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RESEARCH ARTICLE

Chemical Constituents and Pharmacological Activities of *Arachis hypogaea*. – A Review

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ABSTRACT

Peanut is one of the most important crops in the world, both for vegetative oil and as a protein source. It is the fourth important oilseed crop of the world in production after soybean, cottonseed and rapeseed. It also contains flavonoids, carbohydrate, mineral and vitamins. The previous pharmacological studies showed that peanut exerted antioxidant, hypolipidemic, antiinflammatory , analgesia mediated by opioid receptor affinity, sympathomimetic, endocrine, antimicrobial, antiparasitic, sedative, hypotensive and haemostatic effects. The present review will highlight the chemical constituents and the pharmacological and therapeutic effects of *Arachis hypogaea.*

KEYWORDS

Arachis hypogaea, Peanut, Antioxidant, Hypolipidemic, Sympathomimetic, Endocrine, Antimicrobial, Hypotensive and Haemostatic

INTRODUCTION

Peanut oil is added to ointments and medicinal oils. It is applied rectally in rectal constipation. The pharmaceutical and medical industries use peanut oil as a vehicle for medication in external, enteral or parenteral preparations; the cosmetics industry uses it in skin, sun and massage oil[1].

Peanuts and its products have been a component of the world's diet for years. It is the fourth important oilseed crop of the world in production after soybean, cottonseed and rapeseed. Oil yield of peanut was ranged from 18.6- 20.8 %. Peanut contained about 16.2 – 36% protein. These proteins are classified into albumin (water soluble), globulins (salt soluble) and glutelins (acid/alkaline soluble); the globulins constitute about 87% and consists of arachin and conarachin.

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Peanuts are known to be rich in acidic amino acid, but however deficient in essential amino acids, lysine, methionine and threonine[2-7]. Peanut contains 18% carbohydrates with a starch content of 0.5 – 5%, and sucrose content of 4 – 7%. Peanuts also contained 3% ash which is composed of 26 inorganic constituents of which phosphorus, potassium, magnesium and sulfur are high and virtually unaffected by heat[8]. It is also contains vitamins, minerals, flavonoids and many other biologically active constituents[9-16]. The pharmaceutical and medical industries use peanut oil as a vehicle for medication in external, enteral or parenteral preparations; the cosmetics industry uses it in skin, sun and massage oil[1]. Many pharmacological effects such as antioxidant, hypolipidemic, antiinflammatory, analgesia mediated by opioid receptor affinity, sympathomimetic, endocrine, antimicrobial, antiparasitic, sedative, hypotensive and haemostatic were attributed to the constituents of *Arachis hypogaea*. The aim of the present review is to highlight the

chemical constituents and the pharmacological and therapeutic effects of *Arachis hypogaea*.

Synonyms

Arachidna hypogaea (L.) Moench; *Arachis africana* Lour.; *A. americana* Ten.; *A. asiatica* Lour **.**

Common Names

English**:** Groundnut, Peanut, and Monkey nut; French: Arachide; Spanish: Mani, Cacahuete; Italian: Pistacchio di terra; German: Erdnuss; Portugese: Amendoim; Arabic: Fustic Swdani and Fustik Abeed.

Family

Papilionaceae; Fabaceae

Distribution

Arachis hypogaea is cultivated in all tropical and sub-tropical regions worldwide.

Traditional and Pharmaceutical Uses

Peanut oil is added to ointments and medicinal oils, and applied rectally in rectal constipation. It is also used in dermatology for crusting and scaling of the scalp (with hair), baby care and dry skin. Other applications include use as a bath additive for subacute and chronic eczema and for atrophic eczema and ichthyosis. The pharmaceutical and medical industries use peanut oil as a vehicle for medication in external, enteral or parenteral preparations; the cosmetics industry uses it in skin, sun and massage oil. Domestically, it is used as a salad or cooking oil that is said to lower blood cholesterol levels. Peanut oil is also used in neuralgia and dislocated joints[1].

Part Used

The oil, seeds and leaves are used medicinally for many purposes. Seeds eaten raw, boiled, roasted, salted, steamed, used in confectionary, made into peanut butter, or ground into meals of flours for breadstuffs[1].

Arachis hypogaea contained several active components including flavonoids, phenolic acids, phytosterols, alkaloids, and stilbenes[2].

