

# PASSIFLORA SPECIES - BOON TO ANTICANCER DRUGS: A PHARMACOLOGICAL REVIEW

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## Abstract

Herbal medicine, the backbone of traditional medicine in many countries have played an important role in curing the diseases of humans since ancient time. Medicinal plants are great source of bioactive compounds. In the present review, an attempt has been made to compile the anticancer activity of Passiflora species. Passiflora species have different types of pharmacological activities like antioxidant, anticancer, antimicrobial, immunomodulatory, antidiabetic etc. the major phytochemical in Passiflora are flavanoids. Bioactive compounds of Passiflora responsible its various medicinal properties and their effects at the molecular level need to be investigated in more detail. This review will definitely help for the researchers dealing with Passiflora to know its proper usage as this herb is seemed to be highly valuable.

**Keywords:** Herbal drugs, Passiflora, Anticancer activity, Active compounds.

## INTRODUCTION

The term cancer refers to disease of cells that show uncontrolled proliferation, differentiation, invasiveness and the ability to metastasise. The appearance of such abnormal characteristics reflects their chromosomal abnormality including an expression of abnormal gene sequences (called oncogenes). When such cells proliferate excessively, they form local tumors which can compress or invade nearby normal cellular structures. A small core of cells within this tumor, which retain the ability to undergo repeated proliferation and to metastasise, are called tumor stem cells. The extent of metastasis and deterioration in metabolic processes, resulting from cancer, leads to eventual death of the patient, unless the neoplasm is successfully eradicated by the treatment.

There are four main approaches to treat cancer:

1. Surgical resection
2. Radiotherapy
3. Chemotherapy and
4. Immunotherapy.

Chemotherapy can be used alone or as an adjunct to other forms of therapy.

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## TYPES OF NEOPLASM (TUMOURS)

Neoplasm can be benign or malignant. Benign tumours are generally slow growing, resemble normal cells, remain localized and are usually not harmful. The terms cancer or malignant neoplasms are synonymous. They proliferate rapidly, manifest dedifferentiation, invasiveness, and the ability to metastasise. The malignant neoplasms inflict damage to the surrounding cells and are harmful if left untreated.

## AETIOLOGY OF CANCER

1. Viruses: Both DNA and RNA viruses have been implicated in the aetiology of cancer. DNA viruses that are associated with the cause of various neoplasms are Human Papilloma viruses, Epstein- Barr virus, Human irus-8. RNA viruses implicated in the aetiology of cancer are: Human T-cell lymphotropic virus (HTLV-I and HTLV-II).
2. Environmental and occupational hazards such as exposure to ionizing and UV radiation and exposure to various chemical carcinogens like azodyes, asbestos, benzene and polyvinyl chloride.
3. Diet and habits such as high-fat and low-fiber diet; tobacco smoking and alcohol consumption.
4. Use of drugs like immunosuppressants and some alkylating agents.
5. Genetic factors such as inherited genetic mutations, expression of oncogenes and repression of tumour suppressor genes.[1-4]

Plants produce wide variety of secondary metabolites. Phenolic compounds, terpenes and nitrogen containing compounds are the main three classes of these compounds. They are used to treat wide variety of diseases including cancer.[5-6]

## PASSIFLORA

The genus *Passiflora* contains almost 500 species and it is the largest species in the family *Passifloraceae* (Passion fruit family). It is growing in warm tropical climates as well as cold and subtropical areas. These plants are mainly cultivated for food industry for consumption in both their fresh and processed form. The plants of the genus *Passiflora* are shrubs and herbs, mostly climbers with axillary tendrils. Flowers are bisexual or unisexual, regular.

Alkaloids, phenols, glycosyl flavonoids and cyanogenic compounds are known in the genus. Literature survey has revealed that a number of reports are available on *Passiflora incarnata* and *Passiflora edulis*, while only sporadic reports are there on other species of *Passiflora*.

Its major component is flavonoids, which represent about 2.5% of the phytochemicals present in their extract. In most of these species, flavonoid glycosides are present in high amounts. Extracts from different tissues of these species have potent antipyretic, antioxidant, sedative, tranquilizing,

anxiolytic, anti-inflammatory, anticonvulsant, antihypertensive, and analgesic properties.[5-8]

## ANTICANCER STUDIES

Ricardo G. Amaral et al. conducted a study to evaluate the potential cytotoxic and antitumor activities of *Passiflora alata* leaf extract (PaLE). They conducted the study in S180-tumor bearing mice. Utilizing the MTT test method, in vitro experiments are carried out. HepG2, S180, PC3, K562, and K-562 were the cell lines utilised. PaLE demonstrated better efficacy (IC<sub>50</sub> 30 g/mL) and a CPI > 75% against PC3 and S180 cell lines. PaLE demonstrated anticancer efficacy when administered intraperitoneally (at dosages of 36.75 and 44.99%, respectively). Reduced body mass correlated with decreased food intake, increased spleen bulk correlated with an increase in the white pulp of the spleen on a histological level, and increased total leukocyte count correlated with altered lymphocyte-neutrophil ratios were all signs of toxicological alterations. They came to the conclusion that PaLE had less harmful antitumor action.[9]

