ANTICANCER EFFECT OF PSIDIUM GUAJAVA (GUAVA) AND ITS LEAVES

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ABSTRACT

Cancer is a complicated condition brought on by the cumulative effect of numerous genetic mutations. Fruit consumption has been linked to a lower risk of developing a number of cancers, which is primarily due to the phytochemicals they contain. The use of chemo preventive substances and functional foods appears to aid in this process, acting by hormonal, anti-inflammatory, anti-angiogenic, and antioxidant mechanisms. The Psidium guajava has pigments with a high potential for function that play a role in the fight against cancer antioxidant performance. Exposing some chemical compounds from Psidium guajava is the goal of the current review. fractions and their relationship to an anti-carcinogenic effect. The evidence backs up the anticancer theory. Cancer is the top cause of death globally. The most prevalent cancer types reported are cancers of the thyroid, bladder, liver, breast, prostate, leukemia, and blood. Extracts of guajava, which contain a wide variety of polyphenols, exhibit pharmacological traits such as anti-inflammatory and antioxidant actions. The study's sole objective would be to determine the benefits of adopting natural cancer treatments.

Keyword : - *cancer ,Psidium guajava ,antioxidant , polyphenols*

Introduction

One of the top causes of death worldwide is cancer. India has an age-standardized mortality rate (ASMR) for cancer of 63.1 per 100,000, with men making up 65.4 and women 61.0, respectively. This number is around half of the global ASMR for cancer, which is 100.7 per 100,000 people (84.2 for women and 120.8 for males). The numbers make it clear that cancer is a terrible disease that has to be treated right away before it claims more lives. Consequently, through a , Recent research has identified the guava leaves' anticancer properties, toward cancer therapy and prevention. Guava botanical name is Psidium guajava. It is a tree or shrub of the family Myrtaceae. According to the FAO (Food and Agriculture Organization) of the United Nations. There are 2.3 million tons guavas produced worldwide India is the world's top country for the production of guava. The roots, fruits, and leaves of the guava plant have all been traditionally used as medicines, according to recent pharmacological studies, it used to treat gastrointestinal disorders (diarrhoea and stomach pain), diabetes mellitus, hypertension, inflammation astringent and antibacterial. Flavonoids, carotenoids, Essential oils and phenolic chemicals are abundant in guava leaves. Guava's phenolic ingredient helps to treat malignant cells and delay the aging process of the skin

1 Review of literature

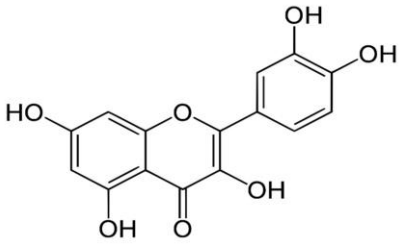
Psidium guajava is a dicotyledonous shrub or small evergreen tree that typically grows 3 to 10 meters high and has numerous branches. The bark is light to reddish brown, thin, smooth, and continuously flaking, and the stems are wavy. The majority of the time, the extensive and superficial root system extends far beyond the canopy. Each has

a few substantial roots but no clear taproot. The opposite, simple leaves have short, 3–10 mm long petioles, an oblong to elliptic blade, prominent veins, and gland-dotted surfaces. Stipules are absent. The flowers are fragrant, with four to six petals and yellow anthers, and they are white with incurved petals that are two or three in number in the leaf axils. When ripe, the fruit is small, pear-shaped, 3 to 6 cm long, and reddish-yellow. The fruit has a fleshy pericarp, a seed cavity filled with pulp, and several small seeds. Dark green, elliptic, and oval in shape, guava leaves are distinguished by their obtuse type apex. The antispasmodic, cough sedative, anti-inflammatory, antidiarrheic, antihypertension, anti-obesity, and antidiabetic effects of guava leaves are also well known.

