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Review

Chemical Components and Bioactivities of *Psidium guajava*

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Abstract: *Psidium guajava* commonly known as guava, is one of the economical fruit crops in the Myrtaceae family, grows in tropical and subtropical region. *Psidium guajava* makes a beneficial contribution to the human diet because of their contents in vitamin C, carotenoids and phenolic compounds. Traditionally guava is used for the treatment of various ailments like diarrhoea wounds, rheumatism, lung problems, ulcers etc. The pharmacological studies have demonstrated that this plant possessed antioxidant, hepatoprotective, anti-allergy, antimicrobial, anticancer, antiparasite, antidiabetic, anti-inflammatory and antinociceptive activities, supporting a great therapeutic potential and a wide range of clinical applications. This review summarizes current knowledge about chemical constituents and bioactivities of *Psidium guajava*.

Keywords: *Psidium guajava*; bioactivity; antioxidant activity; antimicrobial activity.

1. Introduction

Psidium guajava commonly known as guava, is belong to the family of Myrtaceae and guagava species. It grows in the tropical and subtropical areas of the world, adapts to different climatic conditions but prefers dry climates. *Psidium guajava* is a fruit, and can be consumed fresh and processed forms, which including beverages, syrup, ice cream and jams (Antonio et al., 2001). It is gaining visibility in the agro-food business due to the attractive characteristics of the fruit, such as flavour, appearance and health properties of nutrients and functional elements. Guava is well accepted by the consumers, and makes a beneficial contribution to the human diet due to rich in minerals and functional components such as vitamins and phenolic compounds (Luiz et al., 2011).

Different parts of the plant have been used extensively in traditional folk medicine. *Psidium guajava* contains a number of active ingredients such as flavonoids, guayavolic acid, guavanoic acid, guajadial, and guajaverin (Gutierrez et al., 2008). Traditionally guava is used for the treatment of various ailments like diarrhoea wounds, rheumatism, lung problems, ulcers etc. It is mainly known for its antispasmodic and antimicrobial properties in the treatment of diarrhoea and dysentery. Meanwhile, guava has also been used as a hypoglycaemic agent. Many studies have demonstrated its biological activities like antidiarrhoeal, antimicrobial, antioxidant, hepatoprotective, anti-allergy, anti-plasmodial, anti-spasmodic, cardioactive, anti-diabetic, anti-inflammatory, anti-nociceptive and antitussive activities (Sanda et al., 2001). This review summarizes the current knowledge about chemical components and bioactivities of *Psidium guajava*.

2. Chemical Components of *Psidium Guajava*

2.1. Chemical Components of Fruit

Psidium guajava is an important medicinal plant. Its fruits show the presence of moisture (77-86%), crude fiber (2.8-5.5%), protein (0.9-1.0%), fat (0.1-0.5%), ash (0.43-0.7%), carbohydrates (9.5-10%), minerals and vitamins. The composition of guava varies significantly with variety, stage of maturity, and season (Mandal et al., 2009).

A water-soluble polysaccharide was isolated from hot aqueous extracts of fruits of *Psidium guajava*. The polysaccharide was found to contain 2-O-methyl-L-arabinose, 2-O-acetyl-D-galactose, and D-methyl galacturonate in a molar ratio of approximately 1:1:1 (Mandal et al., 2009). Pulp and peel fractions of *Psidium guajava* were tested, and both showed high content of dietary fiber (48.55-49.42%) and extractable polyphenols (2.62-7.79%) (Antonio et al., 2001). Guava powder is rich in dietary fibre (43.21%), phenolics (44.04 mg GAE/g) and so on (Verma et al., 2013).

Volatile components in the fruits and leaves of guava plants were isolated by solvent-assisted flavor evaporation and then analyzed by gas chromatography time-of-flight mass spectrometry. In total, 35 components were identified in the guava samples, including 24 terpene hydrocarbons, 2

terpene alcohols, and minor constituents including 1 alcohol, 2 aldehydes, 3 esters, 1 terpene ester and 2 terpene oxides (Chen et al., 2008). Terpene hydrocarbons and C6 compounds were the most abundant components in both the fruits and leaves. Acetic, butyric and hexanoic acids were the predominant acids, trans-2-hexenal and mid hexenal were the predominant aldehydes, and ethyl propanoate, methyl butyrate, ethyl butyrate, methyl hexanoate, ethyl hexanoate, cis-3-hexen-1-yl acetate, hexyl acetate, methyl benzoate, methyl octanoate, ethyl benzoate, phenylpropyl acetate and cinnamyl acetate were also presented, which were responsible for the characteristic guava flavour (Toth-Markus et al., 2005). α-Pinene, β-caryophyllene, α-humulene, β-(Z)-ocimene, and (Z)-3-hexenal were the major components in fruit and leaves. Carbonyls and esters such as 3-hydroxy-2-butanone, 2-heptanone, benzaldehyde, ethyl hexanoate, (Z)-3-hexenyl acetate, hexyl butanoate and ethyl octanoate were only found in the fruit, whereas terpene such as camphene, sabinene, eucalyptol, α-terpinolene, δ-cadinene, and germacrene B were only identified in the leaves (Lee et al., 2011).

Further, guava is rich in vitamin A and a number of carotenoids namely lycopene, α-carotene, β-carotene, zeinoxanthium, 5, 6, 5', 6'-diepoxy-β-carotene and 5, 8-epoxy 3, 3', 4'-trihydroxy β-carotene (Sharma et al., 1999). Lycopene is a principal pigment in this plant. Sixteen carotenoids were isolated from the flesh of Brazilian red guavas, that is, phytofluene, (all-E)-, (9Z)-, (13Z)-, and (15Z)-β-carotene, (all-E)-γ-carotene, (all-E)-, (9Z)-, (13Z)-, and (15Z)- lycopene, (all-E, 3R)-β-cryptoxanthin, (all-E, 3R)-rubixanthin, (all-E, 3S, 5R, 8S)-cryptoflavin, (all-E, 3R, 3'R, 6'R)-lutein, (all-E, 3S, 5R, 6R, 3'S, 5'R, 8'R)-, and (all-E, 3S, 5R, 6R, 3'S, 5'R, 8'S)-neochrome (Mercadante et al., 1999).

