines and mediators.^[27] Reactive oxygen species and pro inflammatory cytokines plays major role to induce inflammatory responses in the body. Due to activation of certain immune mediators and cytokines damaged cells or pathogen infected cells are removed, but in some cases pro inflammatory factors are activated that leads to migration of WBCs in normal condition. Studies revealed high dosage of fruit extract of. *C. guianensis* inhibits the cell migration and also regulates interleukins. Anti-inflammatory effect of the plant extract can be used as great therapeutics in wound healing.^[34]

Anti-stress activity

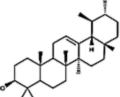
Studies demonstrates the methanolic extracts works as anti-stressor. They observed hormones like glucocorticoid, glyceride level has controlled after providing methanolic extract. Also, the stress has decreased gradually on dose depended manner.^[35] In stress conditions, glucocorticoids present in a low level that can be stimulated by methanolic extract of the plant. This hormone helps to stimulate glucone ogenesis in order to produce more glucose that gives instant energy to body and relieve stress condition. While, glycerides are the lipid ester molecule that stores energy. In stress conditions it plays key role in restoring homeostasis in the cells when it gets expose to certain stress conditions. On other

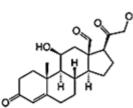


Stigmasterol



Alkaloid



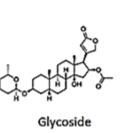


α-Amirin



Terpenoid

Saponin



Steroid



Figure 3: Important Primary and Secondary Metabolites present in Couroupita guianensis.





hand, it regulates cell to cell communications by maintaining ion channels to fight against the stress.^[4,5]

Anti-cancerous activity

Alcoholic extract of *C. guianensis* fruit contains saponin which acts as anti-cancerous agents. The extract inhibits the cell invasion by promoting apoptosis or programmed cell death. Also, it helps to scavenge the free radicals in body to protect the cells from oxidative damage. Saponin molecules bound to death receptors present on cancer cell and activates cascade of protein caspases simultaneously and other hand it produces more amount of cytochrome c to form an apoptosome.^[5] Therefore it mediates apoptosis of cancer cell. Also, high doses of alcoholic extract of fruit pulp induce the inflammatory response by dilution and swelling of intracellular membranes.^[36]

Insecticidal activity

In case of greenhouse cultivated tomato the aqueous extract of *C. guianensis* was more active against nymphs and eggs of Bemisiatabaci. The insect feeds on a wide variety of solanaceous and ornamental crops including tomato, brinjal, cotton okra and cause dry leaf, tomato curl leaf and chlorotic spots etc.,^[3]

Anxiolytic activity

Studies demonstrated that aqueous and methanolic extracts of the fruit have anti-anxiolytic effect in mice when given at a certain dosage. They concluded that extract as a good treatment to treat anxiety and anxiety-related diseases in different mouse models.^[2,4,37]

FUTURE PROSPECTIVES

C. guianensis extracts have multiple impacts on treating a variety of disorders; they have the potential to have a significant impact on society by replacing traditional pharmaceuticals used in the medical field. Recent research has discovered the pharmacological properties of extracts derived primarily from leaves, stems, bark and flowers. As a result, more research is needed to identify phytochemicals that modulate metabolism in animal models. C. guianensis is a versatile large tree that produces phytochemicals such as alkaloids, phenolic compounds, hydrocarbons and terpenoids, which have been used to have mostly antimicrobial, anti-depressant and anti-cancerous activity, but the exact mechanism by which secondary metabolites such as saponins act as an anti-cancerous element and glycosides regulate blood glucose in diabetes mellitus is still unknown to all. This overview discusses the phytochemical and physiological activities used by plants, as well as their biological targets in the treatment of various ailments. Now, researchers face a significant problem in determining the mechanism of action of phytochemicals that are currently unknown.

CONCLUSION

C. guianensis is known for its medicinal values. Studies using *in vivo* and *in vitro* models using different parts of *C. guianensis* revealed that it has anti-cancerous, anti-microbial, anti-biofilm and insecticidal activities. Moreover, plant extract showed strong antioxidant activity. Few researchers have isolated phytocompounds using plant parts, however their biological activities were not tested. Research is required on individual compounds effect on different cell lines as well as *in vivo* models.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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