Fig 1

1.1 CHEMICAL COMPOSITION /PHYTOCHEMISTRY

Guava leaf isolates have been proven to be effective antitumor, anticancer, and cytotoxic drugs in studies using animal models. Quercetin and other bioactive polyphenolic chemicals, as well as ferulic, caffeic, and gallic acids, are present in guava leaves, and these components largely define the bioactive and therapeutic qualities of the leaves. These phenolic substances, sometimes referred to as secondary metabolites, have potent antioxidant and immunostimulant properties. Guava leaves are a great source of several macro- and micronutrients that are good for health, as well as bioactive substances. They contain 82.47% moisture, 103 mg ascorbic acid, 3.64% ash, 0.62% fat, 18.53% protein, 12.74% carbs, and 1717 mg gallic acid equivalents (GAE)/g total phenolic component. Phenolic Substances are responsible for the anticancer activity. They contain high-quality bioactive polysaccharides, proteins, lipids, essential oils, vitamins, and minerals, as was discussed in the preceding sections. Guava leaves include phenolic acids, flavonoids, triterpenoids, sesquiterpenes, glycosides, alkaloids, and saponins, among other secondary metabolites. Guava leaves benefit from the antioxidant qualities of phenolic compounds , which are important bioactive components. Generally speaking, these phenolic chemicals are crucial for controlling a variety of physiological and metabolic processes in the human body. Using tandem mass spectrometry with a diode array detector and high-performance liquid chromatography, 72 distinct phenolic compounds from guava leaves have been identified. Significant anticancer activity was demonstrated by guava's dichloromethane leaf extract and its active components, guajadial, psidial A, and psiguadial A and B, in both an effective in vivo tumor growth inhibition as well as in vitro.

Phytochemicals	Structure	Uses
Quercetin		**destroys cancerous cells, substance has the ability to cause the release of apoptosis in colon cancer cells Caco-2 and HT-29 by triggering cytochrome C in the mitochondria. Furthermore, it showed an interactive involvement of the chemotherapy medication cisplatin in by the inactivation of protein kinase C both in vivo and in vitro.**

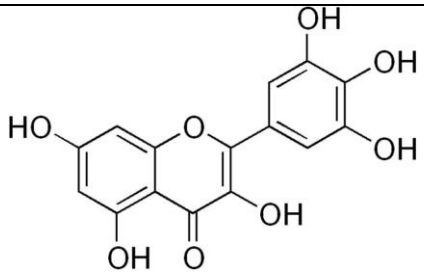
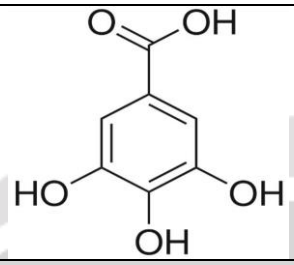
Myricetin		**Anti-Cancer qualities, in preventing brain damage, heart disease, diabetes, and skin cancer. which prevents the growth of cancer cells and promotes cell-protective autophagy as well as in vivo and in vitro apoptosis**
Gallic acid		**diabetes, inflammation, cancer, and as an antioxidant. the anticancer activity of GA is related to the induction of apoptosis**

Table 1

The majority of the substances found in guava leaves include phenolic compounds, lipids, essential oils, gallic acid, catechin, epicatechin, rutin, tannin, saponin, alkaloids, and sesquiterpenes. Flavonoids include morin-3-O-glycoside, morin-3-O-arabinoside, quercetin, and quercetin-3-O arabinoside. A number of terpenoid chemicals have recently been identified and analyzed from guava leaf extract. Certain meroterpenoids among the identified compounds exhibited antifungal and anticancer properties. The volatile composition of guava leaves varies depending on the locale; for instance, Chinese guava leaves contain β-caryophyllene, copaen, azulene, eucalyptol, etc. [12].β caryophyllene, β-elemene, β-selinol, and α-humine are found in Brazilian guavas [13], while trans-nerolidol, globulol, and D-limonene are found in Egyptian guavas [14]. Indian guava has been found to contain caryophyllene, limonene, caryophyllene oxide, and other compounds recently [15]. Generally speaking, terpenoids with antibacterial and anticancer properties include limonene, β-caryophyllene, 1,8-cineole, β-elemene, and others [16,17].

