

Insights into the Potent Anticancer Activity of *Couroupita Guianensis* Aubl. - A Review

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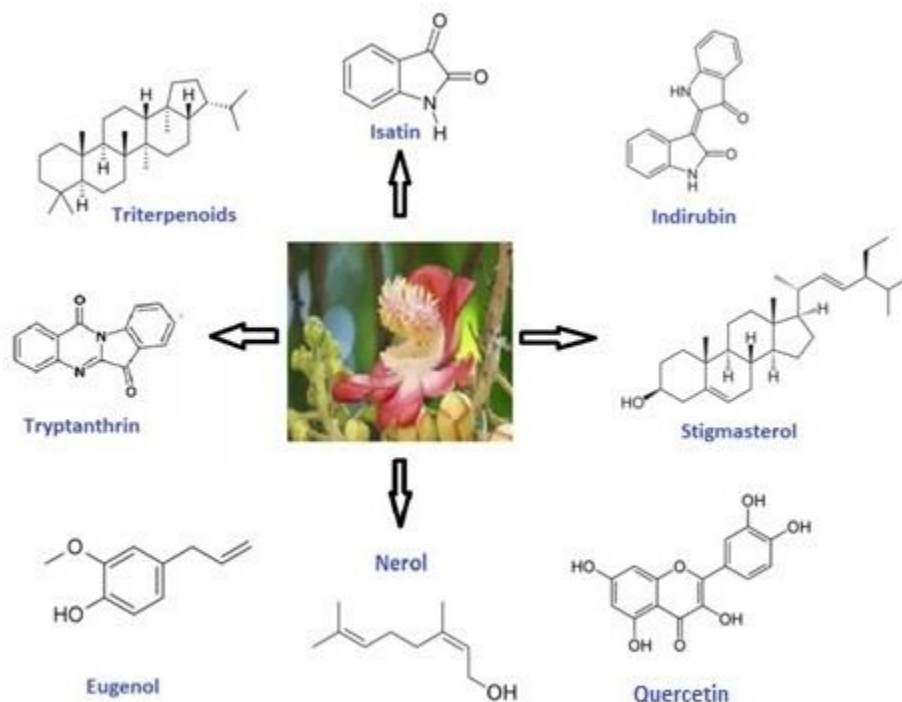
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Abstract:

Since olden times, phytochemicals have made significant contributions to humanity because of their useful medicinal properties. *Couroupita guianensis* Aubl, commonly known as Cannonball tree belongs to the family Lecythidaceae one such plant rich in phytochemicals with potential pharmacological actions. Cannonball tree has gathered global attention because of its huge medicinal values including antibiotic, anti-inflammatory, antimicrobial, antimycobacterial, analgesic, antiarthritic, anti-biofilm, antifertility, antipyretic, antistress, antiulcer, antidermatophytic, antidiarrheal, wound healing, immunomodulatory activities and anti cancer. It has been reported that *C. guianensis* is a rich reserve of useful bioactive molecules, specifically the presence of isatin, quercetin, stigmasterol, tryptanthrin, courouputone A, courouputone B, steroids, triterpenoids, eugenol, linoleic acid and indirubin is praiseworthy. The present review covers in-depth scientific survey of anti cancer activity of the above sacred plant which may facilitate further useful research for the benefit of mankind.

Key words: Phytochemicals, *Couroupita guianensis*, Lecythidaceae, anticancer.

Graphical abstract:



Introduction:

Couropita guianensis is a large deciduous, evergreen tree that generally grows to a height of 20-25 meters. Leaves are alternate, oblong-obovate, up to 20 centimeters long, entire to slightly serrate and hairy on the veins beneath. Inflorescence is racemose, arising from the trunk and other large branches. Flowers are reddish with a yellow tinge on the outside, fragrant, with stamens borne on an overarching androphore. Fruit is a large, reddish-brown globose, 15 to 24 centimeters, with a woody capsule, and each containing 200 to 300 seeds. Pollination is done by bees and bats. The tree bears, also directly on the trunk and main branches, large globose woody fruits; they look like big rusty cannonballs hanging in clusters, like balls on a string.

The common name is in reference to the unusual, bordering-on-the bizarre, woody, globose, hard-shelled, reddish-brown fruits of this tree which mature to a cannonball size of 8-10 in diameter. On windy days, the fruits often bang against each other on the tree creating a sound reportedly resembling like a cannonade. Each fruit

contains 200-300 seeds which are embedded in an ill-smelling, soft red pulp which turns bluish-green when exposed to air. Each fruit typically takes 1 year or more to mature. When ripe, fruits drop from the tree, usually splitting open as they hit the ground with an explosive splat. Large, pleasantly fragrant, rose-pink to red flowers are seen to bloom. Each flower has a 6-lobed calyx and 6 spreading petals which contains 2 types of stamens (fertile stamens and sterile staminoides) which are attached on a cream-colored androphore. Each flower is reported to bloom for only one day. Flowers and subsequent fruits are located on drooping, naked, thick, tangled, vine-like stems (extrusions to 2-6' long) which emerge directly from the trunk and large branches. Simple, elliptic to ovate to oblong leaves (6-8" long) are primarily clustered near the branch ends. Leaves are alternate or in apical whorls. Leaf margins are entire or finely serrate. Veins on leaf undersides are pubescent. Leaves typically drop once, but sometimes twice, per year, usually in response to dry weather, hence the designation of deciduous for this tropical tree¹.



Cannon ball tree bearing fruits and flower

Anticancer potency:

It was reported that, flowers of Cannonball tree contain isatin which is known to have cytotoxic activity against human carcinoma cell lines. This highlights its potential use as a chemotherapeutic agent against cancer. Isatin is well known to start the Apoptosis process by involving with the DNA fragmentation².

