



## RESEARCH ARTICLE

### A COMPREHENSIVE INVESTIGATION OF THE SECONDARY METABOLITES OF PSIDIUM GUAJAVA

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#### ABSTRACT

*Psidium guajava* L., commonly known as guava, is a globally significant fruit tree valued not only for its nutritional benefits but also for its rich phytochemical profile. This paper provides a comprehensive investigation into the secondary metabolites produced by *P. guajava*, highlighting their diversity, biosynthesis, and biological significance. Secondary metabolites are organic compounds that are not directly involved in the normal growth, development, or reproduction of plants but play important roles in defense mechanisms, ecological interactions, and potential therapeutic applications. Phytochemical studies have identified a wide range of secondary metabolites in various parts of *P. guajava*, including leaves, fruits, barks, and seeds. These compounds mainly consist of phenolic acids, flavonoids, tannins, terpenoids, and essential oils. Among them, flavonoids such as quercetin, catechin, and rutin dominate the metabolic profile and are implicated in the plant's antioxidant activity. Phenolic acids, including gallic acid and ellagic acid, exhibit strong free-radical scavenging properties, contributing to the plant's potential in managing oxidative stress. Tannins and terpenoids further enhance the plant's defense against herbivores and pathogens. The secondary metabolites of *P. guajava* have shown promising pharmacological activities antimicrobial, anti-inflammatory, anticancer, antidiabetic, and hepatoprotective effects making the plant a significant candidate for further nutraceutical and pharmaceutical research. This review emphasizes the need for more in-depth studies on extraction methods, metabolite characterization, and clinical evaluations

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## INTRODUCTION

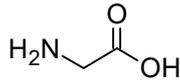
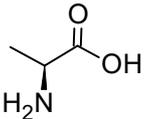
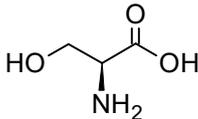
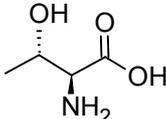
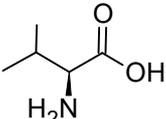
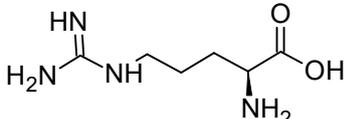
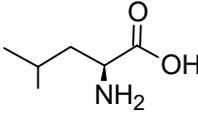
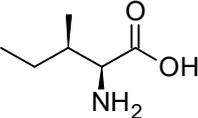
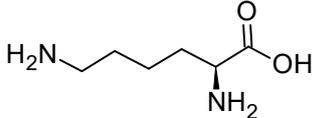
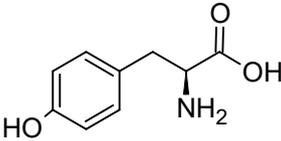
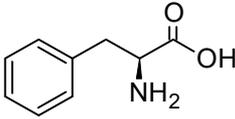
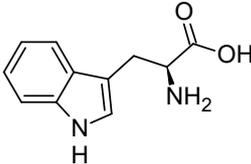
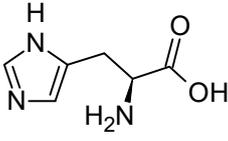
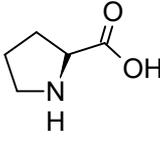
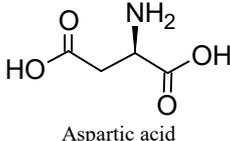
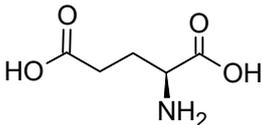
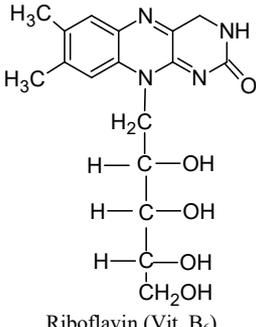
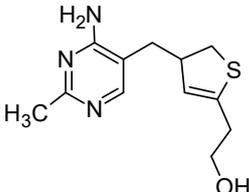
*Psidium guajava* Linn. (family: Myrtaceae) is a semi-deciduous tropical tree and its fruit called Guava (*amrud* in Hindi). The tree is common throughout the world specially all warm areas of tropical America, west India, Asia and Africa, and other subtropical countries including India. Guava is a delicious fruit, which is very nutritious and exceptionally rich in ascorbic acid and several minerals useful for human health (Wilson 1980). The well-known guava jelly is tonic for heart and is effective in constipation. Ripe fruit is a good laxative and aperients, the stem bark and root bark are good astringent and are recommended for gout. The fruit, a berry, when unripe is considered indigestible, while the ripe one is a good aperients. The fruit contains a high percentage of vitamin C, carotene, vitamin B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, free sugars (glucose, fructose and sucrose), pectin and water soluble arabanose<sup>1</sup>. The guava industry provides a variety of processed products<sup>2</sup>. Root bark is an astringent and given to children in diarrhoea and root preparation with fruit is considered to be useful in jaundice<sup>3</sup>. The root bark is successfully employed in chronic infantile diarrhoea in the form of concentrated decoction. The water in which fruits are soaked is good thrust in diabetes<sup>4-8</sup>. Due to their astringent properties, mature guava fruits, leaves, roots, barks and immature fruits are used in local medicines to treat gastrointestinal diseases, diarrhoea and dysentery. Guava consumption has been reported to significant, reduce serum total cholesterol, triglycerides and blood pressure and help in the increase high-density lipoprotein (HDL) or