1.2 Antioxidant compound

Secondary plant metabolites with specific polyphenols, particularly in the leaves of the guava, may have inherent antioxidant, anti-inflammatory, and antiviral effects. Ascorbic acid (vitamin C), flavonoids (apigenin), and lycopene are the most often mentioned guava components that have been proposed to have anticancer effects in vitro. Guavas contain phenolic chemicals, particularly flavonoids, which are potent antioxidants and play a significant role in reducing the action of free radicals in the body. Flavonoids significantly reduce the risk of oxidative cell damage. As a result, they can help prevent cancer and premature skin ageing. Phenolic compounds' health promoting abilities are mostly based on their antioxidant activity, particularly as free radical scavengers and metal chelators that can catalyze the peroxidation of lipids. It has been proven that polyphenols, including flavonoids and vitamin C, can mitigate the toxicity, mutagenicity, and carcinogenicity of a variety of substances. Thenmozhi and Rajan. (2015) Determining the quantity of bioactive substances in an ethanolic extract of leaves is important step. In comparison to the aqueous extract, ethanolic extract has higher quantities of phenol (9.33 mg/g), tannin (4.30 mg/g), flavonoids (6.42 mg/g), and saponin (3.67 mg/g). The study's findings showed that the ethanolic extraction included more phytochemicals than the aqueous extract did. Psidium guava leaves contain five chemical components, including one new one, according to Begum et al. (2004). Pentacyclic triterpenoid guajanoic acid, -sitosterol, uvaol, oleanolic acid, and ursolic acid have all been found. The total phenolic content of ethanol guava leaf extracts was higher than that of water guava leaf extracts, according to Qian and Nihorimbere (2004). The same findings from the investigations by Chiari et al. (2012) and Thenmozhi and Rajan (2015) demonstrated that ethanol guava leaf extraction (GLE) had better radical-scavenging activity than water GLE due to the larger level of phenolic content. Additionally, according to Mailoa et al. (2013), ethanol is superior to acetone as a solvent for removing tannin from guava leaves since it extracts more tannin. produced 2.351 mg/g of tannin as a result. Psidium guajava leaves were extracted qualitatively using ethanolic and aqueous methods, revealing the presence of tannin, phlobatannins, saponin, flavonoids, steroids, terpenoids, triterpenoids, carbohydrate, polyphenol, and glycoside in both extracts.

2. Possible Anticancer Guava Components

The leaves of the guava, in particular, contain secondary plant compounds that may have intrinsic antioxidant, anti-inflammatory, and antiviral activities. Ascorbic acid (vitamin C), flavonoids (apigenin), and lycopene are the most often mentioned guava components that have been proposed to have anticancer effects in vitro. There are a lot more probable compounds in guava plant components (leaves, fruits, bark, etc.) that may have potential anticancer activity, yet just these three are currently briefly mentioned.

2.1 Ascorbic Acid

Vitamin C in its purest form and enough vitamin A are found in guavas. Guava's high ascorbic acid content and/or other ingredients may be the cause of its high antioxidant activity. ascorbic acid could support the formation of hydrogen peroxide in cancer cells leading to oxidative stress and cell death.

