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Presence of phytochemicals in fruits and leaves of guava (*Psidium guajava* Linn.) for cancer prevention: A mini review

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ABSTRACT

The present review deals with the bioactive compounds (phytochemicals) in the fruits and leaves of guava (*Psidium guajava* Linn.). In the present study, an attempt was done to survey of literatures for exact solvent extraction to know exact phytocompound and characterization by using instruments along with anticancer properties of these phytochemicals present in fruits and leaves of guava. The compilation of available literatures of last 10 years can be suitable ready references for future experimental study as *in vitro* and *in vivo* as well as new drug design as phytomedicines for cancer therapy.

Keywords: Bioactive compounds, *Psidium guajava*, Guava fruits and leaves, Cancer therapy, Phytomedicines

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INTRODUCTION

The guava tree (*Psidium guajava* Linn.) is a medicinal plant belonging the family Myrtaceae and found in the many places of India. The leaves and fruits are used for the traditional medicine worldwide[1-4]. In India, the fruits are edible food crop as low cost compared to other fruits and poor people can also afford as food [3,5].

The leaves and fruits of guava contain several phytochemicals viz. tannins, phenols, triterpenes, β-avonoids, essential oils, saponins, carotenoids, lectins, vitamins, fibre and fatty acids [5-10] that prevent several diseases such as digestive disorders, cancers and mutations, bacterial infection, menstrual disorders, dermatitis, neurodegenerative disease, diabetes, lung problems, free radical generation, etc. [4-6, 11-13].

Several research works have already been emphasized that crude extracts of guava leaves and fruits are effective for anti-carcinogenicity [14-19] but few scattered animal studies were observed solvent isolated particular phytochemical(s) of leaves and fruits of guava plant potent to prevent cancer [9, 14, 19-22].

Moreover, previous reports were obtained only on phytochemicals extraction and characterization by using instruments as well as separate experimentation on each phytocompound in animal models or cancer cell lines by researchers. The combination studies as extraction and characterization of phytocompounds of guava fruits and leaves as well as experiments on animal models with these extracts are rare [22-23]. Major review works were observed on the disease prevention by using extracts of different parts of guava tree [2, 4, 19, 24].

In the present study an attempt was undertaken to compile research works of last 10 years to know cancer preventive phytochemicals present in the leaf and fruit of *Psidium guajava* Linn. from available literature as a ready reference for future research works for new drug design for cancer treatment.

Study of solvent extraction for isolation and characterization of phytochemicals of fruits and leaves of guava

It is very important to note that extraction by using proper solvent and isolation of exact phytocompound can be

achieved as a suitable therapeutic agent. On the other hand, crude extract can also prevent cancer in *in vitro* as well as *in vivo* assay but exact phytocompound can be potential for new drug design as active ingredient. Numerous phytochemicals present in the fruits and leaves of guava *Psidium guava* Linn. and these were extracted in different solvents such as water, hexane, chloroform, methanol, ethanol, etc. and phytocompounds characterization by using different instruments [9-10 13, 22, 25-27]. Researchers further used these phytochemicals in cancer therapy in animal models and *in vitro* study with cancer cell lines.

Jiménez-Escrig et al. [25] reported that ascorbic acid and tocopherol present in the fruits of *P. guajava* Linn. The extraction of fruit was done by using ethanol. Koo and Mohamed, [26] analysed phytochemicals Myricetin and Apigenin in dried plant samples especially edible part i.e. fruit of guava after extraction and hydrolysis of the flavonoid glycosides. The phytochemicals were determined from the methanol extract by using reversed-phase HPLC.

Arima and Danno [27] analysed phytocompounds that were isolated from leaves of guava (*P. guajava* Linn.), and the structures of these compounds were confirmed based on chemical structure and spectroscopic evidence. The flavonoid glycosides namely Morin-3-O-alpha-L-lyxopyranoside and Morin-3-O-alpha-L-arabopyranoside, and two known flavonoids, Guaijavarin and Quercetin were determined by them. The extraction was done with n-hexane and chloroform and the aqueous phase was extracted with ethyl acetate followed by separation under HPLC.

Chiari et al. [13] studied the phytochemicals in the fruit extract of guava in hydroethanolic and aqueous solutions, which were analysed by using thin-layer chromatography (silica gel 60 F254 aluminum sheets, 20 × 20 cm, 0.2 mm thickness, Sorbent Technologies). The HPLC-UV-PAD fingerprints of the fruit extracts obtained the main classes of phytochemicals were phenolic compounds, flavonoids, tannins, terpenes, steroids and reducing sugars. Interestingly, 70% ethanol was extracted suitable phytochemicals in the fruit.

Ryu et al. [22] identified phytochemicals in 80% methanol extract of the leaves of *P. guajava* Linn. Further, they fractionated with four different solvents such as the *n*-hexane fraction, chloroform fraction, ethyl acetate fraction, *n*-butanol fraction, and water fraction. They identified 60 types of phytocompounds in the *n*-hexane fraction of the leaf extract.