2.2. Chemical Components of Seed

The guava-seed flour's chemical compositions were as follow. A lower protein content (9.2±0.1%) and higher fiber content (67±1%) were observed. The moisture content and the mineral residue (ash) were 8.3±0.4% and 0.7±0.8%, respectively. The protein extraction and fractioning sequence of Brazilian guava seeds (*Psidium guajava*) are albumin (2.25±0.09 g/100 g), globulin (6.05±0.07 g/100 g), prolamin (2.49±0.02 g/100 g) and glutelin (44.01±0.02 g/100 g). The percentages of the insoluble residue were appropriately 89 g/100g. Glutelin is the major protein fraction from guava seed (Fontanari et al., 2008). The crude oil extracted from guava seeds showed high levels of unsaturated fatty acids (88.1%), mainly linoleic acid (78.4%). The tocopherol and total phenolic contents in the oil amounted to 29.2 and 92.3 mg/100 g, respectively (Malacrida et al., 2013).

2.3. Chemical Components of Leaves

The budding leaves of *Psidium guajava* contained huge amounts of soluble polyphenolics

including (in mg/g) gallic acid (348), catechin (102), epicatechin (60), rutin (100), quercetin (102), and rutin (100) (Chen et al., 2009). The leaf oil of *Psidium guajava* contained a mixture of sesquiterpene hydrocarbons (54.9%) and oxygenated sesquiterpenes (20.9%) with β-caryophyllene (18.3%) as the principal sesquiterpene hydrocarbon and selin-11-en-4 α-ol (6.9%), α-cadinol (3.6%), (E)-nerolidol (3.2%) as the main oxygenated sesquiterpenes (Adam et al., 2011). A total of 73 compounds were identified, of which 61 by hydrodistillation and 24 by headspace SPME. In the headspace, the major constituents were hexenal (65.9%), γ-butyrolactone (7.60%), (E)-2-hexenal (7.4%), (E, E)-2,4-hexadienal (2.2%), (Z)-3-hexenal (2.0%), (Z)-2-hexenal (1.0%), (Z)-3-hexenyl acetate (1.3%) and phenol (1.6%), while β-caryophyllene (24.1%), nerolidol (17.3%), 3-phenylpropyl acetate (5.3%) and caryophyllene oxide (5.1%) were the major volatile constituents present in the hydrodistilled oil (Paniandy et al., 2000). Analysis of guava leaf hexane fraction by gas chromatography and gas chromatography-mass spectrometry tentatively identified 60 compounds, such as β-eudesmol (11.98%), α-copaene (7.97%), phytol (7.95%), α-patchoulene (3.76%), β-caryophyllene oxide (3.63%), caryophylla-3(15), 7(14)-dien-6-ol (2.68%), (E)-methyl isoeugenol (1.90%), α-terpineol (1.76%), and octadecane (1.23%) (Ryu et al., 2012). *Psidium guajava* leaves were subjected to extraction, fractionation and isolation of the flavonoidal compounds. Five flavonoidal compounds were isolated, which are quercetin, quercetin-3-O-α-L-arabinofuranoside, quercetin-3-O-β-D-arabinopyranoside, quercetin-3-O-β-D-glucoside and quercetin-3-O-β-D-galactoside (Metwally et al., 2010). Four new triterpenoids along with 13 known ones were isolated from the leaves of *Psidium guajava*. The structures of new compounds were identified as 2α, 3β-dihydroxy-taraxer-20-en-28-oic acid, 2α, 3β, 12α, 13β-tetrahydroxy-urs-28-oic acid, 2α, 3β, 12β, 13β-tetrahydroxy-urs-28-oic acid, and 2α, 3β, 12β, 13α-tetrahydroxy-urs-28-oic acid, respectively, on the basis of comprehensive spectroscopic methods and molecular modeling calculation (Shao et al., 2012).

3. Bioactivities of *Psidium Guajava*

3.1. Antioxidant and Free Radical Scavenging Activities

Antioxidants are substances that can prevent or delay oxidative damage of lipids, proteins and nucleic acids by reactive oxygen species, which include reactive free radicals such as superoxide, hydroxyl, peroxyl, alkoxyl and non-radicals such as hydrogen peroxide and hypochlorous. They scavenge radicals by inhibiting initiation and breaking chain propagation or suppressing formation of free radicals by binding to the metal ions, reducing hydrogen peroxide, and quenching superoxide and singlet oxygen (Lim et al., 2007). *Psidium guajava* fruit has gained attention for its antioxidant potential. The antioxidant potential of guava fruit extracts has been assessed by means of different *in*

vitro antioxidant assays (ABTS, DPPH and FRAP) (Martinez et al., 2012).

The extracts of branch and leaf showed relatively higher antioxidant properties than those of fruits and seeds (You et al., 2011). The guava seed oil exhibited a great DPPH• scavenging activity and antiradical efficiency (Malacrida et al., 2013). Guava leaves essential oil showed a concentration-dependent free radical scavenging activity by inhibiting the DPPH radicals but served as a moderate antioxidant with IC_{50} value of 460.37 ± 1.33 μg/mL. It also possess moderate inhibition of oxidation of β-carotene with percentage of inhibition value of 81.67±1.48% in β-carotene bleaching assay (Lee et al., 2012). The chromatogram data indicated that guava extracts contained phenolic acids, such as ferulic acid, which appeared to be responsible for their antioxidant activity. Correlation analysis indicated that there was a linear relationship between antioxidant potency, free radical scavenging ability and the content of phenolic compounds of guava leaf extracts (Chen et al., 2007).

Psidium guajava fruit peel aqueous extract has the ability to reduce the oxidative stress of pancreas in streptozotocin-induced (45 mg/kg) diabetic rats. The result showed that aqueous extract of *Psidium guajava* fruit peel supplementation can lower malondialdehyde (MDA) and protein carbonyl level and the activity of superoxide dismutase (SOD) and glutathione (GSH) level was higher (Budin et al., 2013). Besides, the antihyperglycemic effect of guava is also associated with its antioxidative activity (Huang et al., 2011). Pink guava puree supplementation can decrease lipid peroxidation and increase antioxidant enzyme activity such as catalase, superoxide dismutase, glutathione peroxidase and glutathione reductase in spontaneous hypertensive rat's blood (Nor and Yatim, 2011).

