

## Chemical Composition and Biological Activities of *Arachis* Species

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**ABSTRACT:** *Arachis hypogaea*, known as the peanut, is native to South America. Peanut contains several active components including flavonoids, phenolic acids, phytosterols, alkaloids, and stilbenes. Some therapeutic effects have been reported for peanut seed extracts, such as antioxidative, antibacterial, antifungal, and anti-inflammatory activities. This paper aims to give an overview of the chemical composition, focusing on secondary metabolites, and of the biological activity of *A. hypogaea*, to stimulate new studies about species of the *Arachis* genus.

**KEYWORDS:** *Arachis hypogaea*, peanut, active constituents, biological activity

### INTRODUCTION

The genus *Arachis* L. (Fabaceae) is native to South America with a probable center of origin in Brazil, in a region extending from the southwest of Mato Grosso do Sul State to the south of Goiás.<sup>1</sup> The genus has 80 described species, grouped into 9 taxonomic sections. The most remarkable section is *Arachis*, because it includes *A. hypogaea*, the most economically important species, considered the fourth oleaginous plant in the world. This species is cultivated in Asia, Africa, and America, mainly for high-quality vegetal oil production, as a feedstock, and as natural or processed food for human consumption.<sup>1,2</sup> Beyond its nutritional characteristics and commercial value, several studies have pointed to the biological properties of *A. hypogaea*. Thus, the present review aims to examine the chemical composition and biological activity of *Arachis* species to stimulate new studies about this genus.

### ACTIVE CONSTITUENTS

The class of compound most found in this genus is that of phenylpropanoid derivatives, mainly stilbenes and flavonoids. These compounds are involved in a defense mechanism against physical injuries and microbial contamination. Indeed, the correlation between the concentration of several compounds and their effects on injuries or contamination has been fully reported. Therefore, this review does not intend to discriminate the described active compounds as having been isolated from healthy plants or from injured ones, considering that it is not rare for the same compounds to be found in both injured (mainly fungal contamination) and healthy specimens.<sup>3–12</sup>

**Stilbene Derivatives.** Since resveratrol was postulated to be involved in the health benefits associated with a moderate consumption of red wine, plant stilbenes have received notable interest.<sup>13</sup> Stilbenes are characterized by a 1,2-diphenylethylene backbone, usually derived from the basic unit *trans*-resveratrol (3,5,4'-trihydroxy-*trans*-stilbene, **1a**), although other structures are found in particular plant families.<sup>14</sup> Ring A usually carries two hydroxy groups in the *m*-position, whereas ring B is replaced by

hydroxy and methoxy groups in the *o*-, *m*-, or *p*-position. They are synthesized from cinnamic acid derivatives, and the substitution pattern of the cinnamic acids determines that of ring B of the adduct.<sup>15</sup>

Stilbenes are synthesized by a wide range of plant species; however, they are often in plants that are not routinely consumed for food or in the edible tissue. Peanuts (1.3–3.7 μg of resveratrol/g) and peanut butter are considered major dietary sources of stilbenes, along with grapes and their derivatives.<sup>15</sup>

Stilbene synthesis has been associated with resistance to some common peanut diseases, in particular to fungal contamination. As long as peanuts had the ability for phytoalexin production, they were not contaminated with aflatoxins.<sup>9</sup> Also, stilbene production is elicited by injuries, fungal contamination, insect damage, and other attacks.<sup>9,16</sup> However, stilbenes can be found in uninfected and uninjured plants, albeit in minor amounts.

The stilbenes that have been reported for several varieties from *A. hypogaea* in different organs from the plant, such as leaves, roots, and seeds, seem to be derived from *trans*-resveratrol (**1a**), such as piceid (**2**),<sup>17–19</sup> isopentadienylresveratrol (IPD) (*trans*-3'-isopentadienyl-3,5,4'-trihydroxystilbene, **3**),<sup>20</sup> piceatannol (3,4,3',5'-tetrahydroxy-*trans*-stilbene, **4**), arachidin-1 [*trans*-4-(3-methyl-1-butenyl)-3,5,3',4'-tetrahydroxystilbene, **5**], arachidin-2 (**6**), arachidin-3 [*trans*-4-(3-methyl-1-butenyl)-3,5,4'-trihydroxystilbene, **7**],<sup>11,21,22</sup> and *trans*-SB-1 (**8**).<sup>22</sup>

After an experiment using spores of *Aspergillus caelatus* NRRL to elicit phytoalexin production in peanuts, the stilbenes **1a**, **3**, and **5–8** were isolated, as well as chiricanine A (*trans*-4'-deoxyarachidin-2, **9**), arahypin-1 (*trans*-4'-deoxyarachidin-3, **10**), arahypin-2 [*trans*-3'-(2'',3''-dihydroxy-3''-methylbutyl)resveratrol, **11**], arahypin-4 [*trans*-4-(2'',3''-dihydroxy-3''-methylbutyl)-4'-deoxyresveratrol, **12**], arahypin-3 [*trans*-4-(2'',3''-dihydroxy-3''-methylbutyl)resveratrol, **13**], and arahypin-5 (**14**).<sup>8</sup> Keen