Peanut kernel contains about 16.2 – 36% protein. These proteins are classified into albumin (water soluble), globulins (salt soluble) and glutelins (acid/alkaline soluble); the globulins constitute about 87% and consists of arachin and conarachin. Peanuts are known to be rich in acidic amino acid, but however deficient in essential amino acids, lysine, methionine and threonine[3].

The amino acid composition of raw peanut and defatted flour (g/100 g of edible portion respectively) were : tryptophan 0.25 and 0.51, threonine 0.88 and 1.79 , isoleucine 0.91 and 1.84, leucine 1.67 and 3.38, lysine 0.93 and 1.87 , methionine 0.32 and 0.64 , cystine 0.33 and 0.67 , phenylalanine 1.34 and 2.71 , tyrosine 1.05 and 2.12, valine 1.08 and 2.19, arginine 3.09 and 6.24 , histidine 0.65 and 1.32 , alanine 1.03 and 2.07, aspartic Acid 3.15 and 6.37, glutamic Acid 5.39 and 10.91, glycine 1.55 and 3.14, proline 1.14 and 2.30, and serine 1.27 and 2.57[4].

Peanut protein and its hydrolysate were compared with a view to their use as food additives. The effects of pH, temperature and protein concentration on some of their key physicochemical properties were investigated. Compared with peanut protein, peanut peptides exhibited a significantly higher solubility and significantly lower turbidity at pH values 2-12 and temperature between 30 and 80°C. Peanut peptide showed better emulsifying capacity, foam capacity and foam stability, but had lower water holding and fat adsorption capacities over a wide range of protein concentrations (2-5 g/100 ml) than peanut protein isolate[5].

Peanut is the fourth important oilseed crop of the world in production after soybean, cottonseed and rapeseed[6].

Oil yield and physical properties of the six varieties of *Arachis hypogaea* in Pakistan was assayed. Oil yield ranged from 18.6- 20.8 %, the state of the oil at room temperature was liquid , the odour was agreeable and the color ranged from bright , light , amber to golden yellow. The percentage (%) composition of fatty acids in the tested varieties was capric 0.0-

5.85, lauric 5.57-8.10, myristic 0.07-0.09, palmitic 4.10-4.85, palmitoleic 0.59-0.62, stearic 0.67-0.70, oleic 41.67-44.20, linoleic 19.58- 20.77, linolenic 0.12-0.14, arachidic 1.18-1.73, behenic 1.14-1.93, and lignoceric 0.10-0.17[7].

Peanut contained 18% carbohydrates with a starch content of 0.5 – 5%, and sucrose content of 4 – 7%. Peanuts also contained 3% ash which is composed of 26 inorganic constituents of which 0phosphorus, potassium, magnesium and sulfur are high and virtually unaffected by heat[8].

However, N and P concentrations decreased steadily from plant age 2 to 21 weeks; K increased nearly a full percent from week 2 to week 6 before decreasing slightly with further age; Ca and S were erratic but did not decrease significantly over the whole time period; Mg tended to increase slowly to weeks 10-12 and then decrease slightly; Mn decreased slightly throughout; Zn increased to week 6, then decreased markedly to week 21; Cu and B changed only slightly[9].

The peanut plant (Arachis hypogaea L.), when infected by a microbial pathogen, is capable of producing stilbene including resveratrol pterostilbene and arachidin series. Stilbenoids are polyphenolic compounds that are isolated from peanut plant materials strictly in the trans olefinic configuration. The trans-olefin structure of the parent stilbene skeleton is an important determinant of bioactivity. The major stilbenoids bear isopentenyl, isopentyl, or isopentadienyl moieties arising from prenylation. Prenylation plays a major role in the diversification of many natural aromatic compounds, including those from peanuts[10-14].

Eight flavonoids and two indole alkaloids were isolated from water-soluble fraction of peanut skins. Two of the flavonoid glycosides were identified as isorhamnetin 3-O-[2-O-beta-glucopyranosyl-6-O-alpha-rhamnopyranosyl]-beta-glucopyranoside and 3',5,7-trihydroxy isoflavone-4'-methoxy-3'-O-beta-glucopyranoside. The alkaloids were identified as 2-methoxyl-3-(3-indolyl)-propionic acid and 2-hydroxyl-3-[3-(1-N-methyl)-indolyl]-propionic acid[15].

Ten proanthocyanidins were isolated from the PSE. They included epicatechin-(2β→O→7, 4β→6)-epicatechin-(4β→6)-epicatechin., proanthocyanidin monomers, dimers, trimers and tetramers[16].