The gas chromatography-mass spectrometry (GC-MS) analysis revealed the identification of phytocompounds such as Pyrogallol, vitamin E, Palmitic acid, Caryophyllene oxide, Copaene, Alloaromadendrene, Caryophyllene, Sitosterol, α-Bulnesene, α-copaene, squalene, etc. in the methanol, chloroform and hexane extracts [28].

Chiari-Andréo et al. [13] identified different phytocompounds such as Kaempferol 3-O-xylosyl-rutinoside, Quercetin, Quercetin 3-O-diglucoside, Catechin, -)- Epicatechin 8-C-galactoside, etc. in the guava fruits. The total ion chromatogram obtained by negative-ion HPLC/MS/MS of E70 *P. guajava* L. extract.

Borah et al. [10] determined the phytochemical composition of the essential oil extracted from the leaves of *P. guajava* Linn. The leaves were hydro-distilled and phytocompounds were identified using GC-MS. Among 27 phytochemicals, major phytocompounds viz. α-Terpinyl acetate, Trans-caryophyllene, Nerolidol, α-Cadinol, α-Copaene and minor phytocompounds viz. α-Humulene and (-)-Caryphyllene oxide were identified as essential oil by them.

Cancer preventive phytochemicals in fruits and leaves of guava

The carcinogenesis is a matter of great concern worldwide and researchers are showing interest on natural products to prevent cancer. It was also known that common phytochemicals present in the fruits and leaves of guava *P. guava* Linn. led to anti-inflammatory as well as anticarcinogenic properties studied by several researchers (Table 1) are as follows:

Sato et al. [15] stated that phytocompounds viz. Ascorbic acid, Apigenin and Lycopene in the fruits of guava (*P. guava* Linn.) have potent anticarcinogenic effect while phytochemicals such as Gallic acid, Catechin, Epicatechin, Quercetin and Rutin in the leaves of guava observed to prevent breast cancer. They also reported guava fruit extract have ability to prevent cell proliferation of cancer cell lines during *in vitro* study. Nevertheless, Ascorbic acid of guava fruits also showed antioxidative properties.

Kim [20] revealed that phytocompound Kaempferol of guava (*P. guava* Linn.) leaves has potent anticarcinogenic and antiproliferative properties on thyroid cancer cell lines. It was also reported that leaves of guava increased the rate of free radical scavenging activities supported antioxidant properties.

Ryu et al. [22] investigated different phytochemicals such as β-Eudesmol, α-Copaene, Phytol, α-Patchoulene, β-Caryophyllene oxide, Caryophylla-3(15), 7(14)-dien-6-ol, (*E*)-Methyl isoeugenol, α-Terpineol, Hexadecane and Octadecane in the leaves of guava (*P. guava* Linn.) after n-hexane fraction. They observed that guava leaf hexane fraction (GHF) was the prominent inducer of cytotoxic and apoptotic effects in PC-3 (prostrate-cancer) cells. These mechanisms of GHF apoptotic potential were correlated with the suppression of AKT (protein kinase)/mTOR (mammalian target of rapamycin)/S6K1 (Ribosomal protein S6 kinase beta-1) and MAPK (Mitogen-activated protein kinases) signalling pathways. The GHF showed a correlation with down-regulation of several above-mentioned proteins, which remediate cell proliferation, cell survival, metastasis, and angiogenesis.

Bontempo et al. [21] investigated that the fruits of the guava *P. guajava* Linn. extract has potential for cancer prevention on both haematological and solid neoplasias. It has also observed that the extract of fruits reduced the tumour formation due to induction of apoptosis and differentiation. The *ex vivo* myeloid leukaemia blasts revealed that fruits were able to induce cell death but did not exhibit anti-cancer effects on all malignant cells investigated, indicating selective activity against specific tumour. According to them, active antineoplastic phytocompounds of the fruits involved Ursolic acid, Oleanolic acid, Arjunolic acid, Glucuronic acid, Oleandolic acid, Morin3-O-a-L-lyxopyranoside, Morin-3-O-a-Larabinopyranoside, Pentane-2-thiol, Guaijavarin and Quercetin respectively.

El-Ahmady et al. [23] determined the dominant phytocompounds were β-Caryophyllene and Limonene in the *P. guajava* Linn. as fruit oil and β-Caryophyllene and Selin-7(11)-en-4α-ol as leaf oil. It was observed both essential oils have the ability to prevent free radical generating activities and effective for antioxidant activities. This antioxidative ability may prevent the cancer and inflammation.

Chen et al. [14] evaluated antioxidant and the antiproliferative abilities of guava fruit (peel and flesh) on four cancer cell lines such as human lung cancer cells (A549), human breast cancer cells (MCF-7), human hepatoma cells (HepG2) and human colon cancer cells (HT-29) through the MTT assay. The phytocompounds viz. Catechin, Galangin, Homogentisic acid, Gallic acid, Kaempferol and Cyanidin 3-glucoside were reported suitable for antioxidant, antiproliferative and anticancer agents.