3.2. Antibacterial Activity

The antibacterial activity of guava extracts against 21 strains of foodborne pathogens were determined-*Listeria monocytogenes* (five strains), *Staphylococcus aureus* (four strains), *Escherichia coli* O157:H7 (six strains), *Salmonella Enteritidis* (four strains), *Vibrio parahaemolyticus*, and *Bacillus cereus*, and five food spoilage bacteria: *Pseudomonas aeroginosa*, *P. putida*, *Alcaligenes faecalis*, and *Aeromonas hydrophila* (two strains) (Hoque et al., 2007). In another study, four antibacterial flavonoids (morin-3-O-lyxoside, morin-3-O-arabinoside, quercetin, and quercetin-3-O-arabinoside) were isolated from *Psidium guajava* leaves (Rattana and Phumk, 2010). In addition, the extract from leaves of *Psidium guajava* showed higher antimicrobial activity against Gram-positive bacterial and fungal strains (Nair et al., 2007).

Aqueous extracts of *Psidium guajava* was more potent in inhibiting the growth of pathogenic *Proteus mirabilis*, *Streptococcus pyogenes*, *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* than the organic extracts and can be used for the formulation of oral antibacterial drugs to manage surgical, skin and soft tissue infections (Abubakar et al., 2009). Methanolic extract of guava

leaf at minimum bactericidal concentration inhibited the growth of multidrug resistant strain (MDR) by 80%. Time-kill assay revealed that methanolic extract (4 mg/mL) killed MDR bacteria within 10 h (Anas et al., 2008). The peptide Pg-AMP1 was isolated from guava seeds and purified using a red-sepharose Cl-6B affinity column followed by a reversed-phase HPLC (Vydac C18-TP), leading to a clear growth reduction in *Klebsiella* sp. and *Proteus* sp., which are the principal pathogens involved in urinary and gastro-intestinal hospital infections. Pg-AMP1 showed potential to contribute to development of novel antibiotics from natural sources (Pelegrini et al., 2008). Because of the highest antibacterial and antifungal activities of guava leaf extracts, it can be likely natural germicides to prolong vase life of cut flowers (Rahman et al., 2012) and has the potential to control fish diseases caused by *A. hydrophila* (Pachanawan et al., 2008).

The aqueous extracts of *Psidium guajava* exhibited antimicrobial activities with MIC values in the range of 2.61 to 4.69 mg/mL and toxicity values (LC_{50} and EC_{50}) well above its toxic concentrations. *Psidium guajava* extracts containing 11.5 ppm fluoride, showed positive anti-adherence activity and reduced the cell-surface hydrophobicity of the bacteria which might have rendered them less adherent and hence, minimising their adhesion to the tooth surface during the early stage of plaque development. Extracts of *Psidium guajava* may work by first preventing and reducing the adhesion of primary bacterial colonisers to the tooth surface and second, to prevent or inhibit the growth and proliferation of microorganisms adhering on to the tooth surface and may potentiate their antiplaque activities (Fathilah, 2011).

3.3. Anti-diarrhoeal Activity

The extracts of *Psidium guajava* leaf were tested against diarrhea-causing bacteria: *Staphylococcus aureus*, *Salmonella* spp. and *Echerichia coli*. The methanol extract showed the greatest bacterial inhibition. *Staphylococcus aureus* strains were most inhibited by the extracts. Guava leaf extracts and essential oil are very active against *S. aureus* (Goncalves et al., 2008). A hot aqueous extract (decoction) of dried leaves of *Psidium guajava* showed antibacterial activity towards *S. flexneri* and *Vibrio cholerae*. The decoction also inhibited the adherence of *Escherichia coli* and invasion by both enteroinvasive *E. coli* and *Shigella flexneri* to HEp-2 cells. These results indicated that the decoction of *Psidium guajava* leaves was an effective antidiarrhoeal agent (Birdi et al., 2010). Crude aqueous and methanol extracts from leaf and bark of *Psidium guajava* showed strong antibacterial activity against multidrug-resistant *V. cholerae* O1, offered great potential for controlling epidemics of cholera *V. cholerae* O1 (Rahim et al., 2010). A randomized, double-blinded, clinical study on a group of adult patients with acute diarrheic disease also showed that the guava product could decrease the duration of abdominal pain in these patients (Lozoya et al., 2002).

3.4. Antiviral Effects of Psidium guajav against H1N1 Viruses

Guava tea markedly inhibited the growth of A/Narita/1/2009 (amantadine-resistant pandemic 2009 strain) at an IC_{50} of 0.05% and the growth of A/Yamaguchi/20/06 (sensitive strain) and A/Kitakyushu/10/06 (oseltamivir-resistant strain) at similar IC_{50} values ranging from 0.24% to 0.42% in AX4 cells, being 3.4- to 5.4-fold more potent than green tea (IC_{50} values: 0.27% for the 2009 pandemic strain and 0.91% to 1.44% for the seasonal strains). Guava tea showed promise to be efficacious for control of epidemic and pandemic influenza viruses including oseltamivir-resistant strains, and its broad target blockage makes it less likely to lead to emergence of viral resistance (Sriwilaijaroen et al., 2012).

3.5. Antihyperglycemic and Antidiabetes Effects

Hyperglycemia causes increased protein glycation and the formation of early glycation products and advanced glycation end products (AGEs) which are major factors responsible for the complications associated with diabetes. *In vitro* studies had supported the antiglycative potential of guava leaves. The antihyperglycemic efficacy and mechanisms of action of *Psidium guajava* in streptozotocin (STZ)-induced diabetic rats were investigated, and found that oral administration of *Psidium guajava* leaf extract (300 mg/kg body weight/day) for 30 days to streptozotocin-induced diabetes rats significantly decreased the levels of blood glucose, glycosylated hemoglobin and improved the levels of plasma insulin and hemoglobin (Subramanian et al., 2009; Soman et al., 2010). The possible mechanism was that the extracts of *Psidium guajava* leaf may protect pancreatic tissues, including islet β-cells, against lipid peroxidation and DNA strand breaks induced by STZ, and thus reduce the loss of insulin-positive β-cells and insulin secretion, as a result, strength the ability of antihyperglycemic (Huang et al., 2011).

The tannins, polyphenolic compounds, flavonoids, pentacyclic triterpenoids, guiajaverin, quercetin etc. were speculated to account for the observed hypoglycemic effects of the plant's leaf extract (Ojewole, 2005). The aqueous guava leaf extract can enhance glucose uptake in rat clone 9 hepatocytes, which revealed that phenolics are the principal component of the extract, high polarity fractions of the guava leaf extract are enhancers to glucose uptake in rat clone 9 hepatocytes, and quercetin is the major active compound which promotes glucose uptake in liver cells (Cheng, 2009). In addition, normal, mild and severely diabetic rat models had shown hypoglycaemic as well as antidiabetic effect of the unripe guava fruit peel aqueous extract (Rai et al., 2009).