2.2 Flavonoids: Apigenin

Plant flavonoids are also recognized for their anticancer action, primarily via immune function modulation, inhibition of tumour cell attachment, signalling, and suppression of angiogenesis in tumours and cellular proliferation. One of the most prevalent flavonoids, apigenin, is a well-known antioxidant found in a variety of fruits and vegetables. The therapeutic potential of polyphenolic chemicals called flavonoids and their derivatives as anticancer medications has been studied. Guava leaves contain apigenin, which by itself inhibits cell proliferation in a variety of cancer cell lines and has also been shown to exhibit beneficial effects by researchers doing in vivo experiments. (Wang et al. 2004). For example, A combination of p53 and ras mutations (cancer cell mutations) were present in three human colon carcinoma cell lines, so Wang et al. (2000) examined apigenin's antiproliferation activity against these cell lines. Apigenin administration led to a dose-dependent decrease in cell number and cellular protein content in human colon cancer cell lines SW480, HT-29, and Caco-2 when compared to untreated control cultures. They suggested that apigenin appeared to be cytostatic rather than cytotoxic in its reduction of cell proliferation. It might be possible to stop the development or spread of cancer by adding extrinsic cell cycle regulators to the body's existing cell cycle machinery. In human colon carcinoma cell lines, apigenin has also been demonstrated to block the cell cycle in the G2/M stage. Additionally, KB cell line P388 of human mouth epidermal carcinoma is significantly inhibited from proliferating when exposed to guava leaf oil. Guava's leaf extracts have antitumoral properties, which on a molecular level may be explained by the inhibition of the NFkB pathway. A transcription factor called NF-B controls the expression of genes involved in important biological processes like apoptosis, development, and immune/inflammatory responses. Guava leaf or bark's antiproliferative effects could also be brought on by decreasing the levels of chemokines like interleukin-8 and eosinophil cationic as a result protein. This would only be applicable in vivo, where immune cells can react to chemotactic proteins. Wang et al. (2004) It was suggested that apigenin-related flavonoids in food "may cooperatively protect against colorectal cancer through concurrent blocking of cell cycle progression." Testing against human cells used seven apigenin analogues. colon cancer cells SW480 and Caco-2 were compared for cell cycle, cell number, and viability. There were seven apigenin analogues tested; five of them (acacetin, chrysin, luteolin, (Quercetin, Kaempferol) were able to stop the cell cycle at the G2/M phase. The Certain dietary flavonoids related to apigenin may provide protection, according to research. through simultaneous blocking of cell-cycle progression against colorectal cancer. four human pancreatic cancer cell lines—AsPC-1 (human Caucasian adenocarcinoma), CD18 (human pancreatic cancer), MIA PaCa2 (human Caucasian pancreatic carcinoma), and S2-013 (human pancreatic cancer)—reported that apigenin inhibited pancreatic cancer cell growth. Both time- and dose-dependent apigenin in vitro tests showed inhibition of DNA synthesis and cell proliferation in these cell lines. According to Ujiki et al., "Apigenin may be a useful drug for the treatment or prevention of pancreatic cancer" because due to the inhibition of G2/M arrest and cyclin B-associated cdc2 activity, it slows the development of pancreatic cancer cells. Although Wang and colleagues (2007) did not investigate the proliferation of cancer cell lines, they did investigate the potential antioxidant properties of guava leaves. The extracts from distilled water, 65% ethanol, and 95% ethanol revealed a 50% effective concentration (EC50) on scavenging hydroxyl radicals of 0.63, 0.47, and 0.58 g/L, respectively, to test the antioxidative activity of flavonoids. These extracts had respective flavonoid contents of 3.28, 30.71, and 55.98 g/kg leaves. These researchers came to the conclusion that flavonoids might be one of the antioxidant components in guava leaves even though the EC50 was not dose dependent when compared to the flavonoid content.

2.3 Lycopene

Another potential guava component that may have anticancer properties is lycopene. The carotenoid lycopene, which is naturally found in guava juice, may offer cancer protection by limiting free radical damage. When it comes to oxygen and free radicals, lycopene is very reactive. Additionally, it has antimetastatic activity and has been linked to the apoptosis and antiproliferation of some cancer cells. High-performance liquid chromatography was used by Chandrika et al. (2008) to measure the carotenoid content of watermelon and guava, despite the fact that guava has

high lycopene concentrations. They claimed that watermelon is not the best source of lycopene and that guava (specifically the Horana red variety) is. Higher lycopene intake and have been linked in epidemiological studies that are both prospective and retrospective. According to their findings, lycopene promotes "anti-metastatic activity, apoptosis and antiproliferation in cancer cells, as well as the upregulation of the antioxidant response." Because oral lycopene accumulates in and is localized to the nucleus of prostate epithelial cells, according to in vivo research, it may lower the risk of prostate cancer. anti-Cancer effects - P. guajava extract was effective in controlling both solid and hematological neoplasia's. The induction of apoptosis and differentiation was found to be closely related to the antitumor actions of P. guajava extract . A substantial antioxidant concentration in guava may have contributed to its anti-cancer capabilities, according to nearly half of the studies .

2.4 Quercetin

It is possible to separate quercetin, quercetin-3-O-glucopyranoside, and morin from leaves. These substances exhibit antioxidant properties. Quercetin exhibits antioxidant properties. It has a substantially higher reducing power than all additional substances. It's regarded as the most dynamic and strong antioxidant found in guava leaves

3 Guava leaves exert their anticancer effect by

Guava leaves inhibit multiple signalling pathways in cancer cells in order to have their anticancer effects. They have the ability to stop cancer cells from growing and to encourage apoptosis, which kills the cells. Research has demonstrated that the anticancer properties of guava leaves are achieved through the modulation of intracellular signalling pathways involved in cell growth and proliferation

4 In vitro anticancer studies

In human mouth epidermal carcinoma (KB) cells, guava leaf oil demonstrated the most anti-proliferative effect, according to a study by Manosroi et al. With an IC50 value of 0.0379 mg/ml, 4.37 times more potent than vincristine. Myricetin and apigenin are the primary flavonoids found in guavas; according to Manosroi et al. (2006), myricetin is a strong anticarcinogen, an excellent antioxidant, and an antimutagen.