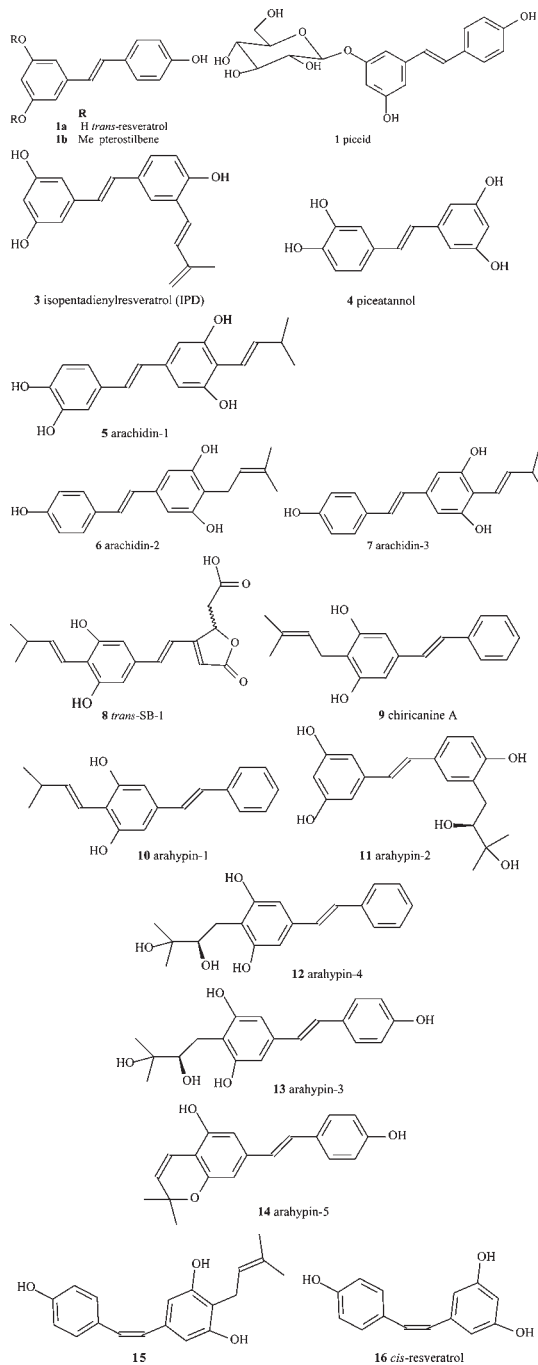
**Received:** December 12, 2010

**Revised:** March 20, 2011

**Accepted:** March 22, 2011

**Published:** March 22, 2011

and Ingham characterized the *cis*-3,5,4'-trihydroxy-4-isopentenylstilbene (**15**) from American varieties of *Arachis*.<sup>23</sup> Ingham also isolated the *cis*-isomer of resveratrol (**16**) from the infected hypocotyls of *A. hypogaea*.<sup>24</sup>

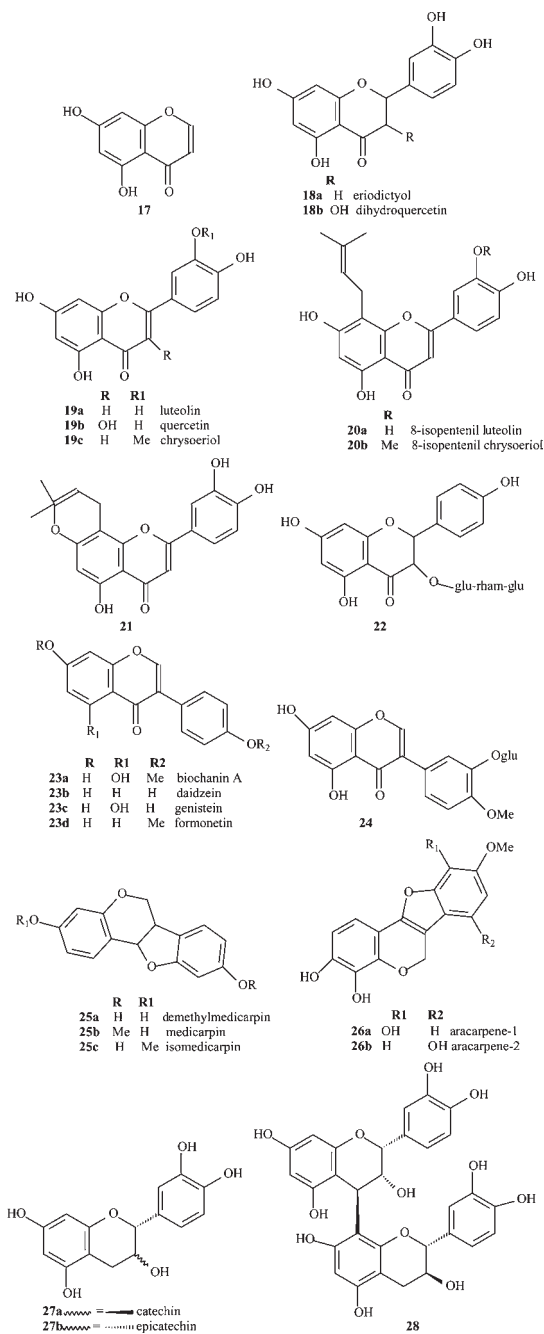


From hairy roots of *A. hypogaea* were isolated resveratrol (**1a**) and its derivative pterostilbene (**1b**).<sup>25</sup>

**Flavonoid Derivatives.** Flavonoids and derivatives can be found in both infected and uninfected *Arachis* plants. From peanut pods 5,7-dihydroxychromone (**17**), eriodictyol (**18a**), and luteolin (3',4',5',7-tetrahydroxyflavone) (**19a**),<sup>3,16</sup> dihydroquercetin (**18b**),<sup>26</sup> and chrysoeriol (**19c**) were isolated, as well as the derivatives 8-isopentenyl-luteolin (**20a**), 8-isopentenylchrysoeriol (**20b**), and 4',5-dihydroxy-2'',2''-dimethylpyrano[5'',6'':7,8]-

flavone (**21**).<sup>27</sup> The isorhamnetin glucoside (**22**) was also isolated from the water-soluble fraction of peanut skin,<sup>28</sup> whereas quercetin (**19b**) was isolated from the exudate of germinating peanut.<sup>29</sup>