good cholesterol<sup>9-10</sup>. Furthermore high concentration of pectin in guava fruit may play a significant role in reduction of cholesterol and thereby decreases the risk of cardiovascular diseases<sup>11</sup>. The leaves and bark of the guava tree have long history of uses for medicinal purposes and are still employed today for the same. A tea made from the leaves and bark has been used by many tribes for diarrhoea and dysentery, and employed for stomach upset, vertigo and to regulate menstrual periods. In traditional practice, guavas leaves are still employed as a natural medicine. Locally decoction of the leaves is an efficacious gargle for the swollen gums, ulceration of the mouth and in scurvy. In cholera, for arresting vomiting and diarrheic symptoms the decoction of the leaves is used. Also applied commonly in rheumatism, epilepsy, cerebral affection and nephritis. Ground leaves are used as poultice. The plant is used for prevention and treatment of scurvy in Asia and Africa. Guava juice has been reported to possess hypoglycemic activity in both mice and humans (Cheng and Yang, 1983). In addition, guava leaves have been used to treat many ailments including cough and pulmonary diseases in Bolivia and Egypt. Young guava leaves are used in India as a remedy against cough. People in China use guava leaves as an anti-inflammatory and haemostatic agent. A decoction of the leaves is used for the treatment of cholera<sup>12</sup>. The leaves of this plant have been employed for dying and tanning and investigation have shown the presence of waxes, resins, sugars and essential oils<sup>13</sup>.