Pharmacological Effects

Duke et al mentioned that peanut induced the following pharmacological effects: panaleptic; antiaggregant; antiapoptotic; anticariogenic; antidiabetic; antidote; antidote; antiinflammatory; antiischemic; antioxidant; antiparkinsonian; antiradicular; antitumor, colon; anxiolytic; aperient; aphrodisiac; apoptotic; astringent; bechic; cardioprotective; cerebroprotective; chemopreventive; COX-2-inhibitor; cyanogenetic; demulcent; diuretic; emollient; estrogenic; febrifuge; fungicide; goitrogenic; hemostat; hypocholesterolemic; hypotensive; hypothermic; hypotriglyceridemic; iOS-inhibitor; lactagogue; laxative; litholytic; neuroprotective; NOinhibitor; osteogenic; pancreaprotective; pectoral; peptic; radioprotective; serotoninergic; tonic; vasoconstrictor; and vasorelaxant[17].

Antioxidant and Hypolipidemic Effects

Peanut peptide exhibited in vitro antioxidant properties measured in terms of reducing power, scavenging of hydroxyl radical, and scavenging of DPPH radical[5]. Flavonoids isolated from water-soluble fraction of peanut skins exerted free radical scavenging activity and protein glycation inhibitory effects[2, 15].

The effect of water soluble polyphenolic extract of peanut skin (PE) was investigated for its hypolipidemic properties and improvement of lipid homoeostasis in rats. 300mg/kg body weight of (PE) induced significantly reduced body weight and epididymal fat. Plasma and liver triglyceride (TG) and cholesterol (TC) levels were significantly reduced while faecal secretion of TG and TC was greatly increased upon PE administration. Liver mRNA expression of enzymes involved in fatty acid synthesis, such as fatty acid synthase (FAS),

sterol receptor element binding protein (SREBP)-1c, acetyl-CoA carboxylase (ACC1) and lipid uptake genes, such as PPARγ, were decreased, while PPARα was up-regulated by administration of PE[18].

Feeding a high-cholesterol diet with a water-soluble peanut skin polyphenol fraction to rats reduced their plasma cholesterol level, with an increase in fecal cholesterol excretion. The hypocholesterolemic effect was greater with the lower-molecular-weight rather than higher-molecular-weight polyphenol fraction. This effect attributed to some oligomeric polyphenols which reduced the solubility of dietary cholesterol in intestinal bile acid-emulsified micelles[19].

The effects of peanut (*Arachis hypogaea*) consumption on oxidant-antioxidant status and lipid profile in Streptozotocin (STZ) induced diabetic rats were investigated. Rats were given standard rat chow supplemented with 0.63 g % peanut for 12 weeks. The supplementation with peanut in the diabetic group led to significantly higher HDL-C levels and lower atherogenic index (AI) levels compared to diabetic group. Peanut consumption increased GSH levels significantly both in control and diabetic groups[20].

Most of peanet stilbenoids inhibited intracellular generation of reactive oxygen species (ROS) in PMA inducedHL-60 cells. Three stilbenids compounds produced a strongest antioxidant effect. Twelve compounds demonstrated significantly high antioxidant properties which were comparable to those of Trolox. Although, the majority of stilbenoids demonstrated moderate cytotoxicity toward HL-60 cells, but the antioxidant effect was observed at much lower concentrations confirming that the antioxidant effect was not related to cytotoxic effect[14,21].

Antiinflammatory Effects

The anti-inflammatory of proanthocyanidins isolated from peanut skin were tested on inflammatory cytokine production and melanin synthesis in cultured cell lines. Peanut skin extract (PSE, 200 µg/mL) decreased melanogenesis in cultured human melanoma HMV-II co-stimulated with phorbol-12-myristate-13-acetate. It also decreased production of inflammatory cytokines (PSE at 100 µg/mL), tumor necrosis factor-α and interleukin-6, in cultured human monocytic THP-1 cells in response to lipopolysaccharide. Proanthocyanidins of peanet showed suppressive activities against melanogenesis and cytokine production at concentrations ranging from 0.1-10 µg/mL. Among the tested compounds, suppressive activities of proanthocyanidin dimers or trimers in two assay systems were stronger than those obtained with monomer or tetramers. These data indicate that proanthocyanidin oligomers from peanut skin have the potential to reduce dermatological conditions such as inflammation and melanogenesis[2,16].