The isoflavones biochanin A (**23a**), daidzein (**23b**), and genistein (**23c**)<sup>30</sup> and formonnetin (**23d**)<sup>31,32</sup> can also be found, besides glucoside (**24**)<sup>28</sup> and medicarpin (**25b**) and demethylmedicarpin (**25a**).<sup>31,32</sup> It is important to consider that demethylmedicarpin (**25a**) seems to be a degradation product from medicarpin (**25b**). Isomedicarpin was isolated from aerial parts of *A. hypogaea* (**25c**).<sup>33</sup>

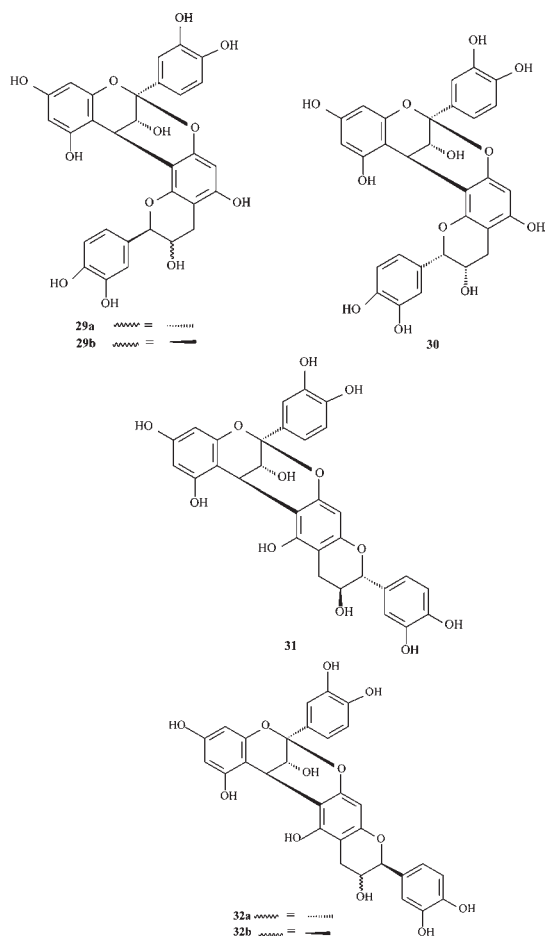


Medicarpin (**25b**) was able to promote bone mass and strength achieved at the end of the growth period, commonly designated peak bone mass (PBM), in a *ex vivo* model and likely acts via estrogen receptor  $\beta$  (ER $\beta$ ) in osteoblasts.<sup>34</sup>

This compound was also isolated from fungus-infected leaves of *A. hypogaea*, as well as the pterocarpan arcarpene-1 (**26a**) and arcarpene-2 (**26b**).<sup>35</sup> Pterocarpan is a class of compounds considered to have the highest antifungal activity among the phytoalexins in the flavonoid-based group of compounds.<sup>36</sup>

The ethyl acetate fraction from aqueous extract of peanuts skin gave catechin (**27a**), epicatechin (**27b**), the condensation product **28**, and the proanthocyanidins A<sub>1</sub> (**29a**) and A<sub>2</sub> (**29b**).

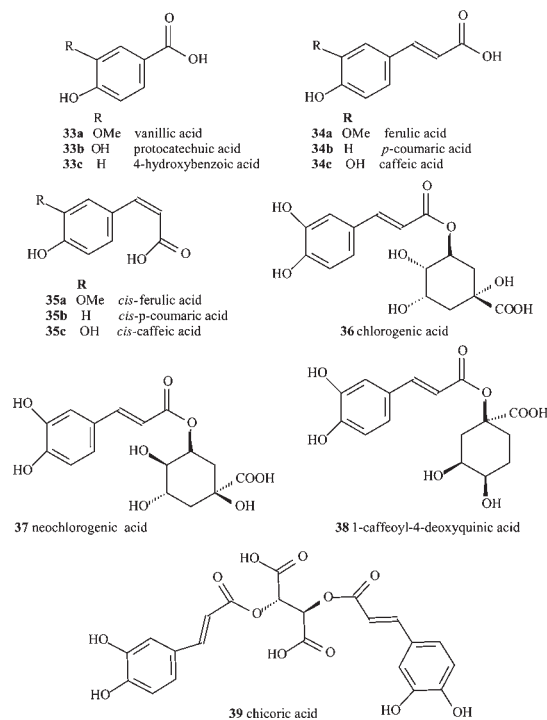
Roasted peanut skins exhibit a considerable content of proanthocyanidin.<sup>37</sup> Six A-type proanthocyanidins were isolated from the water-soluble fraction of peanut skins, the proanthocyanidins A<sub>1</sub> (**29a**), A<sub>2</sub> (**29b**), and **29a** epimer (**30**), as well as compounds **31**, **32a**, and **32b**.<sup>38</sup>



**Phenolic Acids.** From exudate of germinating peanut were isolated the phenolic acids vanillic (4-hydroxy-3-methoxybenzoic acid, **33a**), protocatechuic (3,4-dihydroxybenzoic acid, **33b**), ferulic (4-hydroxy-3-methoxycinnamic acid, **34a**), and caffeic (4-hydroxycinnamic acid, **34b**).<sup>29</sup>

From peanut roots inoculated with mycorrhizal and *Rhizobium*, besides vanillic (**33a**), protocatechuic (**33b**), ferulic (**34a**), and *p*-coumaric (**34b**) acids, 4-hydroxybenzoic acid (**33c**), caffeic acid (**34c**), the *cis*-isomers from **34a**, **34b**, and **34c** (**35a**–**35c**, respectively), and chlorogenic acid (**36**)<sup>5</sup> were isolated. Ferulic (**33a**) and *p*-coumaric (**33b**) acids were also isolated as major compounds from dry-roasted peanuts.<sup>39</sup> Compounds **1a**, **2**, and **34a**–**34c** were also detected in peanuts submitted to combined ultrasound and ultraviolet treatments.<sup>40</sup>

Chlorogenic acid (**36**) was also isolated from leaves of *A. paraguariensis*, besides neochlorogenic (**37**) and 1-caffeoyl-4-deoxyquinnic acid (**38**).<sup>41</sup>



Chicoric acid (**39**)<sup>42</sup> was isolated from partially opened vegetative quadrifoliate leaf buds of peanuts presenting late leaf spot disease fungus (*Cercosporidium personatum*), insect tobacco thrips (*Frankliniella fusca*), and potato leafhopper (*Empoasca fabae*).