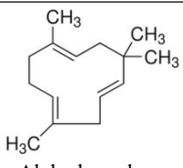
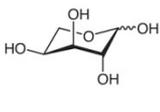
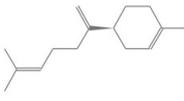
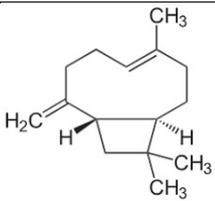
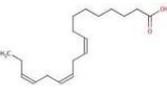
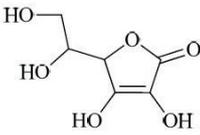
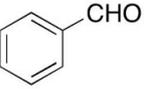
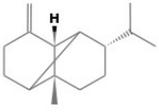
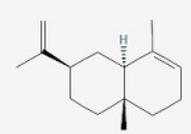
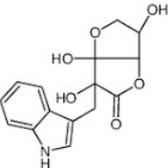
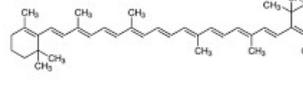
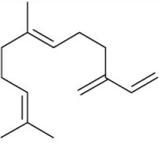
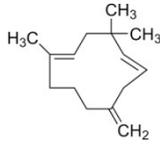
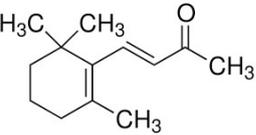
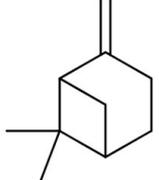
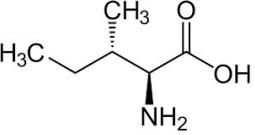
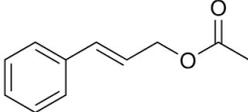
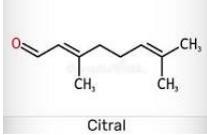
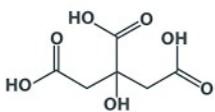
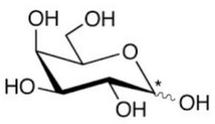
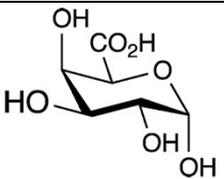
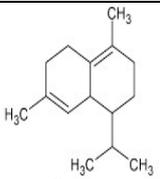
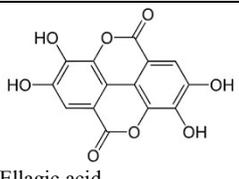
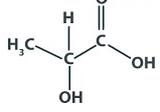
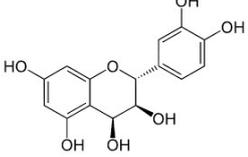
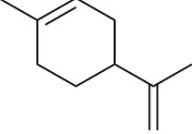
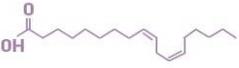
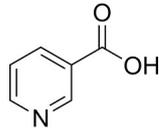
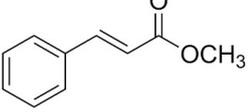
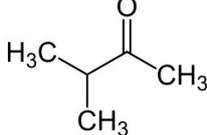
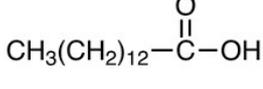
Table 1.

S.No.	Country	Medicinal properties and uses
1.	Cuba	Cold, Dysentery, Dyspepsia
2.	Asia and America	Astringent, Bactericide, Bowel, Bronchitis, Cachexia, Cholera, Colic, Convulsion, Diarrhoea, Epilepsy, Fever, Gingivitis, Jaundice, Nausea, Nephritis, Respiratory, Rheumatism, Sore, Spasm, Tonic, toothache, Wound.
3.	Ghana	Astringent, Cough, Diarrhoea, Dysentery, Laxative, Toothache.
4.	Haiti	Astringent, Antiseptic, Cicatrizant, Dysentery, Diarrhoea, Epilepsy, Hemostat, Piles, Scabies, Sore, Itch, Sorethroat.
5.	Malaya	Dermatosis, Diarrhoea, Epilepsy, Hysteria.
6.	Mexico	Stomachache, Deafness, Diarrhoea, Itch, Scabies, swelling, Ulcer, Vermifuge, vulnerary.
7.	Philippines	Astringent, Sore, wound.

**Chemical constituents:** The major chemical constituents of the leaves of *P. guajava* are listed<sup>14</sup> in below.

 Glycine	 Alanine	 Serine
 Threonine	 Valine	 Arginine
 Leucine	 Isoleucine	 Lysine
 Tyrosine	 Phenyl alanine	 Tryptophan
 Histidine	 Proline	 Aspartic acid
 Glutamic acid	 Riboflavin (Vit. B <sub>6</sub> )	 Thiamin (Vit. B <sub>1</sub> )

Continue

 Alpha-humulene	 Arabinose	 Beta-bisabolene	 Beta-caryophyllene
 Alpha-linolenic acid	 Ascorbic acid	 Benzaldehyde	 Beta-copaene
 Alpha-selinene	 Ascorbigen	 Beta-carotene	 Beta-farnesene
 butanol	 Beta-humulene	 Beta-ionone	 Beta-pinene
 Isoleucine	 Cinnamylacetate	 Citral	 Citric acid
 D-galactose	 D-galacturonic acid	 Delta-cadinene	 Ellagic acid
 Lactic acid	 Leucocyanidins	 Limonene	 Linoleic acid
 Niacin	 Methylcinnamata	 Methylisopropylketone	 Myristic acid

**Chemical constituents:** The major chemical constituents of the leaves of *P. guajava* are listed<sup>14</sup> in below.