Ashraf et al. [28] reported that *P. guajava* Linn. contained several phytochemicals in the leaves and observed anti-inflammatory and modulation of the NF-kB activation. The activation of NF-kB-regulated genes were associated with cellular transformation, proliferation, angiogensis, invasion, tumour cell survival and metastasis. Although, these phytochemicals have also potent anticarcinogenic properties.

Table 1. Anti-carcinogenic properties of phytochemicals in leaf and fruit of guava

Sl. No.	Leaves or Fruits	Bioactive compounds	Preventive properties	References
1.	Fruits	Ascorbic acid, Apigenin and Lycopene	Anticarcinogenic, antiproliferative and antioxidative	Sato et al., [15]
2.	Leaves	Gallic acid, Catechin, Epicatechin, Quercetin and Rutin	Anti-breast cancer	Sato et al., [15]
2.	Leaves	Kaempferol	Anticarcinogenic, antiproliferative and antioxidative	Kim, [20]
3.	Leaves	β-Eudesmol, α-Copaene, Phytol, α-Patchoulene, β-Caryophyllene oxide, Caryophylla-3(15), 7(14)-dien-6-ol, (*E*)-Methyl isoeugenol, α-Terpineol, Hexadecane and Octadecane	Anticarcinogenic and antitumorigenic	Ryu et al., [22]
4.	Fruits	Ursolic acid, Oleanolic acid, Arjunolic acid, Glucuronic acid, Oleandolic acid, Morin3-O-a-L-lyxopyranoside, morin-3-O-a-Larabinopyranoside, Pentane-2-thiol Guaijavarin and Quercetin	Anticarcinogenic induced apoptosis, antiproliferative, non-malignancy, antineoplastic effect	Bontempo et al., [21]
5.	Fruits	β-Caryophyllene and Limonene	Antiinflammatory and anticarcinogenic	El-Ahmady et al., [23]
6.	Leaves	β-Caryophyllene and Selin-7(11)-en-4α-ol	Antiinflammatory and anticarcinogenic	El-Ahmady et al., [23]
7.	Fruits	Catechin, Galangin, Homogentisic acid, Gallic acid, Kaempferol and Cyanidin 3-glucoside	Antioxidant, antiproliferative and anticarcinogenic	Chen et al., [14]
8.	Leaves	Caryophyllene, vitamin E, α-Copaene, Heneicosane, Pyrogallol, palmitic acid, Caryophyllene oxide, Alloaromadendrene, Sitosterol, α-Bulnesene and Squalene	Antiinflammatory, and anticarcinogenic	Ashraf et al., [28]
9.	Fruits	3-Methoxysinensetin, Kaempferol, Kaempferol 3-O-xylosyl-rutinoside, Quercetin, Schottenol ferulate, 3-Methoxysinensetin and Sesamolinol 4'-O-b-D-glucosyl (1->6)-O-b-D-glucoside	Anticarcinogenic and antioxidant	Chiari-Andréo et al., [9]
10.	Fruits	Lycopene	Antioxidative and anticarcinogenic	Kaur et al., [19]
11.	Leaves	Kaempferol	Anticarcinogenic	Kaur et al., [19]
12.	Leaves	Gallic acid, Catechin, Epicatechin, Rutin and Quercetin	Anticarcinogenic and antiproliferative	Bijauliya et al., [24]

Chiari-Andréo et al. [9] reported fruit phytochemicals such as Quercetin, Kaempferol, Schottenol of guava (*P. guajava* Linn.), which had strong antioxidant effect on superoxide dismutase (SOD) enzyme. This antioxidant activity may lead to prevent oxidative stress and possibly cancer.

Kaur et al. [19] reviewed that Lycopene in the fruits of guava (*P. guajava* Linn.) showed powerful antioxidative properties, which helped the body to prevent from the harmful free radicals and increased the generation of free radicals may lead to cancer. According to them, guava fruit is suitable for decreased oxidative damage and prevent cancer. On the other hand, guava leaf phytochemical namely Kaempferol has potent anticarcinogenic properties.

Bijauliya et al.[24] reviewed that aqueous extract of phytochemicals such as Gallic acid, Catechin, Epicatechin, Rutin and Quercetin of leaves of guava (*P. guajava* Linn.) observed anticarcinogenic properties. This extract containing phytochemicals are suitable for antiproliferative and antitumorigenic effect.

CONCLUSIONS

It is concluded from above-mentioned compilation of different research works that phytochemicals or bioactive compounds mainly polyphenols and flavonoids as well as essential oils of guava (*P. guajava* Linn.) fruits and leaves are suitable for antioxidative, antiproliferative, antitumorigenic and anticarcinogenic potential. Moreover, the solvent

extraction is very essential to isolate exact phytochemical and each phytoconstitute can be used as phytomedicine for future drug design in cancer therapy. This present review work was compiled from available literatures with special reference to the process of isolation of phytochemicals by using instruments and experimentation on different cancer cell lines and colorimetric assay with these phytochemicals for cancer therapy as ready references for the academicians, researchers, pharmaceutical industries, etc. Further, it is suggested functional assay and bioavailability along with different pharmacological tests to detect specific cancer treatment by individual phytochemical.

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