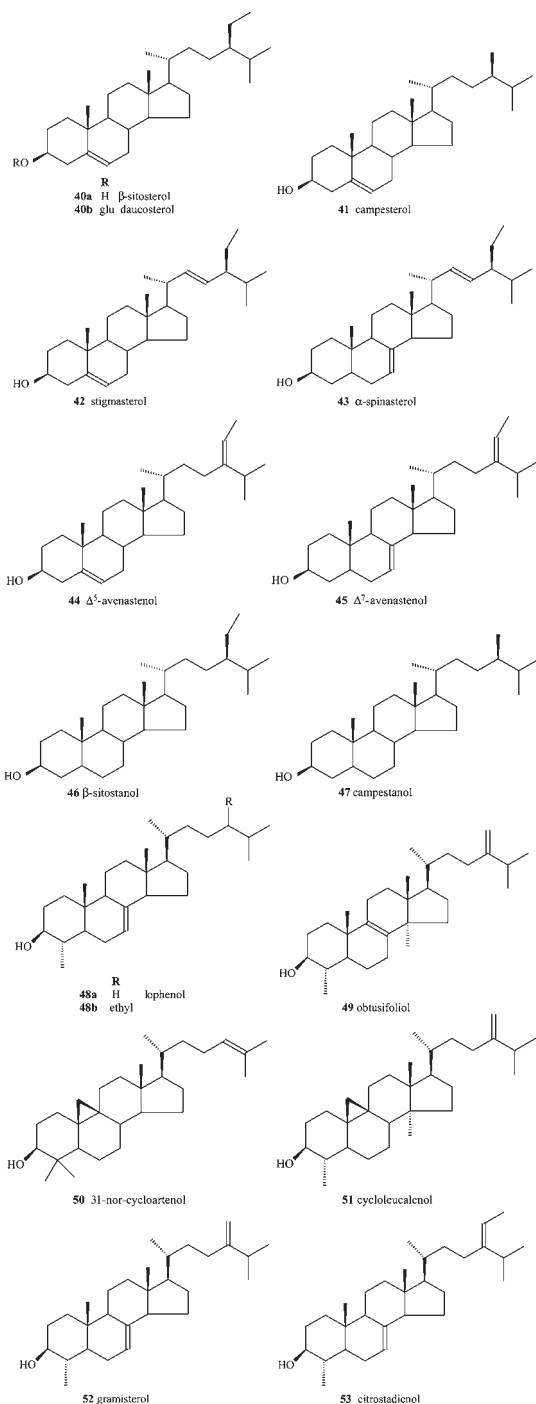
**Phytosterols.** In peanut butter, oil and groundseed were found  $\beta$ -sitosterol (**40a**), campesterol (**41**), stigmasterol (**42**),  $\alpha$ -spinasterol (**43**),  $\Delta^5$ -avenasterol (**44**),  $\Delta^7$ -avenasterol (**45**), sitostanol (**46**), and campestanol (**47**).<sup>43–50</sup> A similar steroid composition was found in other *Arachis* species such as *A. sylvestris*, *A. pintoi*, *A. chinquitana*, *A. appresipila*, *A. kretschmeri*, *A. matiensis*, *A. trinitensis*, *A. kempff-mercadoi*, *A. diogoi*, *A. benensis*, *A. valida*, *A. helodes*, *A. kuhlmannii*, *A. williamsii*, *A. hoehnei*, *A. villosa*, *A. stenosperma*, *A. fastigiata* var. *fastigiata*, and *A. fastigiata* var. *peruviana*.<sup>44,47</sup> According to the authors,<sup>47</sup> there were no significant changes in steroid content.  $\beta$ -Sitosterol (**40a**) was also isolated from aerial parts of *A. hypogaea*, as well as daucosterol (**40b**).<sup>33</sup>

Other phytosterols can be found in *Arachis*: lophenol (**48a**), 24-ethyllophenol (**48b**), obtusifoliol (**49**), 31-norcycloartenol (**50**), cycloleucalenol (**51**), gramisterol (**52**), and citrostadienol (**53**).<sup>45,51</sup>

**Triterpenes.** The presence of triterpene in peanut oil is not surprising, considering that triterpenes and sterols are synthesized via the same metabolic route and *Arachis* oil is rich in sterols, mainly  $\beta$ -sitosterol (**40a**). The most usual triterpenes in peanut seem to be cycloartenol (**54**), cycloartenol (**55a**), cyclobranol (**55b**), 24-methylenecycloartenol (**56**),  $\beta$ -amyrin (**57**), and lupeol (**58**).<sup>45,51,52</sup>

From roots were isolated sophoradiol (**59a**) and soyasapogenol B (**59b**).<sup>53</sup> Soyasapogenol B (**59b**) was also isolated from aerial parts.<sup>33</sup> From groundnuts were isolated **59b** and its glucoside soyasaponin I (**59c**).<sup>54</sup>