Opioid Receptor Affinity

Cho-K1 cells stably transfected with opioid receptor subtypes µ, Δ, and κ was used to assay the affinity to opioid receptors. Compound GC-143-8 was run in competition binding against all three opioid subtypes (µ, κ, and Δ). One of peanet stilbenoids showed opioid receptor affinity. Combined use of this compound and analgesic agents may result in lower amounts of the latter needed to block pain. However, it is likely that the specific position and number of hydroxy groups in the structure of the stilbenoid may be responsible for opioid receptor binding[14].

Sympathomimetic Effects

The active ingredient of A. hypogaea such as resveratrol can act as a sympathomimetic compound and induce aggregation of melanophores of tadpole B. Significant skin lightening activity of the extract of A. hypogaea and its active ingredient resveratrol was observed on the tail melanophores of tadpole. The pigment cells responded by distinct aggregation leading to skin lightening, this effect was reversible, as re-immersion in physiological saline made the melanophores return to their normal intermediate state. These

melanin aggregating effects were completely blocked by propanolol (beta blocker) and partially blocked by prazosin (alpha blocker) and were also found to be highly potentiated by reserpine[22].

Immunomodulating and Anticancer Effects

Peanut-skin procyanidin A1 inhibited degranulation downstream of protein kinase C activation or Ca^{2+} influx from an internal store in RBL-2H3 cells. Peanut skin contained large amounts of polyphenols having antiallergic effects. Peanut-skin extract (PSE) inhibited the degranulation induced by antigen stimulation of rat basophilic leukemia (RBL-2H3) cells. A low-molecular-weight fraction from PSE, PSEL, also had inhibitory activity against allergic degranulation. The polyphenol was identified as procyanidin A1. It inhibited the degranulation caused by antigen stimulation at the IC_{50} of 20.3 µM. Phorbol-12-myristate-13-acetate (PMA) and 2,5,-di(tert-butyl)-1,4-hydroquinone (DTBHQ)-induced processes of degranulation were also inhibited by procyanidin A1[23]. Peanut stilbenoids demonstrated the inhibition of NF-κB dependent transcription in SW1353 cells induced by phorbol myristate acetate (PMA) with IC50 values in the range of 12-22.5 µg/mL. Many peanut stilbenoids inhibited both NF-kB and Sp-1 at significantly lower concentrations (0.025 and <0.025 µg/mL, respectively) [14,24].

Cytotoxicity of stilbenes was determined against a panel of four human tumor cell lines [SK-MEL (malignant melanoma); KB (oral epidermal carcinoma); BT-549 (breast ductal carcinoma); and SKOV- 3 (ovary carcinoma)]; and two noncancerous cell lines [Vero (African green monkey kidney fibroblasts) and LLC-PK11 (pig kidney epithelial cells)]. More than half of the peanut stilbenoids inhibited the activity of inducible nitric oxide synthase (iNOS) in LPS-induced macrophages resulting in a decrease of nitric oxide (NO) levels. Arachidin-1 was the most potent inhibitor (IC50 = 1.9 µg/mL). Many other stilbene compounds also demonstrated considerable inhibition of iNOS activity. Moderate cytotoxicity was observed among limited number of peanut stilbenoids in a panel of mammalian kidney cells (Vero and LLC-PK11) and cancer cells (SK-MEL, KB, BT-549, and SK-OV-3) up to the peak concentration tested (25 µg/mL). The highest but moderate cytotoxicity was exhibited in all cell lines by arachidin-1[14].

Endocrine Effects

Aldosterone antagonistic action of various vegetable oils was investigated. Consistent and marked antagonism was seen only with arachis oil at all doses. The potent aldosterone antagonist is believed to be contained in the unsaponifiable portion of the oil. Antagonistism of aldosterone modified sodium reabsorption and urinary secretion of sodium and potassium. 0.05 ml of the oil in mice largely antagonized the action of 10 *ug* aldosterone[25].

A goitrogenic factor is believed to be located in the chromogenic tegument of the peanut. Arachoside and glycosides isolated from the peanuts inhibited the formation of inorganic iodine and thyroxine and resulted in a major increase in the urinary secretion of iodine and phenols.

Introduction of refined peanut oil to form 10% of the food ration of immature mice increases uterine weight[26-27].

Phytoestrogens are plant-derived compounds that structurally or functionally mimic mammalian estrogens and therefore are considered to play an important role in the prevention of cancers, heart disease, menopausal symptoms and osteoporosis. Peanut (*Arachis hypogaea* L.) showed high levels of phytoestrogens including isoflavones (formononetin and biochanin A, 729 ug/g dry weight)[28-31].