Water-soluble solids showed higher superoxide dismutase-like activity and lipid peroxidation inhibition ability than ethanol-soluble solids *in vitro*, suggesting that anti-peroxidation of lipids is a possible mechanism for guava leaves to retard the progress of type 2 diabetes (Chuang et al., 2008).

Long-term administration of guava leaf extracts increased the plasma insulin level and glucose utilization in diabetic rats. The activities of hepatic hexokinase, phosphofructokinase and glucose-6-phosphate dehydrogenase in diabetic rats fed with aqueous extracts were higher than in the normal diabetic group, which provided evidence to support the antihyperglycemic effect of guava leaf extract and the health function of guava leaves against type 2 diabetes (Oh et al., 2005; Shen et al., 2008). Guava leaf extracts are potent antiglycation agents, which can be of great value in the preventive glycation-associated complications in diabetes (Wu et al., 2009). The extract of guava leaf is an excellent anti-LDL glycative agent whose potential therapeutic uses can be extended to the prevention of a variety of cardiovascular and neurodegenerative diseases associated with glycations (Hsieh et al., 2007). There are also studies supporting that guava fruit could protect kidney against diabetic progression via its anti-oxidative, anti-inflammatory and anti-glycative effects (Lin and Yin, 2012).

3.6. Anti-inflammatory Activity

Psidium guajava leaf extracts can inhibit the main developer of acne lesions: *Propionibacterium acnes* (*P. acnes*). It may be beneficial in treating acne especially when they are known to have anti-inflammatory activities (Qa'dan et al., 2005). *Psidium guajava* ethyl acetate extract inhibited Th2 chemokine expression in keratinocytes by inducing HO-1 expression and suppressing the activation of NF-κ B and STAT1 co-stimulated with TNF-α and INF-γ (Han et al., 2011). *Psidium guajava* water extract (PGW) on 2, 4-dinitrochlorobenzene (DNCB)-induced atopic dermatitis (AD)-like skin lesions in NC/Nga mice. Treatment of cream containing PGW onto DNCB-induced AD-like skin lesions in NC/Nga mice ameliorated lesion intensity scores, levels of IgE, thymus and activation-regulated chemokine (TARC), TNF-α, and IL-4 in serum and ears. These results suggested a possible therapeutic application and adjunctive agent to control pruritus in atopic dermatitis and other inflammatory skin diseases (Choi et al., 2012).

Anti-inflammatory activity of the essential oils from the leaves of *Psidium guajava* was accessed in the lipopolysaccharide-induced pleurisy model by measuring the inhibition of total leukocyte, neutrophil and eosinophil migration in the mice pleural lavage after oil treatment with the oils at 100 mg/kg. Eosinophil migration was inhibited by the essential oils (76%). This efficacy was correlated with the presence of β-pinene and β-caryophyllene in the oils and synergistic effects associated with the presence of α-pinene. It indicated that guava may be useful to treat inflammatory diseases by the mechanisms that include the inhibition of eosinophil migration (Siani et al., 2013).

The tannins, poyphenolic compounds, flavonoids, ellagic acid, triterpenoids, guiajaverin, quercetin, and other chemical compounds present in the *Psidium guajava* are speculated to account for the observed anti-inflammatory and analgesic effects of the plant's leaf extract. The anti-inflammatory

property of the aqueous leaf extract was investigated in rats, using fresh egg albumin-induced pedal (paw) edema, while the analgesic effect of the plant extract was evaluated by the "hot-plate" and "acetic acid" test models of pain in mice. *Psidium guajava* aqueous extract produced dose-dependent in certain range and significant inhibition of fresh egg albumin-induced acute inflammation (oedema) and significant analgesic effects against thermally and chemically induced nociceptive pain in mice (Ojewole, 2006).

3.7. Anti-allergic Effects

The effects of *Psidium guajava* ethyl acetate extract (PGEA) on IgE-mediated allergic responses in rat mast RBL-2H3 cells were investigated. PGEA reduced antigen-induced release of β-hexosaminidase and histamine in IgE-sensitized RBL-2H3 cells. PGEA suppressed antigen-induced phosphorylation of Syk, LAT, Gab2, and PLC γ 2 but not Lyn, and inhibited antigen-induced phosphorylation of downstream signaling intermediates including MAP kinases and Akt. The anti-allergic effects of PGEA *in vitro* suggested its possible therapeutic application to inflammatory allergic diseases, in which its inhibition of inflammatory cytokine production and Fc epsilon RI-dependent signaling events in mast cells (Han et al., 2011).

3.8. Anti-parasite Effects

In vitro anti-parasitic assay was studied using the Vero cells as host for *T. gondii,* guava leaves essential oil showed promising result with EC_{50} of 3.94 ± 0.39 μg/mL, as compared to the standard drug clindamycin (EC_{50} value of 6.24 ± 0.53 μg/mL). The potential therapeutic activity of guava leaves essential oil may have contributed by the *in vitro* inhibition of free radicals associated with toxoplasmosis pathology (Lee et al., 2013).

Ethanolic extracts from the leaves of *Psidium guajava* were evaluated for anti-trypanosoma and cytotoxicity activities in the bloodstream species of *Trypanosoma brucei brucei* (BS427) and HEK293 in 384-well Alamar Blue assays, respectively. The results showed that the extracts inhibited the growth of *T. b. brucei* with an IC_{50} of 6.3 μg/mL and 48.9 μg/mL for 80% and 20% ethanolic preparations respectively, with corresponding activity of less than 50% against HEK293 at the highest screening dose of 238.10 μg/mL. The estimated selectivity index of the extracts compares favourably with reference drugs (pentamidine and diminazene) (Adeyemi et al., 2011). *Psidium guajava* leaf extract has trypanocidal properties which could be attributed in parts to the broad antimicrobial and iron chelating activity of flavonoids and tannins respectively. Iron chelation has been suggested by several reports as an effective way of killing trypanosomes. The prime target was the enzyme, ribonucleotide reductase whose activity was central to DNA synthesis prior to cell division as obtained in

trypanosomiasis infection (Adeyemi et al., 2009). The aqueous extract was able to reduce the trypanosomosis associated lipid peroxidation as well as raise the level of GSH in the infected but treated animals significantly ($P < 0.05$) and lower the MDA concentrations in the treatment group (Akanji et al., 2009).