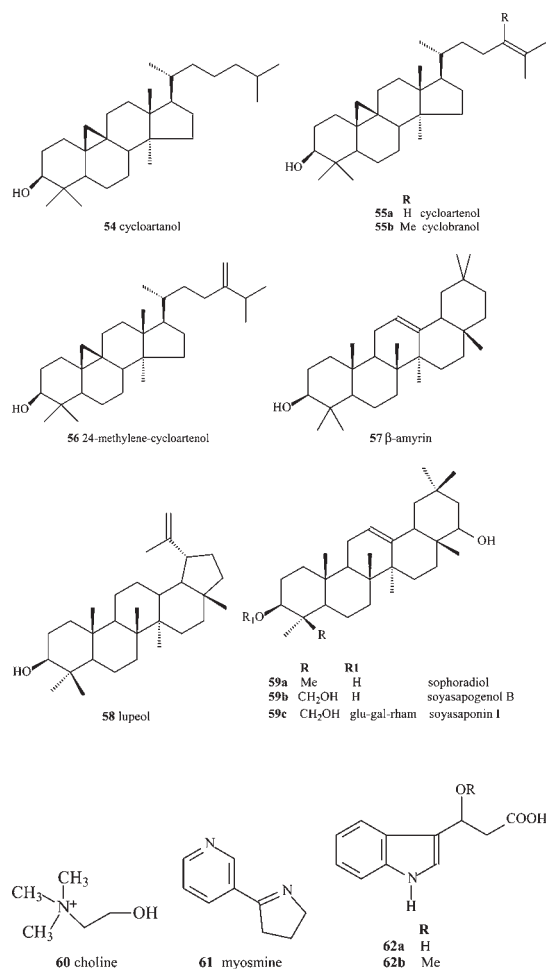
**Alkaloids.** There are few reports of the occurrence of alkaloids in the *Arachis* genus. Probably the first report of these compounds in *Arachis* was made by Mooser (1904), which described the alkaloid named arachine.<sup>55</sup> However, Moll (1961) showed that arachine was, in fact, choline (**60**).<sup>56</sup>



Myosmine [3-(1-pyrroline-2-yl)pyridine, **61**] was first structurally identified as a tobacco alkaloid present along with nicotine in tobacco smoke, presenting low toxicity to mammals.<sup>57</sup> Myosmine (**61**) was detected in untreated and roasted groundnuts, as well as in the oil from both untreated and roasted groundnuts.<sup>57</sup>

From the water-soluble fraction of peanut skins were isolated 2-hydroxy-3-[3-(1-N-methyl)indolyl]propionic acid (**62a**) and 2-methoxy-3-(3-indolyl)-propionic acid (**62b**).<sup>28</sup>

**Fatty Acids.** The following fatty acids were detected in several varieties of peanut (*A. hypogaea*): palmitic (16:0), stearic (18:0), oleic (18:1), linoleic (18:2), arachidic (20:0), eicosenoic (gadoleic) (20:1), behenic (22:0), and lignoceric (24:0) acids.<sup>58–60</sup> However, no significant differences could be found among varieties.<sup>46,52</sup> The same fatty acid composition was found in other species from the *Arachis* genus, such as *A. sylvestris*, *A. pinto*, *A. chinquitana*, *A. appresipila*, *A. kretschmeri*, *A. matiensis*, *A. trinitensis*, *A. kempff-mercadoi*, *A. diogoi*, *A. benensis*, *A. valida*, *A. helodes*, *A. kuhlmannii*, *A. williamsii*, *A. hoehnei*, *A. currentina*, *A. durannensis*, *A. monticola*, *A. batizocoi*, *A. cardenasii*, *A. villosa*, *A. stenosperma*, *A. fastigiata* var. *fastigiata*, and *A. fastigiata* var. *peruviana*.<sup>44,47,61</sup> Peanut, peanut oil, and peanut butter from six varieties of *A. hypogaea* from Nigeria and two from Turkey also presented capric (10:0), lauric (12:0), myristic (14:0), palmitoleic (16:1n-7), and linolenic acids (18:3).<sup>58,62</sup>



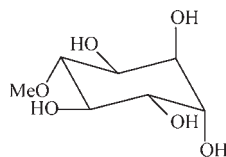
The fatty acid composition usually varies among species, except for stearic acid.<sup>47</sup> Oleic and linoleic acids were the major components of the fatty acid fraction from groundnut oil.<sup>52,63</sup>

**Other Compounds.** The inositol D-pinitol (**63**) was isolated from groundnuts.<sup>64</sup> Among vitamins, 5-formyltetrahydrofolate was found to be the most important folate vitamin in peanut.<sup>65</sup> Peanuts are a good source of tocopherol (vitamin E).<sup>48</sup>

The characteristic odor from raw or roasted peanut is due to several compounds such as 2- and 3-methylbutanal, phenylacetaldehyde, ethyl 2-methylbutanoate, ethyl 3-methylbutanoate, butanoic acid, methylbutanoic acid, 4-vinylphenol,



2-methoxyphenol, 2-methoxy-4-vinylphenol,  $\beta$ -pinene, limonene,  $\alpha$ -terpineol, and sulfur compounds such as 3-(methylthio)-propionaldehyde, 4-hydroxy-2,5-dimethyl-3(2*H*)-furanone, ethyl 2-methylbutanoate, 2,5-ethyl-3-dimethylpyrazine, 2,3-diethyl-5-methylpyrazine, (*Z*)-2-nonenal, (*E,E*)-2,4-decadienal, (*E*)- $\beta$ -damascenone, 4-hydroxy-3-methoxybenzaldehyde, and others.<sup>66</sup>



63 D-pinitol

## ■ BIOLOGICAL ACTIVITIES OF *A. HYPOGAEA*

The traditional use of peanuts for a medicinal purpose has been reported since ancient times. In 2003, a Qualified Health Claim was approved, stating that eating 42 g of nuts per day may reduce the risk of heart disease.<sup>67</sup> Peanut skins are used to treat chronic hemorrhage and bronchitis in China.<sup>38</sup> Groundnut extracts have been used in the management of diabetic patients in northern Nigeria.<sup>68</sup> In fact, *Arachis* is used to lower cholesterol, aid weight loss, and prevent cardiovascular diseases and cancer.<sup>69</sup>

Peanuts have been shown to have a favorable nutrient profile, presenting several highly valued dietary constituents, including dietary fibers, proteins, micronutrients, and phytochemicals such as phytosterols, phenolics, stilbenes, and arginine,<sup>70,71</sup> which elicit several biological effects, including cardioprotective, anti-inflammatory, anticancer, and others. Indeed, resveratrol (**1a**), luteolin (**19a**), quercetin (**19b**), and many other phytochemicals have already been isolated from peanut tissues, including industrial residues (shells, leaves, roots, etc.), presenting many biological activities.