Antimicrobial and Antiparasitic Effects

Peanut seed extracts exerted antioxidative, antibacterial activities[2]. Peanut peptides also exerted antimicrobial effects. They were active against *Escherichia coli* O157:H7 and *Listeria* monocytogenes[32].

Peanut stilbenoids appear to play roles in plant defense mechanisms, they were evaluated for

their effects on economically important plant pathogenic fungi of the genera Colletotrichum, Botrytis, Fusarium, and Phomopsis[14,24,33].

The toxicity of peanet stilbenoids was evaluated on adult mosquito and mosquito larvae. Six stilbenoids showed the highest activity and high lipophilicity activity. The lipophilicity characteristics seem to play a role in the toxicity of natural peanut stilbenoids to adult. Peanut stilbenoids with higher lipophilicity rapidly induced parentheses followed by death[14].

The amoebicidal activity of ethanol extracts of Arachis hypogaea L. (peanut) was evaluated in vitro. Acanthamoeba were isolated from keratitic patients, cultivated on 1.5% non-nutrient agar, and then incubated with different concentrations of plant extracts which were further evaluated for their cysticidal activity. The results showed that all extracts had significant inhibitory effect on the multiplication of Acanthamoeba cysts as compared to the drug control (chlorhexidine) and non-treated control, and the inhibition was time and dose dependent. The ethanol extract of A. hypogaea had a remarkable cysticidal effect with minimal inhibitory concentration (MIC) of 100 mg/ml in all incubation periods, while the concentrations of 10 and 1 mg/ml were able to completely inhibit growth after 48 and 72 h, respectively. The concentrations 0.1 and 0.01 mg/ml failed to completely inhibit the cyst growth, but showed growth reduction by 64.4-82.6% in all incubation periods [34].

Sedative Effect

Peanut (*Arachis hypogaea* L.) leaf aqueous extracts (PLAE) have received a long reputation as an abirritative remedy to ease various sleep disorders. The clinical studies confirmed the hypnotic effects of Arachis hypogaea[35-36].

The sedative effects of peanut (*Arachis hypogaea* L.) leaf aqueous extracts on brain ATP, AMP, adenosine and glutamate/GABA of rats was investigated. intragastrically administrated of peanut (*Arachis hypogaea* L.) leaf aqueous extracts (PLAE, 100 and 500 mg/kg body weight BW) and peanut stem aqueous extracts (PSAE, 500 mg/kg BW) for at least 14 days. The results showed that the brain lactate were significantly elevated ($p < 0.05$) in rat cerebrums after PLAE administrations, compared with control and PSAE groups. In respect of brain energy system, significant degradations of the brain adenosine triphosphate (ATP) ($p < 0.05$) were observed in the brain-stems and even the whole brains of rats though PLAE treatments. Moreover, the brain adenosine monophosphate (AMP) were clearly decreased ($p < 0.05$) in rat cerebrum and brainstem regions, while the brain adenosine revealed an increasing propensity ($p = 0.076$) in the cerebrums of freely behaving rats. The γ-aminobutyric acid (GABA) concentrations were statistically ($p < 0.05$) enhanced and the ratios of Glutamate/GABA were simultaneously reduced ($p < 0.05$) in rat brainstems, no matter which one dose (100 or 500 mg/kg BW) of PLAE were used[37].

Hypotensive and Haemostatic Effects

Bioactive Peptides with Antihypertensive Effects against Angiotensin Converting Enzyme (ACE) [32]. The active ingredient of A. hypogaea such as resveratrol can act as a sympathomimetic compound, its effects was completely blocked by propanolol (beta blocker) and partially blocked by prazosin (alpha blocker) and were also found to be highly potentiated by reserpine[22].

There is a haemostatic principle in the peanut flour, which is said to improve the condition of haemophiliacs. The protease inhibitor acts on the fibrinolytic system, primarily as an antiplasmin[38].

Contraindications and Adverse Effects

No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. Many people are dangerously allergic to peanuts[1,17].

Dosage

As a rectal enema, use 130 ml of oil at body temperature. For use in a bath, the recommended concentration is 4 ml per 10 liters of water. Adults should bathe for 15 to 20

minutes 2 to 3 times weekly. Children and babies should bathe for a few minutes 2 to 3 time's weekly[1,17].

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