A study to evaluate the anticancer potential of five plants was carried out by Victor Kuete et al. The cytotoxicity of the extracts was assessed using the MTT assay, and the cell cycle, apoptosis, mitochondrial membrane potential (MMP), and reactive oxygen species were all measured using flow cytometry. Ten extracts from five plants-*Alchornea floribunda*, *Annona muricata*, *Euphorbia prostata*, *Pachypodium staudtii*, and *Passiflora edulis*-displayed IC<sub>50</sub> values < 20 g/mL during initial screening utilising leukaemia CCRF-CEM cells. They were next examined in 8 additional cell lines and in regular AML12 hepatocytes. All of the chosen extracts had an IC<sub>50</sub> value below 40 ng/mL and were effective against leukaemia CEM/ADR5000 cells. Extracts from *Annona muricata* leaves (AML) and seeds (AMS), and *Passiflora edulis* fruit (PEF) had IC<sub>50</sub> values below 1 µg/mL against CCRF-CEM cells and below 10 µg/mL against its MDR subline CEM/ADR5000 cells. AML, AMS and PEF induced MMP-loss-mediated apoptosis in CCRF-CEM cells. [10]

Valentina Ramirez et al. performed anticancer Studies of ethanolic extracts and phytochemicals from *Passiflora* genus have shown promissory biological activity for cancer chemoprevention. They used Caco-2 and SW480 colorectal adenocarcinoma cells for the study. The effect of the extract on cell viability was evaluated by MTT assay. Apoptosis-inducing effect and cell cycle regulation was assayed by flow cytometry. They got half maximal inhibitory concentration (IC<sub>50</sub>) of the extract over both cell lines and also, it was observed the inhibition of cellular proliferation after 48 hours of exposure to the extract. The extract altered the distribution of cell cycle phases by increasing SubG1 and G2/M populations. Their results suggest that *P. edulis* is a potential source of phytochemical compounds with anticancer properties for the management of colorectal cancer patients.[11]

Dheeban SP et al performed analysis of cytotoxic and apoptotic action of *Passiflora foetida* extract. They use methanolic extract of *P. foetida* to find out cytotoxic and apoptotic effect and used HeLa cell line cultures with different concentrations of the extract (25, 50, 75, 100, and 125 µg/ml), and thereby the activity was ratified by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay and propidium iodide staining. The functional groups of the active component was identified by using FTIR. [12]

Annalisa Chiavaroli et al. conducted study on *Passiflora foetida* extracts for their phytochemical profile, enzyme inhibitory, and antioxidant potentials. In silico, in vitro and ex vivo studies were also carried out on methanol and water extracts for predicting pharmacokinetics and pharmacodynamics. In this regard, extracts were applied to pathogen dermatophytes cultures, isolated mouse skin tissues, and neuronal HypoE22 cells. The extract's ability to inhibit changes in prostaglandin E2 (PGE2), l-dopa, and serotonin caused by hydrogen peroxide was stressed. Similar chemicals were found in both the infusion and the methanolic extracts, according to chemical analyses. By reducing the quantity of PGE2 produced by hydrogen peroxide, *P. foetida* water and methanol extracts also demonstrated protective skin characteristics in ex vivo investigations. From their study *P. foetida* extracts could represent potential sources of pharmaceuticals and nutraceuticals. [13]

Meenakshi Sundaram Muthuram et al. investigated antitumor potential of ethanolic extract of *Passiflora incarnata* on Ehrlich ascites carcinoma. They performed in vitro studies to investigate the antitumor potential. Active components in the extract were identified by using GC-MS. They also made attempt to understand the mechanism of action using in silico methods. They concluded that *Passiflora incarnata* extract shows significant antitumor activity. [14]

Ricardo Guimaraes et al. performed anticancer screening of ethanolic extract of 14 species of *Passiflora*. They selected *P. alata*, *P. sapsularis*, *P. cincinnata*, *P. Gibertii*, *P. maliformis*, *P. malleophylla*, *P. murchonata*, *P. morifolia*, *P. quadrangularis*, *P. racemosa*, *P. setacea*, *P. suberosa*, *P. tenuifolia*, and *P. vitifolia* for their study. They performed in vitro studies mainly in 3 cell types HCT-116, OVACAR-8 and SF-295. Doxorubicin was the standard drug used for the comparison. They concluded that among the 14 species *P. alata* have highest anticancer activity. [15]

## CONCLUSION

From the above research survey, it was concluded that traditional medicine is safe and has many therapeutic applications. Of many medicinal plants *Passiflora* species is one of the important herbs which have multiple pharmacological properties. The scientific research on different *Passiflora* species suggest its strong anticancerous

activity. Even though, *Passiflora* has various medicinal properties since ages, there is a colossal necessity to scientifically explore and evident its medicinal values at molecular level with help of various latest biotechnological tools and techniques. There are also research opportunities to better utilize *Passiflora* for human consumption.

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