The leaves of *A. hypogaea* have astringent action and several biological properties. They are used therapeutically against abdominal pain, bronchitis, constipation, and flatulence.<sup>72</sup> Peanut also has therapeutic effects as a solvent for bleeding in hemophiliacs.<sup>73</sup>

Peanuts are a rich source of magnesium, folate, fiber,  $\alpha$ -tocopherol, copper, and arginine,<sup>74</sup> and dietary consumption of peanuts has been stimulated.<sup>70</sup> Although the biological activity of pure compounds has been proved, the intake of peanuts or their extract may sometimes be more favorable than the ingestion of pure phytochemicals. For example, the absorption of luteolin (**19a**) was proved to be more efficient from peanut hull extract than that of the pure compound.<sup>75</sup>

**Anti-inflammatory Activity.** Usually all tested peanut stilbenoids presented anti-inflammatory activities; this could be attributed to the fact that stilbenoids bear a 4'-hydroxyl group, as the most important determinant of bioactivity.<sup>76</sup> Arachidin-1 (**5**), piceatannol (**4**), and resveratrol (**1a**) could effectively inhibit lipopolysaccharide (LPS)-induced nitric oxide (NO) production; piceatannol (**4**) presents strongest inhibitory potency on LPS-induced prostaglandin E<sub>2</sub>/NO production, C/EBP $\delta$  gene expression, and nuclear factor- $\kappa$ B activation.<sup>77</sup> In general, arachidin-1 (**5**), piceatannol (**4**), and resveratrol (**1a**) perform effective anti-inflammatory activity following an identical mechanism but with different potencies among molecules. The authors suggested these compounds might be of importance in further development for nutraceutical or chemopreventive applications.<sup>77</sup>

Resveratrol (**1a**), in an ex vivo model, inhibited TNF- $\alpha$  and IL-6 released from macrophages, thereby suppressing macrophage-CM-induced inflammatory response in adipocytes.<sup>78</sup> Also, resveratrol exerts anti-inflammatory effects in microglia and astrocytes by inhibiting different pro-inflammatory cytokines and key signaling molecules.<sup>79</sup>

Resveratrol (**1a**) treatment of mice presented protection against colitis through up-regulation of SIRT1 in immune cells in the colon.<sup>80</sup>

**Antitumor Activity.** There is evidence suggesting a protective role of phytosterols, especially  $\beta$ -sitosterol (**40a**), in colon, prostate, and breast cancer.<sup>81</sup> Because peanuts and their products, such as peanut oil, peanut butter, and peanut flour, are good sources of phytosterols, consuming these products can bring health benefits.<sup>81</sup>

Piceatannol (**4**), arachidin-1 (**5**), and resveratrol (**1a**) also showed high cytotoxicity in mouse macrophages.<sup>77</sup> On the basis of in vitro, ex vivo, and animal studies, resveratrol (**1a**) and derivatives inhibit cellular events associated with the beginning, promotion, and progression of tumors.<sup>82–84</sup> Resveratrol inhibits free radical formation, which will inhibit tumor formation; it acts as an antimutagen, because it induces the quinone reductase able to detoxify carcinogens; moreover, it inhibits the development of preneoplastic lesions.<sup>15</sup>

Depending on the concentration and cell type, resveratrol (**1a**) can act as a pro-oxidant molecule, and this effect could be an important action mechanism for its anticancer and pro-apoptotic properties.<sup>85</sup>

Arachidin-1 (**5**), arachidin-3 (**7**), isopentadienylresveratrol (**3**), and resveratrol (**1a**) have been isolated from germinating peanut kernels and characterized as antioxidant and anti-inflammatory agents. Some studies have indicated that **1a** induces programmed cell death (PCD) in human leukemia HL-60 cells, and the anticancer activity of these stilbenoids was determined in the same lineage cells. Arachidin-1 (**5**) had the highest efficacy in inducing PCD in HL-60 cells, with an approximately 4-fold lower EC<sub>50</sub> than resveratrol (**1a**), causing mitochondrial membrane damage, activation of caspases, and nuclear translocation of apoptosis-inducing factor and resulting in chromosome degradation and cell death. Therefore, **5** induces PCD in HL-60 cells through caspase-dependent and caspase-independent pathways. Arachidin-1 (**5**) demonstrates its efficacy as an anticancer agent by inducing caspase-independent cell death, which is an alternative death pathway of cancer cells with mutations in key apoptotic genes.<sup>86</sup>

Oral administration of resveratrol at a daily dose of 15 mg/kg was effective as chemopreventive treatment for pulmonary metastasis of the challenged CT26 cells. More than 57.1% of the CT26-challenged BALB/c mice treated with resveratrol were free of tumor nodules in their lungs. Of further merit is the observation that resveratrol-treated mice that survived were highly resistant (100%) to tumor colonization by the second challenge of CT26 cells.<sup>87</sup>

Hypotin, a protein isolated from *Arachis* seeds, showed anti-proliferative activity toward human liver hepatoma Bel-7402 cells.<sup>88</sup>