3.9. Anticancer Activity

The aqueous extract of *Psidium guajava* leaves (PE) bears an extremely high content of polyphenolic and isoflavonoids, it could be used as an anti-tumor chemoprevention in view of anti-angiogenesis and anti-migration. By the means of morphology of cells, cell cycle characteristics and apoptosis and performed immunostaining, differentiation and western blot analyses, the results showed that the *Psidium guajava* extract exerted anti-cancer control on both haematological and solid neoplasias. Guava extract's antitumour properties were found to be tightly bound to induction of apoptosis and differentiation. The using of *ex vivo* myeloid leukaemia blasts corroborated that *Psidium guajava* was able to induce cell death. Analyses of guava pulp, peel and seeds identified the pulp as being the most relevant component for causing cell cycle arrest and apoptosis, whereas peel was responsible for causing cell differentiation. *Psidium guajava* extract was able to exert anti-cancer activity on cultures *in vitro* and *ex vivo*, supporting the hypothesis of its anti-malignant pro-apoptotic modulation (Bontempo et al., 2012). Using the neutral red cytotoxicity assay, the IC_{50} of *Psidium guajava* was determined at 29.0 ± 0.4 μg/mL, indicating the plant extracts equally potent for the treatment of cancerous oral epidermal lesions (Fathilah et al., 2010). In addition, PE effectively inhibited the expressions of VEGF, IL-6 and IL-8 cytokines, and MMP-2 and MMP-9, and simultaneously activated TIMP-2 and suppressed the cell migration and the angiogenesis. Thus it can be used as an effective adjuvant anti-cancer chemopreventive (Peng et al., 2011). Furthermore, *Psidium guajava* extracts are efficacious for the prevention of tumor development by depressing Tr cells and subsequently shifting to Th1 cells (Seo et al., 2005).

The acetone extracts of guava branch (GBA) had cytotoxic effects on HT-29 human colon cancer cells. The GBA showed highly cytotoxic effects via the MTT reduction assay, LDH release assay, and colony formation assay. In particular, the GBA of the 250 μg/mL showed 35.5% inhibition against growth of HT-29 cells. *Psidium guajava* extracts produced significant ($p < 0.05$) cytotoxicity in OV2008 and Kasumi-1 cell lines, the IC_{50} value was 200 μg/mL (Lee et al., 2010). The IC_{50} of PE for DU145 cells was similar to 0.57 mg/mL. Aqueous extract of *Psidium guajava* budding leaves has shown to possess anti-prostate cancer activity in a cell line model. It decreased Bcl-2/Bax ratio, inactivation of phosphor-Akt, activation of phosphor-p38, phospho-Erk1/phospho-Erk2, molecular action mechanism of PE to induce apoptosis in LNCaP cells was elucidated. Compatible with the *in*

vitro study findings, treatment with PE (1.5 mg/mouse/day) significantly diminished both the PSA serum levels and tumor size in a xenograft mouse tumor model. Besides, guava leaf hexane fraction was the most potent inducer of cytotoxic and apoptotic effects in PC-3 cells and inhibited the AKT/mTOR/S6K1 signaling pathway and induced apoptosis in prostate cancer cells (Ryu et al., 2012). Thus, PE is a promising anti-androgen-sensitive prostate cancer agent (Chen et al., 2010).

3.10. Hepatoprotective Effect

In the acute liver damage induced by different hepatotoxins, *Psidium guajava* leaf methanolic and ethyl acetate extracts significantly reduced the elevated serum levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and bilirubin in carbon tetrachloride and paracetamol induced hepatotoxicity. Meanwhile, *Psidium guajava* leaf aqueous extract significantly reduced the elevated serum levels of alkaline phosphatase, alanine aminotransferase and bilirubin in carbon tetrachloride induced hepatotoxicity. Histological examination of the liver tissues supported the hepatoprotection. Thus, the methanolic extract of leaves of *Psidium guajava* plant possesses better hepatoprotective activity compared to other extracts (Roy et al., 2010). Psiguadials A and B, two novel sesquiterpenoid-diphenylmethane meroterpenoids were isolated from the leaves of *Psidium guajava*, which exhibited potent inhibitory effects on the growth of human hepatoma cells (Shao et al., 2010).

3.11. Gastro Protective Effect

The best alternatives to synthetic medicines for the treatment of gastric ulcer disorders are the natural products found in plants. The methanol extracts of the leaves of *Psidium guajava* were tested in three different ulcer models viz. aspirin (ASP), pyloric ligation (PL) and ethanol (EtoH) induced ulcer models in rats. The treatment of *Psidium guajava* at varying doses (100 mg/kg and 200 mg/kg) significantly ($p < 0.001$) inhibited the gastric lesions induced by ASP (70.5%), PL (65.07%) and EtoH (70.4%) respectively and the potency was found to be equivalent as compared to the standard drug, omeprazole. Secretory volume, acid secretion and increased gastric pH in the gastric were reduced. The results suggested that *Psidium guajava* possessed gastro protective as well as ulcer healing properties (Raja et al., 2012).

4. Conclusions and Prospects

Psidium guajava is an important food crop and medicinal plant with immense pharmacological potential, such as antioxidant, anti-inflammatory, anti-allergic, anti-diarrhoeal, gastroenteritis protective, wounds healing, anti-acne, anti-dental plaque, anti-coughs, anti-diabetes, anti-liver diseases, and anticancer activities. Further research, more clinical trials and product development are

needed to make *Psidium guajava* as a more important and significant food and medicine for the public health.

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References

Abubakar, E. M. M. (2009). The use of *Psidium guajava* Linn. in treating wound, skin and soft tissue infections. *Sci. Res. Essays*, **4**: 605-611.

Adam, F., Vahirua-Lechat, I., and Deslandes, E. (2011). Aromatic plants of French Polynesia. V. Chemical composition of essential oils of leaves of *Psidium guajava* L. and *Psidium cattleyanum* Sabine. *J. Essent. Oil Res*., **23**: 98-101.

Adeyemi, O. S., Akanji, M. A., and Oguntoye, S. A. (2009). Ethanolic leaf extract of *Psidium guajava*: Phyto-chemical and trypanocidal activity in rats infected with *Trypanosoma brucei*. *J. Med. Plant Res*., **3**: 420-423.