The fruits sweet musky odour, when ripe, may be round, ovoid or pear shaped, 2 to 4 inches long with 4 or 5 protruding floral remnants (sepals at the apex and the skin is light, yellow and thin. Next to skin is a layer of granular flesh, 1/8 to 1/2 inches thick, white yellowish light or dark pink or near red juicy, acid, sub acid or sweet and flavorful. The central pulp, lightly darker in tone is juicy and normally filled with very hard, yellowish seeds. Seed count ranges from 112 to 535 but some guava are seedless or nearly so<sup>15-18</sup>.

The plant has been investigated for its chemical constituents by many workers and different parts of finds use in the Indian indigenous system of medicine specially the leaves and the bark<sup>19-21</sup>. From the benzene extract of flowers and leaves,  $\beta$ -sitosterol<sup>22</sup>, oleanolic acid<sup>23</sup>, quercetin and ellagic acid<sup>24</sup> were obtained. Ellagic acid is reported to 'have astringent, haemostatic and antihemorrhagic properties and oleanolic acid has antihepatotoxic effects and these constituents may be responsible for some of the medicinal uses of *P. guajava*<sup>24-25</sup>. Soliman and Farid isolated a new triterpene acid "psidiolic acid" from the ether soluble fraction of the methanol extract of defatted leaves Lator on ather and hui reported that psidiolic acid is a mixture of four acids viz.oleanolic, ursolic, cratogenic (maslinic acid) together