Isoflavones are an important group of the phytochemicals that have been reported not only to have anticarcinogenic properties but also to play a role in the mitigation of osteoporosis in postmenopausal women.<sup>30</sup>

**Antifungal Activity.** The protein hypogin was isolated from seeds of peanut and shows inhibitory activity on the growth of the

fungi *Mycosphaerella arachidicola*, *M. berkeleyii*, *Fusarium oxysporum*, and *Coprinus comatus*.<sup>89,90</sup> Hypotin exerted potent antifungal action against various fungal species, including *Pythium aphanidermatum*, *Botrytis cinerea*, *Alternata alternata*, *Physalospora piricola*, *Fusarium solani*, and *F. oxysporum*.<sup>88</sup> From roots of peanut two antifungal proteins named PAFP-I and PAFP-II were purified to homogeneity and characterized, and these showed strong in vitro growth inhibition of *Trichoderma viride*, *B. cinerea*, and *Cladosporium* spp.<sup>91</sup>

The chromone **17** presented antimicrobial activity against soil pathogenic fungi *R. solani* and *Sclerotium rofsii*.<sup>92</sup> This suggests **17** plays a role in the protection of peanuts against fungal contamination, together with resveratrol (**1a**) and derivatives. Furthermore, the stilbene derivative **3** was inhibitory to both spore germination and hyphal extension of the fungus *Aspergillus flavus*.<sup>20</sup>

**Antibacterial and Antiproliferative Activity.** The aqueous extract from peanut leaves presented antibacterial activity against *Enterobacter aerogenes* and *Klebsiella pneumoniae*.<sup>72</sup> The ethanol extract was also active against *K. pneumoniae*. In contrast, these extracts were inactive against *Escherichia coli*, *Proteus mirabilis*, *Proteus vulgaris*, and *Salmonella typhimurium*.<sup>72</sup>

Hypotin exerted antibacterial activity toward the Gram-positive bacterium *Staphylococcus aureus*. However, this protein did not present any effect against Gram-negative strains.<sup>88</sup>

**Antioxidant Effects.** The antioxidant activity of peanuts has been widely reported. Several authors describe different models to assess this activity,<sup>29,93,94</sup> usually attributed to the phenolic contents.<sup>39,95</sup> The methanol extract from peanut presented 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging activity. The isolated stilbenes resveratrol (**1a**), IPD (**3**), arachidin-1 (**5**), and arachidin-3 (**7**) displayed potent antioxidant activity; in particular, arachidin-1 (**5**) showed equivalent or even better antioxidant activity than BHT did.<sup>76</sup> The compounds quercetin (**19b**), 3,4-dihydroxybenzoic acid (**33b**), ferulic acid (**34a**), and 4-hydroxycinnamic acid (**34b**) presented potent antioxidant activity in DPPH as well as ABTS assays.<sup>29</sup>

In dry-roasted peanuts, *p*-coumaric acid (**34b**) seems to be responsible for the major antioxidant activity among the isolated polyphenols.<sup>39</sup> The antioxidant capacity of whole extracts from roasted peanut skins was determined by various methods (i.e., total antioxidant capacity, ORAC, DPPH test, and reducing power), and the results showed that these extracts present high antioxidant activity, mainly due to the polyphenol content.<sup>37</sup>

The volatile fraction from a Pakistani cultivar of peanut exhibits antiradical activities by both DPPH and phosphomolybdenum complex methods, as well as an antioxidant potential similar to that of butylated hydroxytoluene (BHT).<sup>96</sup>

**Hypoglycemic and Hypolipidemic Activities.** Frequent nut consumption, including that of peanut, is associated with a reduced risk of developing diabetes and cardiovascular disease. The exact mechanisms are not known but may relate to beneficial changes in blood lipids and reduction in oxidative damage and inflammatory biomarkers.<sup>97</sup> The low-density lipoprotein-cholesterol (LDL-C)-lowering response of peanut studies is greater than expected on the basis of the blood cholesterol-lowering equations that are derived from changes in the fatty acid profile of the diet. Thus, in addition to a favorable fatty acid profile, peanuts contain other bioactive compounds that explain their multiple cardiovascular benefits.<sup>71</sup>

Peanut shell ethanol extract was screened for inhibitory effects on pancreatic lipase (PL) and lipoprotein lipase (LPL) activities

as well as on lipolysis of 3T3-L1 adipocytes. Treated Wistar rats showed increased fecal lipid excretion compared to that of the control group. Body weight, body weight gain, and liver size were significantly lower in rats fed the high-fat diet with 1% of extract than in those fed the high-fat diet alone. Additionally, the rats treated with peanut extract showed reduced triacylglycerol content in the liver, as well as serum glucose and insulin. The observed decline in intracellular lipolytic activity of cultured 3T3-L1 adipocytes suggests that peanut ethanol extract may reduce the levels of circulating free fatty acids. The observed effects may, at least in part, be attributed to the fat absorption inhibition in the digestive tract and the decrease in adipocyte lipolysis.<sup>98</sup> Also, resveratrol (**1a**) presented reversed inflammation-related adverse changes in adipokines, facilitated insulin signaling transduction by phosphorylation modification of IRS-1, and improved insulin sensitivity in 3T3-L1 cells.<sup>78</sup>

In an experiment with streptozotocin-induced diabetic rats, diet supplementation with peanut in the diabetic group led to significantly higher high-density lipoprotein-cholesterol (HDL-C) levels and lower atherogenic index (AI) levels compared to a control group. In addition, peanut consumption increased glutathione (GSH) levels significantly in both control and diabetic groups, showing that peanut consumption may improve oxidant-antioxidant status in healthy and diabetic rats without increasing blood lipids, suggesting that peanut consumption may have protective effects against cardiovascular complications of diabetes.<sup>99</sup>