Adeyemi, O. S., Sykes, M. L., and Akanji, M. A. (2011). Anti-trypanosomal and cytotoxic activity of ethanolic extracts of *Psidium guajava* leaves in Alamar Blue based assays. *Veterinarski Arhiv*, **81**: 623-633.

Akanji, M. A., Adeyemi, O. S., Oguntoye, S. O., and Sulyman, F. (2009). *Psidium guajava* extract reduces trypanosomosis associated lipid peroxidation and raises glutathione concentrations in infected animals. *Excil. J*., **8**: 148-154.

Anas, K., Jayasree, P. R., Vijayakumar, T., and Kumar, P. R. M. (2008). In vitro antibacterial activity of *Psidium guajava* Linn. leaf extract on clinical isolates of multidrug resistant *Staphylococcus aureus*. *India J. Exp. Biol*., **46**: 41-46.

Antonio, J. E., Mariela, R., Raquel, P., and Fulgencio, S. C. (2001). Guava fruit (*Psidium guajava* L.) as a new source of antioxidant dietary fiber. *J. Agric. Food Chem.*, **49**: 5489-5493.

Birdi, T., Daswani, P., Brijesh, S., Tetali, P., Natu, A., and Antia, N. (2010). Newer insights into the mechanism of action of *Psidium guajava* L. leaves in infectious diarrhea. *BMC Complem. Altern. Med*., **10**: Article number 33.

Bontempo, P., Doto, A., and Miceli, M. (2012). *Psidium guajava* L. anti-neoplastic effects: Induction of apoptosis and cell differentiation. *Cell Proliferat*., **45**: 22-31.

Budin, S. B., Ismail, H., and Chong, P. L. (2013). *Psidium guajava* fruit peel extract reduces oxidative

stress of pancreas in streptozotocin-induced diabetic rats. *Sains Malays*., **42**: 707-713.

Chen, H. Y., and Yen, G. C. (2007). Antioxidant activity and free radical-scavenging capacity of extracts from guava (*Psidium guajava* L.) leaves. *Food Chem*., **101**: 686-694.

Chen, H. C., Sheu, M. J., Lin, L. Y., and Wu, C. M. (2008). Volatile constituents of six cultivars of mature guava (*Psidium guajava* L.) fruits from Taiwan. *Acta Horticul.*, **765**: 273-277.

Chen, K. C., Hsieh, C. L., Huang, K. D., Ker, Y. B., Chyau, C. C., and Peng, R. Y. (2009). Anticancer activity of rhamnoallosan against DU-145 cells is kinetically complementary to coexisting polyphenolics in *Psidium guajava* budding leaves. *J. Agric. Food Chem*., **57**: 6114-6122.

Cheng, F. C., Shen, S. C., and Wu, J. S. B. (2009). Effect of guava (*Psidium guajava* L.) leaf extract on glucose uptake in rat hepatocytes. *J. Food Sci*., **74**: H132-H138.

Choi, J. H., Park, B. H., Kim, H. G., Hwang, Y. P., Han, E. H., Jin, S. W., Seo, J. K., Chung, Y. C., and Jeong, H. G. (2012). Inhibitory effect of *Psidium guajava* water extract in the development of 2,4-dinitrochlorobenzene-induced atopic dermatitis in NC/Nga mice. *Food Chem. Toxicol*., **50**: 2923-2929.

Chuang, P. T., Shen, S. C., Wu, N. J., and Wu, J. S. B. (2008b). Anti-peroxidation effect of guava (*Psidium guajava* Linn.) leaf soluble solids in vitro and in streptozotocin/nicotinamide-induced diabetic rats. *J. Sci. Food Agric*., **88**: 2173-2179.

de Lima, R. K., Cardoso, M. D., Andrade, M. A., Nascimento, E. A., de Morais, S. A. L., and Nelson, D. L. (2010). Composition of the essential oil from the leaves of tree domestic varieties and one wild variety of the guava plant (*Psidium guajava* L., Myrtaceae). *Rev. Bras. Farmacogn*., **20**: 41-44.

Fathilah, A. R., Sujata, R., Norhanom, A. W., and Adenan, M. I. (2010). Antiproliferative activity of aqueous extract of *Piper betle* L. and *Psidium guajava* L. on KB and HeLa cell lines. *J. Med. Plant Res*., **4**: 987-990.

Fathilah, A. R. (2011). *Piper betle* L. and *Psidium guajava* L. in oral health maintenance. *J. Med. Plant Res*., **5**: 156-163.

Fontanari, G. G., Souza, G. R., Batistuti, J. P., Neves, V. A., Pastre, I. A., and Fertonani, F. L. (2008). DSC studies on protein isolate of guava seeds *Psidium guajava*. *J. Therm. Anal. Calorim*., **93**: 397-402.

Goncalves, F. A., Neto, M. A., Bezerra, J. N. S., Macrae, A., de Sousa, O. V., Fonteles, A. A., and Vieira, R. H. S. F. (2008). Antibacterial activity of guava, *Psidium guajava* Linnaeus, leaf extracts on diarrhea-causing enteric bacteria isolated from seabob shrimp, *Xiphopenaeus kroyeri* (Heller). *Rev. Inst. Med. Trop. Sp*., **50**: 11-15.

Gutierrez, R. M. P., Mitchell, S., and Solis, R. V. (2008). *Psidium guajava*: A review of its traditional uses, phytochemistry and pharmacology. *J. Ethnopharmcol.*, **117**:1-27.

Han, E. H., Hwang, Y. P., and Kim, H. G. (2011a). Ethyl acetate extract of *Psidium guajava* inhibits

IgE-mediated allergic responses by blocking Fc epsilon RI signaling. *Food. Chem. Toxicol*., **49**: 100-108.

Han, E. H., Hwang, Y. P., Choi, J. H., Yang, J. H., Seo, J. K., Chung, Y. C., and Jeong, H. G. (2011b). *Psidium guajava* extract inhibits thymus and activation-regulated chemokine (TARC/CCL17) production in human keratinocytes by inducing heme oxygenase-1 and blocking NF-kappa B and STAT1 activation. *Environ. Toxicol. Pharm.*, **32**: 136-145.