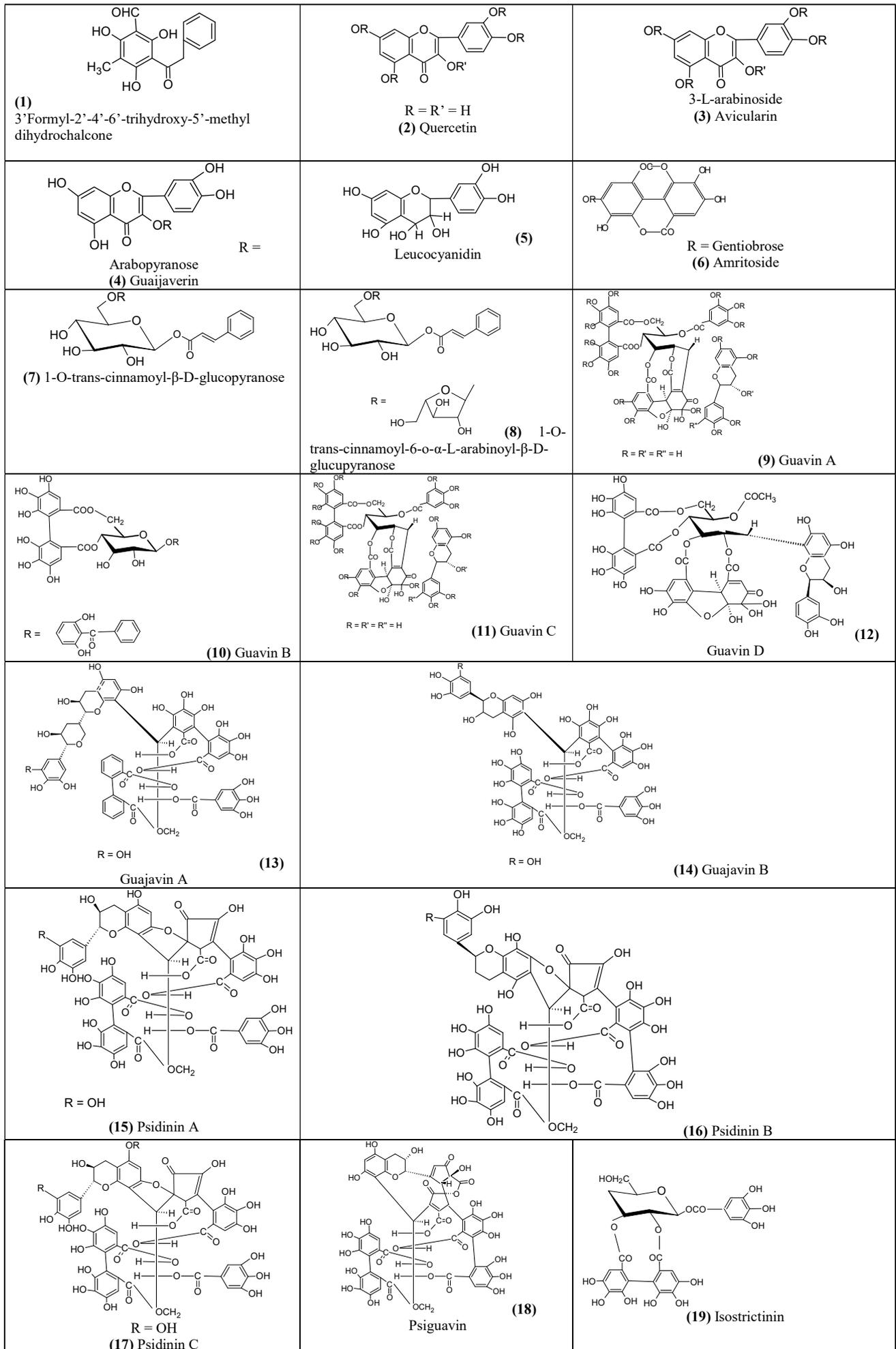


Table on.2

S. No.	Class	Name	Molecular Formula	Molecular Wt.	Ref. no.
1.	Chalcone	3'-Formyl-2'-4'-6'-trihydroxy-5'-methyl dihydrochalcone (1)	C <sub>17</sub> H <sub>16</sub> O <sub>5</sub>	300	31
2.	Polyphenol	Quercetin (2)	C <sub>15</sub> H <sub>10</sub> O <sub>7</sub>	302	32-33
3.	Polyphenol	Avicularin (3)	C <sub>20</sub> H <sub>18</sub> O <sub>11</sub> .H <sub>2</sub> O	452	33
4.	Polyphenol	Guajaverin (4)	C <sub>20</sub> H <sub>18</sub> O <sub>11</sub> .H <sub>2</sub> O	452	32-33
5.	Polyphenol	Leucocyanidin (5)	C <sub>27</sub> H <sub>26</sub> O <sub>12</sub>	558	32
6.	Polyphenol	Amritoside (6)	C <sub>46</sub> H <sub>46</sub> O <sub>28</sub>	1046	32-34
7.	Carbohydrate ester	1-O-trans-cinnamoyl-β-D-glucopyranose (7)	C <sub>16</sub> H <sub>18</sub> O <sub>7</sub>	322	35
8.	Carbohydrate este	1-O-trans-cinnamoyl-6-o-α-L-arabinoyl-β-D-glucopyranose (8)	C <sub>21</sub> H <sub>26</sub> O <sub>11</sub>	454	35
9.	Complex Tannin	Guavin A (9)	C <sub>56</sub> H <sub>40</sub> O <sub>32</sub> .9H <sub>2</sub> O	1224	36-38
10.	Complex Tannin	Guavin B (10)	C <sub>33</sub> H <sub>26</sub> O <sub>17</sub> .H <sub>2</sub> O	694	39
11.	Complex Tannin	Guavin C (11)	C <sub>56</sub> H <sub>40</sub> O <sub>33</sub> .5H <sub>2</sub> O	1240	36-38
12.	Complex Tannin	Guavin D (12)	C <sub>56</sub> H <sub>40</sub> O <sub>29</sub> .6H <sub>2</sub> O	1176	36-38
13.	Complex Tannin	Guajavin A (13)	C <sub>33</sub> H <sub>40</sub> O <sub>32</sub> .6H <sub>2</sub> O	944	40
14.	Complex Tannin	Guajavin B (14)	C <sub>56</sub> H <sub>38</sub> O <sub>32</sub> .H <sub>2</sub> O	1222	40
15.	Complex Tannin	Psidin A (15)	C <sub>55</sub> H <sub>39</sub> O <sub>31</sub> .5H <sub>2</sub> O	1194	40
16.	Complex Tannin	Psidin B (16)	C <sub>55</sub> H <sub>36</sub> O <sub>3</sub> .H <sub>2</sub> O	1192	40
17.	Complex Tannin	Psidin C (17)	C <sub>55</sub> H <sub>38</sub> O <sub>31</sub> .6H <sub>2</sub> O	1194	40
18.	Complex Tannin	Psiguavin (18)	C <sub>55</sub> H <sub>34</sub> O <sub>31</sub> .9H <sub>2</sub> O	1190	40
19.	Complex Tannin	Isostrictinin (19)	C <sub>27</sub> H <sub>22</sub> O <sub>18</sub> .2H <sub>2</sub> O	634	37