4.1 In vitro anticancer studies of guava fruit

According to research, guavas' strong antioxidant content may prevent malignancies that are brought on by free radical and oxidative damage to DNA and other cell components. Based on the edible portion (wet weight), Leong and Shui (2002) determined the antioxidant capacity (AEAC, ascorbic acid equivalent antioxidant capacity) of a few fruits. The maximum antioxidant capacity was observed in ciku, a tropical fruit also known as sapodilla (3396 mg/100 g), which was followed by strawberry (472 mg/100 g), plum (312 mg/100 g), and starfruit (278 mg/100 g), guava (270 mg/100 g), grape seedless (264 mg/100 g). The peel, shell, and pulp of fresh guava fruit were tested for total polyphenol content and antioxidant capacity by Marquina and colleagues (2008). Additionally, processed guava pulp and jam were examined. The guava peel had the highest phenolic content (10 times more antioxidant capacity than pulp), while the jam had the lowest phenolic concentration. Based on the components of guava and possible bio actives with anti-cancer properties found in the fruit, leaves, and bark, numerous studies have been conducted on the fruit. Studies on the anti-proliferative properties of guava leaf extract are scarce, nevertheless. Only seven research, according to Sato et al., were connected to the anti-proliferative activity on cancer cell line by employing extract from guava leaves. This study tested the anti-proliferative effect of guava leaf extract in petroleum ether, methanol, and water on three different forms of cancer. cell lines from human cervical cancer patients, osteosarcoma and breast cancer cells. Regarding human cervical cancer cells, none of the three varieties of guava leaf extract had any anti-proliferative effects. Out of the three extracts, methanol extract and petroleum ether extract had the most anti-proliferative effects on osteosarcoma and breast cancer cell lines. Nevertheless, the non-malignant cell Madine Darby canine kidney (MDCK) is cytotoxically affected by these extracts. It is likely that the cytotoxic effect of the guava methanol and petroleum ether extract accompanied its anti-cancer properties. Therefore, it is necessary to test for other non-malignant cells in order to screen for any adverse effects on normal cells. Ampasavate et al.'s results demonstrated that PG leaf ethanolic extracts have no cytotoxic effects on four leukemic cell lines, promyeloid (HL60), erythroid (K562), both lymphoblastic (Molt4) and monocytic (U937), as well as the human mononuclear cells from peripheral blood (PBMCs). PBMC is also used in cytotoxicity tests to evaluate how anti-proliferative activity affects normal cells. Furthermore, research indicates that guava leaves are a potentially effective anti-cancer agent. Among the extracts tested, petroleum ether extract exhibited the strongest anti-proliferative effect on human breast cancer and osteosarcoma cancer cells. Because petroleum ether extract has a cytotoxic effect in addition to its anti proliferative activity, it is necessary to evaluate this effect in order to determine whether guava is safe for ingestion by humans. Gaining more insight into their molecular mechanism may help in the development of anti-cancer drugs.