The aqueous extract from groundnuts was evaluated for hypoglycemic and hypolipidemic activity on alloxan-induced diabetic rats. The extract promoted a decrease in glucose level, as well as causing a drop in serum triglyceride, total cholesterol, LDL-C, and HDL-C in both normal and diabetic rats.<sup>68</sup> Because of their structure, stilbenes, if absorbed, could accumulate at the water-lipid boundary and might therefore protect LDLs and cellular membranes from oxidative damage.<sup>15</sup> Recent human clinical trials have demonstrated the cardiovascular protective properties of *A. hypogaea* in decreasing LDL-C without reducing HDL-C.<sup>100,101</sup> Peanut, peanut oil, and fat-free peanut flour reduced the cardiovascular disease factor and the development of atherosclerosis in animals consuming an atherosclerosis-inducing diet.<sup>101</sup>

A 30-week, randomized, crossover trial study conducted with healthy Ghanaian adults suggested that regular consumption of peanuts lowers the total cholesterol and triacylglycerol concentrations.<sup>102</sup> In addition, peanut oil consumption can elicit significant blood pressure reduction in normolipidemic adults.<sup>103</sup>

The protein arachin and its hydrolysis products are at least partly responsible for the hypotensive activity of peanuts, due to angiotensin I-converting enzyme (ACE) inhibition activity.<sup>104</sup>

**Antiplatelet Aggregation Activity.** The antiplatelet activity of phenolic compounds isolated from *A. hypogaea* was determined in washed rabbit platelets. Eriodictyol (**18**), luteolin (**19a**), chrysoeriol (**19c**), 8-isopentenyl-luteolin (**20a**), 8-isopentenylchrysoeriol (**20b**), and the luteolin derivative **21** inhibited platelet aggregation induced by arachidonic acid, collagen, platelet-activating factor (PAF), and thrombin in a concentration-dependent manner.<sup>27</sup>

Fat-free peanut flour, peanuts, and peanut oil were evaluated for their effects on cardiovascular disease risk factors in male Syrian golden hamsters. All samples (fat-free peanut flour, peanuts, and peanut oil) were able to retard the development of atherosclerosis in animals consuming an atherosclerosis-inducing diet.

In addition, the results showed they were able to retard the increase of aortic cholesteryl ester, a primary metabolic parameter associated with the development of atherosclerosis, suggesting that peanuts, peanut oil, and fat-free peanut flour retard the development of atherosclerosis.<sup>101</sup>

**Enzyme Inhibition.** Water-soluble fractions from peanut skins present the ability to inhibit hialuronidase activity, because of the presence of tannin and proanthocyanidins.<sup>38</sup>

Protease inhibitors presenting low molecular weights were isolated from peanut seeds. They were able to inhibit bovine trypsin and chymotrypsin.<sup>105–107</sup>

The protein hypogin presents suppressive action on human immunodeficiency virus (HIV) reverse transcriptase and enzymes associated with HIV infection, including  $\alpha$ - and  $\beta$ -glucosidase.<sup>89</sup>

**Sedative and Hypnotic Effect.** The aqueous extract from *A. hypogaea* leaves presented a mildly hypnotic effect on sleep ameliorations in rats.<sup>108</sup>

**Other Effects.** Clinical trials reveal little or no weight change with inclusion of various types of nuts in the diet over 1–6 months, and mechanistic studies indicate this is largely attributable to the high satiety properties of nuts. Additionally, due to resistance of the cell walls of nuts to degradation in the intestinal tract and poor bioaccessibility of lipids, there is a limited efficiency of energy absorption. The literature suggests nuts may be included in the diet, in moderation, to enhance palatability and nutrient quality without posing a threat of weight gain.<sup>103</sup> Also, the consumption of peanuts may augment energy expenditure, suggesting that this food may be useful in the management of obesity.<sup>109</sup>

Allelopathy includes both positive and negative effects of one plant or substance on another through the environment. It plays a key role in both natural and managed ecosystems. In agroecosystems, several weeds, crops, agro-forestry trees, and fruit trees have been shown to exert an allelopathic influence on the crops, adversely affecting their germination and growth. The chromone 17, isolated from peanut shells, presents phytotoxicity (radicle elongation).<sup>92</sup> Also, 17 can inhibit the germination of velvetleaf (*Abutilon theophrasti* Medic) seeds.<sup>110</sup>

The procyanidin level is related to resistance of *Arachis* species against *Aphis craccivora*. The high concentration of procyanidin can inhibit the fertility of this aphid.<sup>111</sup>

The caffeic acid derivatives 36–38 and the flavonoid quercetin 19b can inhibit the development of *Spodoptera litura* larvae. The resistance of *A. paraguayensis* to attachment of these larvae seems to be due to the presence of these compounds.<sup>41</sup>

The saponin-rich fraction from hydroethanol extract of peanuts inhibits both the emergence and development of *Callosobruchus chinensis* larvae, an important pest of stored seeds.<sup>112</sup> The oil of *A. hypogaea* presented toxicity on the larval development of *C. maculatus*.<sup>113</sup>

D-Pinitol (63) presents larvicidal activity against *Aedes aegypti* and *Culex quinquefasciatus*.<sup>64</sup>

The species *A. hypogaea* is commonly remembered as a good source of oil and protein, but studies have shown that peanuts have a strong potential as functional food besides having therapeutic and other biological uses. Peanuts present great diversity of secondary metabolites, and many of them are responsible for plant defense against herbivores or pathogenic microorganisms and for response to damage in any plant tissue, as well as protection against ultraviolet radiation.

Several *Arachis* wild species have higher resistance levels to diseases when compared to *A. hypogaea* germplasm accessions,<sup>114</sup> so it is believed that those species have higher concentrations of these metabolites. Therefore, phytochemical and pharmacological studies with wild species are necessary, seeking new potential genetic resources for application in medicine, agriculture, and food science as for the commercial species.

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