with a new acid called "guajjavolic acid" (C<sub>30</sub>H<sub>48</sub>O<sub>4</sub>)<sup>26-27</sup>. Later on it was concluded that chemically "guajjavolic acid" is 22-hydroxyursolic acid and it may be the same medicinal principle responsible for the treatment of the throat and chest complaints<sup>28</sup>. The major components are: selenene, β-caryophyllene, caryophyllene oxide, squalene, selin-11-en-4α-ol, 1996), morin-3-O-α-L-lyxopyranoside and morin-3-O-α-L-lyxopyranoside, morin-3-O-α-L-arabopyranoside<sup>29</sup>, and ursolic acid<sup>30</sup>. Studies on the leaves of *P. guajava* revealed that they are rich in polyphenols and tannins. A brief review of these compounds is summed up in the table no.2

**Pharmacology Properties:** *Psidium guajava* has been screened and tested for various biological activities and pharmacological properties. The extract of the whole plant of *P. guajava* excluding roots was reported to be devoid of any antibacterial, antifungal, antiviral, antifertility, hypoglycaemic, diuretic and anti-inflammatory activities<sup>41</sup>. The leaves of *P. guajava* inhibit the increase of plasma sugar level in alloxan induced diabetic rats, during glucose tolerance test 11. In addition, the butanol and water-soluble fractions were found to suppress adrenalin induced lipolysis in fat cells from rats epididymal adipose tissues<sup>42</sup>. Several flavonoids, glycosides, terpenoids etc. have been shown to possess antidiabetic properties<sup>43-45</sup>.

**Antibacterial activities:** Three different method namely, disk inhibition zone, total plate count and turbidometric measurements were used to determine the growth inhibition of bacteria by different extracts of *P. guajava*. The aqueous extract (decoction) and MeOH extract were tested on the following bacteria viz. *Staphylococcus aureus*, *Streptococcus pyogenes*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Proteus vulgaris*, *streptococcus epidermis*, *Escherichia coli* and *Klebsiella pneumoniae*<sup>46-49</sup>. The two bacteria *E. coli* and *K. pneumoniae* were found to be resistant against both the extracts while *S. aureus* showed the complete inhibition by aqueous extract. Moderate activity against *S. pyogenes* and *S. epidermis*, low activity against *Salmonella* and *P. aeruginosa* and no activity against *S. marcescens* and *P. vulgaris* were observed.

All *Staphylococcus strains* by were found to be resistant against extract at the concentration of 6.5 mg/ml in all the three methods. On comparison with antibiotics used in the treatment of some diseases, the extract showed similar effects as found with chloramphenicol, cephoxitin and mefloxotin. The activities of all strains of *Staphylococcus coccus* are very important, as *S. aureus* is resistant to different antibiotics. Thus *P. guajava* may be an important source of new antimicrobial compounds<sup>50</sup>.

**Antimutagenic activity:** A number of mutagens, which are thought to be related to cancer induction, genotoxicity and aging, have been

detected in our environment. They are also many factors, which modify their mutagenic activities. Bioantimutagen is defined as a compound modifying the process of mutation repair after DNA is damaged by mutagens, and consequently suppressing mutagenesis<sup>51-52</sup>. Our scientific interest has focused on finding new bioantimutagenic compounds of plant origin, especially for use in cancer chemoprevention. Tomiaki Matsuo and coworkers from Japan investigated one hundred and fifty kinds of plant extracts for their biomutagenic effects on UVC 254(nm) induced mutagenesis using *E. coli*. The primary screening showed that MeOH extract of guava leaves had a high biomutagenic activity. Further investigation concluded the presence of (+)-gallacatechin in the leaves of guava to be responsible for the same<sup>53</sup>. Eight ellagitannins and structurally related polyphenols were identified by HPLC from MeOH and EtOH extracts namely pesunculagin, mcaurimin, stachyurin, tellimagrandin, strictin, casuaritin and 2,3 hexahydroxy diphenyl glucose and 4,6 hexahydroxy diphenylglucose<sup>37</sup>.