Hoque, M. D. M., Bari, M. L., Inatsu, Y., Juneja, V. K., and Kawamoto, S. (2007). Antibacterial activity of guava (*Psidium guajava* L.) and neem (*Azadirachta indica* A. Juss.) extracts against foodborne pathogens and spoilage bacteria. *Foodborne Pathog. Dis*., **4**: 481-488.

Hsieh, C. L., Yang, M. H., Chyau, C. C., Chiu, C. H., Wang, H. E., Lin, Y. C., Chiu, W. T., and Peng, R. Y. (2007). Kinetic analysis on the sensitivity of glucose- or glyoxal-induced LDL glycation to the inhibitory effect of *Psidium guajava* extract in a physiomimic system. *Biosystems*, **88**: 92-100.

Hsieh, C. L., and Peng, R. Y. (2010). Action mechanism and signal pathways of *Psidium guajava* L. aqueous extract in killing prostate cancer LNCaP cells. *Nutr. Cancer*, **62**: 260-270.

Huang, C. S., Yin, M. C., and Chiu, L. C. (2011). Antihyperglycemic and antioxidative potential of *Psidium guajava* fruit in streptozotocin-induced diabetic rats. *Food Chem. Toxicol*., **49**: 2189-2195.

Lee, S. B., and Park, H. R. (2010). Anticancer activity of guava (*Psidium guajava* L.) branch extracts against HT-29 human colon cancer cells. *J. Med. Plant Res*., **4**: 891-896.

Lee, S., Km, Y. S., and Choi, H. K. (2011). Determination of the volatile components in the fruits and leaves of guava plants (*Psidium guajava* L.) grown on Jeju island, South Korea. *Carbohyd. Res*., **23**:52-56.

Lee, W. C., Mahmud, R., Pillai, S., Perumal, S., and Ismail, S. (2012). Antioxidant activities of essential oil of *Psidium guajava* L. leaves. *3rd International Conference on Biotechnology and Food Science (ICBFS 2012)*, pp: 86-91.

Lee, W. C., Mahmud, R., Noordin, R., Piaru, S. P., Perumal, S., and Ismail, S. (2013). Free radicals scavenging activity, cytotoxicity and anti-parasitic activity of essential oil of *Psidium guajava* L. leaves against *Toxoplasma gondii*. *J. Essent. Oil Bear. Pl*., **16**: 32-38.

Lim, Y. Y., Lim, T. T., and Tee, J. J. (2007). Antioxidant properties of several tropical fruits: A comparative study. *Food Chem*., **103**: 1003-1008.

Lin, C. Y., and Yin, M. C. (2012). Renal protective effects of extracts from guava fruit (*Psidium guajava* L.) in diabetic mice. *Plant Food Hum. Nutr.*, **67**: 303-308.

Lozoya, X., Reyes-Morales, H., Chavez-Soto, M. A., Martinez-Garcia, M. D., Soto-Gonzalez, Y., and Doubova, S. V. (2002). Intestinal anti-spasmodic effect of a phytodrug of *Psidium guajava* folia in the treatment of acute diarrheic disease. *J. Ethnopharmacol*., **83**: 19-24.

Luiz, C. C., Carlos, A. F., Santos, F, V., and G, P. P. L. (2011). Antioxidant content in guava (*Psidium*

guajava) and araca (*Psidium spp*.) germplasm from different Brazilian regions. *Plant Genetic Resources: Characterization and Utilization*, **9**: 384-391.

Malacrida, C. R., and Jorge, N. (2013). Fatty acids and some antioxidant copounds of *Psidium guajava* seed oil. *Acta Aliment. Hung.*, **42**: 371-378.

Mandal, S., Sarkar, R., Patra, P., Nandan, C. K., Das, D., Bhanja, S. K., Islam, S. S. (2009). Structural studies of a heteropolysaccharide (PS-I) isolated from hot water extract of fruits of *Psidium guajava* (guava). *Carbohyd. Res*., **344**: 1365-1370.

Martinez, R., Torres, P., Meneses, M. A., Figueroa, J. G., Perez-Alvarez, J. A., and Viuda-Martos, M. (2012). Chemical, technological and in vitro antioxidant properties of mango, guava, pineapple and passion fruit dietary fiber concentrate. *Food Chem*., **135**: 1520-1526.

Mercadante, A. Z., Steck, A., and Pfander, H. (1999). Carotenoids from guava (*Psidium guajava* L.): isolation and structure elucidation. *J. Agric. Food Chem.,* **47**: 145-151.

Metwally, A. M., Omar, A. A., and Harraz, F. M. (2010). Phytochemical investigation and antimicrobial activity of Psidium guajava L. leaves. *Pharmacogn. Mag.* **23**: 212-218.

Nair, R., and Chanda, S. (2007). In-vitro antimicrobial activity of *Psidium guajava* L. leaf extracts against clinically important pathogenic microbial strains. *Braz. J. Microbiol*., **38**: 452-458.

Nor, N. M., and Yatim, A. M. (2011). Effects of pink guava (*Psidium guajava*) puree supplementation on antioxidant enzyme activities and organ function of spontaneous hypertensive rat. *Sains. Malays*., **40**: 369-372.

Oh, W. K., Lee, C. H., Lee, M. S., Bae, E. Y., Sohn, C. B., Oh, H., Kim, B. Y., and Ahn, J. S. (2005). Antidiabetic effects of extracts from *Psidium guajava*. *J. Ethnopharmacol*., **96**: 411-415.

Ojewole, J. (2005). Hypoglycemic and hypotensive effects of *Psidium guajava* Linn. (Myrtaceae) leaf aqueous extract. *Method Find Exp. Clin*., **27**: 689-695.

Ojewole, J. A. O. (2006). Antiinflammatory and analgesic effects of *Psidium guajava* Linn. (Myrtaceae) leaf aqueous extract in rats and mice. *Method Find Exp. Clin*., **28**: 441-446.

Pachanawan, A., Phumkhachorn, P., and Rattanachaikunsopon, P. (2008). Potential of *Psidium guajava* supplemented fish diets in controlling aeromonas hydrophila infection in Tilapia (*Oreochromis niloticus*). *J. Biosci. Bioeng*., **106**: 419-424.

Paniandy, J. C., Chane-Ming, J., and Pieribattesti, J. C. (2000). Chemical composition of the essential oil and headspace solid-phase microextraction of the guava fruit (*Psidium guajava* L.). *J. Essent. Oil Res*., **12**: 153-158.