According to Nurcahyo Iman Prakoso*, Mila Tria Nita [30] Maceration and fractionation techniques were successfully used to manufacture the chemo preventive agent from guava leaves. Screenings with phytochemicals have shown that the terpenoids and flavonoids were present in the n hexane fraction. The ethyl acetate fraction included tannins/polyphenols and flavonoids. and ethanol fraction included terpenoids, flavonoids, tannins/polyphenols. Considering the MTT test, it was discovered that the portion of n-hexane had a high activity. and specificity for cancer cells using the IC50 values for MCF-7, T47D, and the selectivity of HeLa is 8.92, 4.28, and 85.98, respectively. value was more than 10, which was considered to indicate strong selectivity. In a cell line model, an aqueous extract of P. guajava budding leaves has demonstrated anti-prostate cancer action. It has been demonstrated that guava leaf essential oil has a cytotoxic effect on human cervical cancer cell lines.[31] investigated the possibility of maintaining its bioactivity with or without synthetic androgen R1881. It was demonstrated that guava extract inhibited the proliferation of LNCaP cells in both instances and down-regulated the expressions of the prostate specific antigen (PSA) and androgen receptor (AR). PE's cytotoxicity was demonstrated in LNCaP cells by increased LDH release. After being treated with guava extract for 48 hours in a dose responsive manner, the flow cytometry analysis showed cell cycle arrests in G(0)/G(1) phase with a significant number of apoptotic LNCaP cells, which was further validated by the TUNEL assay. The results of phospho-Erk1/phospho-Erk2, phospho-Akt, phosphor-p38, and a lowered Bcl-2/Bax ratio were used to determine the molecular mechanism by which PE causes apoptosis in LNCaP cells. in harmony with the in vitro The results of phospho-Erk1/phospho-Erk2, phospho-Akt, phosphor-p38, and a lowered Bcl-2/Bax ratio were used to determine the molecular mechanism by which PE causes apoptosis in LNCaP cells. In a xenograft mouse tumor model, treatment with guava extract (1.5 mg/mouse/day) significantly reduced both the tumor growth and PSA serum levels, which is consistent with the results of the in vitro investigation. In summary, guava extract exhibits great potential as an anti-androgen-sensitive treatment for prostate cancer.[32] Oxidative stress is the result of producing more free radicals than a cell can neutralize. This can lead to damage to essential components of the cell, including proteins, lipids, carbohydrates, and DNA. Numerous investigations have documented notable modifications in the antioxidant enzyme systems of plasma, such as lipid peroxidation and superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). According to numerous reports, Psidium guajava (PG) exerts an antioxidant effect via restoring enzymatic antioxidants and inhibiting Nuclear Factor-kappa B (NF-kB) activation. According to studies, guava fruits with red pulp flesh had a high concentration of phenolic compounds and a significant number of carotenoids, particularly lycopene. These substances were primarily in charge of the antioxidant activity. Phenolic phytochemicals found in Psidium guajava reduce peroxidation reactions in living things, preventing diabetes, cancer, and heart disease, among other chronic illnesses. Its phenolic components, which include gallic acid, caffeic acid, ascorbic acid, quercetin, guavin, and protocatechunic acid, are linked to these antioxidant qualities. Natural antioxidants may be found in guava leaf extracts and fruits. Research revealed that in the technetium-99 assay, guava fruit also exhibited antioxidant, collagen forming, and radioprotective properties.[34] Numerous research investigations have demonstrated the anti-proliferative properties of 17 Thai medicinal plants belonging to the Psidium guajava family against human oral epidermal carcinoma and murine leukemia cells. Subsequent research revealed that HT-29 cells were cytotoxically affected by guava (Psidium guajava L.) branch (GBA) acetone extracts. By using the MTT reduction assay, LDH release assay, and colony formation assay, the GBA demonstrated extremely cytotoxic effects. At 250 µg/ml, the extract inhibited the proliferation of HT-29 cells. In HT-29 cells, branch extract exhibited distinct apoptotic effects, such as chromatin condensation and sharking. It causes HT-29 cells to become more cytotoxic and enter the sub-G1 phase . Research revealed that Psidium guajava budding leaves contain enormous concentrations of soluble polyphenolics (SP), including gallic acid (measured in milligrams per gramme(348), epicatechin (60), rutin (100), catechin (102), rutin (100), quercetin (102) and to show strong antitumor efficaciousness 63. It might be applied as a Considering anti-tumor chemoprevention, anti-migration and angiogenesis suggested that the For DU145 cells, Psidium guajava's IC50 was 0.57. mg ml–1.[34] According to Yaneenart Suwanwong a, Somchai Boonpangrak,the antioxidant activity of guava fruit extracts was found to be associated with the number of phytochemicals present, according to the findings. Additionally, they had a noteworthy cytotoxic impact on leukemia cells (U937). Compared to the pulp extract, the guava fruit peel extract showed higher levels of phytochemicals and antioxidant and anticancer properties. Kimju guava cultivar exhibited the highest antioxidant activity, while Paen Saidang guava cultivar demonstrated the highest anticancer activity. The current study's findings indicate that the presence of several phytochemicals in Thai guava fruits may confer potential antioxidant and anticancer activities. [35]