**Antidiarrhoeal activity:** Drinking the decoction of the leaves or root, bark, stem of the guava plant, as well as chewing the fresh leaves and have been employed in the acute diarrhoeal diseases for many centuries in folk medicine<sup>54</sup>. George D., Lutterodt, Malaysia in his experiments verified the antidiarrhoeal action of the extracts of *P. guajava* leaf in rats induced by experimental diarrhea using microlax. Measurement of rates of propulsion in the small intestine, in control and experimental groups of male Sprague Dawley rats (200-250g) were carried out as a means of assessing antidiarrhoeal activity of aqueous extract using morphine as the standards drug. Hyper propulsion (diarrhoea) was induced by feeding the rats in a control group with microlax, using phenol red mixed into it as a marker in the intestine, and the mean rate of hyper propulsion was determined. In experimental groups pretreated with internal administration of either morphine or aqueous extracts, 1 hr before the induction of microlax, the percentage inhibition to the hyper propulsion rate (antidiarrhoeal activity was calculated). Both morphine and extract produced a dose response relationship in their antidiarrhoeal effects. A dose of 0.2 ml fresh of morphine sulphate. The antidiarrhoeal action of an alcoholic extract of the leaves was shown to be due to the presence of a flavonoid compound identified as quercetin<sup>55-59</sup>.

**Antiamoebic activity:** The antiamoebic activity of plant extracts was assessed in-vitro according to the procedure described by Ndir and Pousset (1981) using *Entamoeba histolytica* as a test organism. It was isolated from patients with acute amoebic dysentery and metronidazole was used. The aqueous extract of *P. guajava* was among the most active extract and exhibited a strong antiamoebic activity with minimum inhibitory concentration i.e. MIC = 7.81 mg<sup>60</sup>. The property of extract was attributed to the presence of quercetin and its glycosides.

**Anticough activity:** P. jaiarj and coworkers at Bangkok University evaluated the anticough activity of *P. guajava* leaf extract in rats and guinea pigs. The result showed that water extract of the plant at the doses of 2 and 5 g/kg, decreased the frequency of cough induced by capsaicin aerosol by 35 and 54% respectively, as compared to the control, within 10 min injection of the extract, ( $P < 0.01$ ). However, the anticough activity of extract is less potent than of 3 mg/kg dextromethorphan, which decreased frequently of cough by 78 % ( $P, 0.01$ ). An experiment on isolated rat tracheal muscle showed that the extract directly stimulated muscle contraction and also synergies with the stimulatory effect of pilocarpine. This effect was antagonized by atropine. The active leaf ingredient of guava leaves in the experiment was not quercetin. The data confirms that guava leaf extract can be recommended for cough remedy in the primary health care system in remote villages where modern antitussive drug is difficult to obtained<sup>61</sup>.

**Anti hyperglycemic effect:** It is interesting to note that many plant polysaccharides have also been reported to exhibit hypoglycaemic effect<sup>62-64</sup>. Although the fruit of *P. guajava* is known to contain free sugars, yet the fruit extract showed hypoglycaemic effect in alloxan treated mice and patients with diabetes<sup>65</sup>. *P. guajava* fruit has also been shown as a source of antioxidant due to the presence of polyphenols, ascorbic acid and carotenoids<sup>66</sup>. In an experiment by R. Roman Ramos and coworkers, the anti hyperglycemic effect of *P. guajava* was studied on 27 health rabbits, submitted weekly to subcutaneous glucose tolerance tests after gastric administration of water, tolbutamide or the plant extract. The tolbutamide decreased the area under the glucose tolerance curve and hyperglycemic peak

significantly. The glycemic decreases caused by *P. guajava* aqueous extracts were not significant ( $P < 0.05$ )<sup>67-68</sup>.

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