Apoptosis induced by isatin was confirmed by flow cytometry to further elucidate the extent and causes of

apoptosis. Isatin was isolated from the floral parts of cannon ball tree and it exhibited antioxidant activity and cytotoxicity against HL60 cells³.

Rare earth element ytterbium oxide (Yb_2O_3) and ionic liquid (IL) added ytterbium oxide (Yb_2O_3 -IL) nanoparticles (NPs) were synthesized using *Couropita guianensis* Abul leaves extract by hydrothermal method. The synthesized Yb_2O_3 and Yb_2O_3 -IL NPs are of BCC structure and crystalline size of 40 and 35 nm. The MTT

assay of Yb_2O_3 and IL-assisted Yb_2O_3 NPs was received against cancer MCF-7 breast cancer cells. The cytotoxicity of Yb_2O_3 and IL-assisted Yb_2O_3 NPs against cancer cells has a higher effect than standard cells. This mainly interrupts the cell wall of cancer cells, leading to breakage of the MCF-7 breast cancer cell wall and cytoplasmic ingredients in the MCF-7 breast cancer cells. As a result, there is cell death⁴.

The anti-cancer activity of synthesized silver nanoparticles using aqueous extracts from flowers of *Couropita guianensis* against breast cancer cells (MCF-7) and fibroblast cells (L-929) were evaluated using MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay. Potent in vitro cytotoxic activity was found against MCF-7 cells. Ag NPs coated with ingredients in the plant extract, possibly favored the apoptosis induced cell death, thereby, decrease in cell viability was witnessed⁵.

Gold nanoparticles biosynthesizing capability of the flower of pharmacologically important tree *Couropita guianensis* was reported. Rapid, cost-effective, one-step process of synthesis has been achieved. Newly genre gold nanoparticles were characterized by involving UV-vis spectroscopy, FTIR, XRD, SEM, and TEM analysis. Interestingly, as a result of extensive screening on the application of newly synthesized gold nanoparticles their anticancer potential has been discovered using MTT assay, DNA fragmentation, apoptosis by DAPI staining, and comet assay for DNA damage. Cell viability determination was made using MTT assay which was conducted for 120 h. *C. guianensis* flower extract synthesized gold nanoparticles caused a significant cytotoxicity in HL-60 cells in a concentration-dependent manner with the CC50 value of 5.14 Mm⁶.

Palladium nanoparticles (CGPdNPs) using the aqueous fruit extract of *C. guianensis* Aubl was reported as a potent anticancer agent. The cytotoxic activity of CGPdNPs were measured using the MTT (3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide) assay. Moreover, the anticancer prospective of the CGPdNPs in human lung carcinoma cells was notable with 50% of mortality at 121mg/ml⁷.

In-vitro anticancer activity and cellular toxicity of *Couropita guianensis* (CG) towards the Human promyelocytic leukemia HL60 cells, contrasted with the normal cell lines was reported. The anti-cancer properties of *Couropita guianensis* extracted with Chloroform and DMSO (Dimethyl sulfoxide) were analysed and studied throughout. HL60 cell lines were permitted to develop in DMEM (Dulbecco's Modified Eagle's medium) and incubated with differed concentration of DMSO CG extract. MTT assay drew out the best approach to decide the cell feasibility and assessment was done with the optical absorbance at 570nm and 620nm as reference. The

floral extract inhibited 50% growth (IC50) of HL60 cell lines at 10 mg/ml of extract concentration⁸.

It was reported that among all the successive extracts of *C. guianensis*, ethylacetate extract of the stem, crude methanolic extracts of the flower has been used for in vitro cytotoxicity studies. In the cytotoxicity study, based on in vitro antioxidant activity, the potent extracts were chosen for cytotoxicity study on HT-29 cell line. The selected Ethyl acetate leaf extract and Chloroform leaf extract have shown better cytotoxicity. The CTC50 values are 300.0 and 220.0 $\mu\text{g}/\text{mL}$, respectively⁹.

In silico studies of the various phytoconstituents of the above plant have been reported with positive predictions. The phytochemicals such as stigmasterol, quercetin, p-coumaric acid and o-coumaric acid from Cannonball were docked with signalling molecule and protein related to cancer pathway such as BRCA1 breast cancer type 1 susceptibility protein (3PXD) using SwissDock to explore their potential to be used as drugs for these diseases. Although stigmasterol has shown greater affinity with most of these proteins nonetheless, quercetin, p-coumaric acid and o-coumaric acid have also shown moderate binding with the proteins at their catalytic sites and hence can be considered as suitable drug candidates¹⁰. Extracts of *Couropita guianensis* flowers were treated on MCF-7 cell lines when observed, both ethanolic extract (ECG), ethyl acetate extract (EACG) showed in vitro cytotoxic activity. The above results indicated that, both ethanolic and ethyl acetate extracts of *Couropita guianensis* flowers showed in vitro cytotoxic activity against MCF-7 cell lines, when compared with standard tamoxifen, whose cytotoxic activity is less. Cytotoxic properties observed may be due the presence of number phenolic chemical constituents in the extracts. Prior reports suggested that flavonoids and phenolic constituents have exhibited antineoplastic activity¹¹.

Conclusion:

Various biological activities of the plant *Couropita guianensis* has been reported, present review focuses only on the antiproliferative potency of various parts of the plant. Herbal medicines and other products are gaining worldwide attention because of the safety and efficacies when compared to synthetic molecules. Therefore in this context, there is a need for extensive in-vivo and in-vitro research to expose the phytochemicals present in various herbs in the current generation for developing evidence based medicine. This may facilitate new horizons in the development of active therapeutic medicines. The present review provides scientific information that may motivate interest among various researchers to explore such important natural resources for the benefit of mankind.

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