5 ANTICANCER ACTIVITY

Cancer is a multifaceted medical condition characterized by either increased or decreased cell proliferation, which leads to apoptosis. Numerous endogenous and exogenous variables that contribute to the overproduction of reactive oxygen species (ROS) might cause it. Tumor formation, chromosomal breakage and reorganization, DNA cross-

linkage, nucleic acid degradation, lipid peroxidation-induced damage to cell membrane integrity, and single- or double-strand breaks in DNA or RNA are possible outcomes of this. Triterpenoids, sesquiterpenes, tannins, psiguadials, volatile oils, flavonoids, benzophenone glycosides, and other quinones are all found in good amounts in GLs. Psiguadial C and D both inhibit protein tyrosine phosphatase 1B (PTP1B) and human hepatoma cells (HepG2). GLs contain terpenoids and flavonoids that have anticancer effects through immune system regulation. tumor angiogenesis and cell proliferation are impeded as well as signal transmission and tumor cell adhesion being suppressed. Research indicates that these leaves have a strong inhibitory effect on cancer cell lines such as the breast cancer cell lines MDA MB-231 and Michigan Cancer Foundation-7 (MCF-7), the cervical cancer cell line Henrietta Lacks (HeLa), the nasopharyngeal cancer cell line KB, the prostate cancer cell line LNCaP, DU 145, and prostate cancer-3 (PC-3), and the colon cancer cell line colorectal 320 double minutes (COLO320DM). The process of angiogenesis, in which new blood vessels sprout from pre-existing ones, is primarily responsible for the growth of colorectal tumors. Extended angiogenesis plays a critical role in the development of tumors towards malignancy by effectively supplying oxygen and essential metabolites to the growing tumor cells. It also serves as an effective mechanism for the elimination of cellular waste. An investigation of the anticancer and antiangiogenic properties of GL extracts against colorectal cancer that is dependent on angiogenesis was carried out. Rich in vitamin E, β-caryophyllene, and flavonoids (apigenin), guava leaf extracts showed significant antiproliferative action against human colon cancer cell lines Caco-2, HT-29, and SW480. Because β-caryophyllene interacts with the transcription factor HIF-1α, which controls the biological processes linked to hypoxia, tumor metastasis, and tumor mediated angiogenesis, it has antiangiogenic properties. The antiproliferative and antiestrogenic properties of guajadial, a caryophyllene-based meroterpenoid from GLs, were investigated against human breast cancer cell lines. The authors proposed that guajadial inhibits the cell cycle at the G1 phase, acts on estrogenic receptors to induce apoptosis by preventing DNA synthesis, and all three mechanisms to carry out its anticancer action. A related investigation revealed that three benzophenones, which were extracted from guava leaves and named guavinoside B, guavinoside E, and 3,5-dihydroxy-2,4-dimethyl-1-O-(60 O-galloyl-β-D glucopyranosyl)-benzophenone, suppressed the proliferation of HCT116 human colon cancer cells. These substances potently promoted apoptosis in cancer cells and altered the expression of important proteins involved in apoptotic signaling and cell proliferation, such as p53, c-Jun NH2-terminal kinases (p-JNK), extracellular signal related kinases (p-ERK1/2), and cleaved caspases 8 and 9. A different study found that guava leaf extracts inhibited genes related to lung cancer, particularly those implicated in signaling pathways like PI3K-Akt. The leaf extract contained progesterone receptor (PGR), peroxisome proliferator-activated receptor gamma (PPARG), daidzein,ursolic acid, apigenin, genistein, and quercetin, which all strongly inhibited cyclin-dependent kinase 2,6 (CDK2,6), vitamin D3 receptor (VDR), hepatocyte growth factor receptor (MET), epidermal growth factor receptor (EGFR), progesterone receptor (PGR), cyclin-dependent kinase 2,6 (CDK2,6), and interleukin 2 (IL-2). These actions prevented tumor angiogenesis, spread, and extracellular matrix degradation.

6. CONCLUSIONS AND FUTURE DIRECTIONS

Psidium guajava extracts made from different plant parts were studied to see how they affected animal models and human cancer cell lines; all of the results demonstrated the plant's possible anticancer properties. Extracts from P. guajava are not known to be poisonous to human cells, which suggests that they may be a good option for future research into safe and reasonably priced treatments for different kinds of cancer in humans. Particularly, it was discovered that the plant's leaves contained a variety of bioactive substances with possible chemo preventive and anticancer properties. In the interim, additional research into the guava fruit's possible anticancer properties needs to be done. Given that the fruit is widely consumed in tropical and subtropical areas, a better knowledge of its potential as a chemo preventive diet can help reduce the incidence of cancer.

Nanotechnology : Examine the novel strategy of applying nanotechnology to enhance the distribution and effectiveness of guava's active ingredients.

Combination Therapies Explore the fascinating field of fusing the active ingredients of guava with currently available treatments to open up new therapy options for the fight against cancer.

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