Pelegrini, P. B., Murad, A. M., Silva, L. P., dos Santos, R. C. P., Costa, F. T., Tagliari, P. D., Bloch, C., Noronha, E. F., Miller, R. N. G., and Franco, O. L. (2008). Identification of a novel storage glycine-rich peptide from guava (*Psidium guajava*) seeds with activity against Gram-negative bacteria. *Peptides*, **29**: 1271-1279.

Peng, C. C., Peng, C. H., Chen, K. C., Hsieh, C. L., and Peng, R. Y. (2011). The aqueous soluble polyphenolic fraction of *Psidium guajava* leaves exhibits potent anti-angiogenesis and anti-migration actions on DU145 cells. *Evid-Based. Compl. Alt*., 1-8.

Qa'dan, F., Thewaini, A. J., Ali, D. A., Afifi, R., Elkhawad, A., and Matalka, K. Z. (2005). The antimicrobial activities of *Psidium guajava* and *Juglans regia* leaf extracts to acne-developing organisms. *Am. J. Chin. Med*., **33**: 197-204.

Rahim, N., Gomes, D. J., Watanabe, H., Rahman, S. R., Chomvarin, C., Endtz, H. P., and Alam, M. (2010). Antibacterial activity of *Psidium guajava* leaf and bark against multidrug-resistant vibrio cholerae: Implication for cholera control. *Jap. J. Infect. Dis*., **63**: 271-274.

Rahman, M. M., Ahmad, S. H., and Lgu, K. S. (2012). *Psidium guajava* and *Piper betle* leaf extracts prolong vase life of cut carnation (*Dianthus caryophyllus*) Flowers. *Sci. World. J.*, **5**: 123-128.

Rai, P. K., Jaiswal, D., Mehta, S., and Watal, G. (2009). Anti-hyperglycaemic potential of *Psidium guajava* raw fruit peel. *India J. Med. Res*., **129**: 561-565.

Raja, N. R. L., and Sundar, K. (2012). *Psidium guajava* Linn confers gastro protective effects on rats. *Eur. Rev. Med. Pharmacol*., **16**: 151-156.

Roy, C. K., and Das, A. K. (2010). Comparative evaluation of different extracts of leafs of *Psidium guajava* Linn. for hepatoprotective activity. *Pak. J. Pharm. Sci*., **23**: 15-20.

Ryu, N. H., Park, K. R., Kim, S. M., Yun, H. M., Nam, D., Lee, S. G., Jang, H. J., Ahn, K. S., Kim, S. H., Shim, B. S., Choi, S. H., Mosaddik, A., Cho, S. K., and Ahn, K. S. (2012). A hexane fraction of guava leaves (*Psidium guajava* L.) induces anticancer activity by suppressing AKT/mammalian target of rapamycin/ribosomal p70 S6 kinase in human prostate cancer cells. *J. Med. Food*, **15**: 231-241.

Sanda, K. A., Grema, H. A., Geidam, Y. A., and Bukar-Kolo, Y. M. (2011). Pharmacological aspects of *Psidium guajava*: An update. *Int. J. Pharmacol*., **7**: 316-324.

Seo, N., Ito, T., Wang, N. L., Ya, X. S., Tokura, Y., Furukawa, F., Takigawa, M., and Kitanaka, S. (2005). Anti-allergic *Psidium guajava* extracts exert an antitumor effect by inhibition of T regulatory cells and resultant augmentation of Th1 cells. *Anticancer Res*., **25**: 3763-3770.

Shao, M., Wang, Y., and Liu, Z. (2010). Psiguadials A and B, two novel meroterpenoids with unusual skeletons from the leaves of *Psidium guajava*. *Org. Lett*., **12**: 5040-5043.

Shao, M., Wang, Y., Huang, X. J., Fan, C. L., Zhang, Q. W., Zhang, X. Q., and Ye, W. C. (2012). Four new triterpenoids from the leaves of *Psidium guajava*. *J. Asian Nat. Prod. Res*., **14**: 348-354.

Sharma, S., Rajat, K., Prasad, R., and Vasudevan, P. (1999). Biology and potential of *Psidium guajava*. *J. Sci. Res. India*, **58**: 414-421.

Shen, S. C., Cheng, F. C., and Wu, N. J. (2008). Effect of guava (*Psidium guajava* Linn.) leaf soluble solids on glucose metabolism in type 2 diabetic rats. *Phytother. Res*., **22**: 1458-1464.

Siani, A. C., Souza, M. C., and Henriques, M. G. M. O. (2013). Anti-inflammatory activity of essential oils from *Syzygium cumini* and *Psidium guajava*. *Pharm. Biol*., **51**: 881-887.

Soman, S., Rauf, A. A., Indira, M., and Rajamanickam, C. (2010). Antioxidant and antiglycative potential of ethyl acetate fraction of *Psidium guajava* leaf extract in streptozotocin-induced diabetic rats. *Plant Foods for Hum. Nutr*., **65**: 386-391.

Sriwilaijaroen, N., Fukumoto, S., and Kumagai, K. (2012). Antiviral effects of *Psidium guajava* Linn. (guava) tea on the growth of clinical isolated H1N1 viruses: Its role in viral hemagglutination and neuraminidase inhibition. *Antivir. Res.*, **94**: 139-146.

Toth-Markus, M., Siddiqui, S., Kovacs, E., Roth, E., and Nemeth-Szerdahelyi, E. (2005). Changes in flavour, cell wall degrading enzymes and ultrastructure of guava (*Psidium guajava* L.) during ripening. *Acta. Aliment. Hung*., **34**: 259-266.

Verma, A. K., Rajkumar, V., Banerjee, R., Biswas, S., and Das, A. K., (2013). Guava (*Psidium guajava* L.) powder as an antioxidant dietary fiber in sheep meat nuggets. *Asian Austral. J. Anim*., **26**(6): 886-895.

Wu, J. W., Hsieh, C. L., Wang, H. Y., and Chen, H. Y. (2009). Inhibitory effects of guava (*Psidium guajava* L.) leaf extracts and its active compounds on the glycation process of protein. *Food Chem*., **113**: 78-84.

You, D. H., Park, J. W., Yuk, H. G., and Lee, S. C. (2011). Antioxidant and tyrosinase inhibitory activities of different parts of guava (*Psidium guajava* L.). *Food Sci. Biotechnol*., **20**: 1095-1100.