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Peanuts
A source of medically important resveratrol

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Abstract

Peanuts have a long history as a healthy snack food. Products made from peanuts have been used to provide valuable protein for the body. Although it contains a high amount of fat, most of the fat in peanuts is in the form of polyunsaturated and monounsaturated fats. Peanuts can be processed into a multitude of products from peanut butter to peanut oil to peanut candy. Due to their versatility and relative stability, these products have been used in various places from the home to the ballpark, to the school lunchroom, and even the hospital kitchen. Now, in addition to being a source of good protein, peanuts can also be cited as a source of the phytochemical, resveratrol. Resveratrol concentration varies between peanut parts, processed products, and cultivars. Several studies have shown that resveratrol may help to prevent cardiovascular disease by inhibiting adhesion of monoclonal antibodies and neutrophils to vein endothelial cells, thus preventing antherosclerosis. Resveratrol also may help prevent cancer in the promotion and progression phase by inhibiting proliferation of cancer cells and vascularization to cancer cells. With this association with resveratrol, peanuts are being touted not only as a health food, but also a functional food, capable of preventing cardiovascular problems and cancer. This overview is intended to review the functional role of resveratrol in peanuts.

Introduction

Peanuts (***Arachis hypogaea* Linn.**), a member of the Papilionaceae family, have been cultivated for its use as a non-meat protein source (Woodroof, 1973). Although peanuts may be considered a source of fat, the majority of the fat is unsaturated and, in particular, the monounsaturated fat oleic acid (Woodroof, 1973). Each product including roasted peanuts, peanut butter, and peanut oil involves a process to remove the shell and skin and further processes to either coat the remaining kernel or to grind or press it down.

Although not new to the phytochemical world, resveratrol is a phytochemical often associated with red wine and grapes, and is now associated with peanuts as well (Dixon, 2001). The de novo process involving the production of resveratrol involves the injuring of the kernel (Dixon, 2001). The level of resistance and cultivar affect the level of resveratrol found in individual peanuts (Arora and Strange, 1991; Sanders *et al*, 2000). Resveratrol content also varies between peanut products and specific parts of the peanut (Sobolev and Cole, 1999; Ibern-Gomez *et al*, 2000).

Peanut and other nut consumption and in general has shown favourable results in relationship to cardiovascular disease (Fraser *et al*, 1992; Hu *et al*, 1998). Laboratory studies involving resveratrol have shown that it may prevent monocyte and neutrophil adhesion in atherogenesis and reshape arterial cells to aid in stress (Ferrero *et al*,1998; Bruder *et al*, 2001). Studies into cancer also reveal that resveratrol may have a favourable effect on preventing cancer through acting on the promotion and proliferation phases, as well as preventing neovascularization to tumour cells (Jang *et al*, 1997; Kimura and Okuda, 2001; Wolter *et al*, 2001).

This review seeks to address the issues surrounding the presence and functional role (cardiovascular and chemopreventive) of resveratrol in peanuts, as well as the issues surrounding the processing, regulation, and health issues of peanuts and peanut products.

Nutritional composition of peanuts

Although peanuts are often associated with tree nuts, peanuts are grown in the ground. Peanuts begin as the seeds of the ovary from the peanut plant (Figure 1). Peanuts contain anywhere from 21-36.4% protein, 18% carbohydrates, and 36-54% fat (Woodroof, 1973). In their natural state, one ounce of peanuts contains at least 10% of the recommended daily intake for vitamin E, folate, niacin, magnesium, copper, phosphorus, and potassium. Of their fat content, 30-35% is polyunsaturated, and 40-45% is oleic, a monounsaturated fatty acid (Woodroof, 1973). Peanuts contain about 2.4-2.6 grams of fibre per ounce (Kris-Etherton *et al*, 2001). Peanuts, along with other legumes, are considered a part of the meat and meat alternative group in the Food Guide Pyramid (Whitney and Rolfes, 1996). However, in the diabetic exchange lists, peanut products are considered part of the fat group (American Diabetes Association 1995). Throughout the world there are several different kinds of peanuts. Each is used for a specific purpose from animal feed to the manufacture of roasted peanuts, peanut butter, peanut oil, and a multitude of other products.

Peanuts allergies

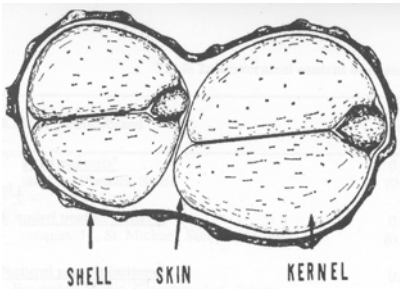
To date, peanuts are considered one of the top eight foods that cause anaphylactic reactions. Much research has been conducted into the nature of peanut especially into hereditary issues and resolution of the allergy over time in children. In a study conducted by Hourihane *et al* (1996) in USA, the prevalence of hereditary peanut allergies in children were compared between a sample of 622 individuals who filled out questionnaires, and 50 individuals who took part in skin tests and open peanut challenges. In the questionnaire portion, the researchers found that allergies in general were more common in maternal relatives than paternal relatives of children with reported peanut allergies (39% vs. 23%). It was also found that peanut allergies were even more common in relatives in the same generation (6.9% siblings vs. 1.07% aunts and uncles and 0.12% grandparents). In the skin test the researchers found that 14% of those who reported having a peanut allergy had a negative skin test and five of these individuals also had a negative peanut challenge test. Of those allergic to peanuts, 32% also were allergic to tree nuts.

Although peanut allergies do persist in some, researchers have found that in other children the allergy "resolves" after a period of time. In a study by Hourihane *et al* (1998), 30 children with persistent or resolved documented peanut allergies were given skin tests and food challenges. Neither group differed in the age of onset of peanut allergies. The average age of onset was 11 months. In the "resolvers" group, 8 of the 15 children had negative skin tests, and 5 had reactions around 4-5 mm; while 11 of the 14 "persisters" had positive skin tests greater than 6 mm. The cut-off for a positive reaction was 3 mm. Twelve of the "persisters" went on to try peanuts and had no anaphylactic reactions, the other two did not try peanuts. As with the previous study, more "persisters" were allergic to other foods (9 out of 15) than "resolvers" (2 out of 15). Commonly reported signs of allergic reactions included rash, tightening of the throat, breathing difficulties, and facial changes (swelling).

As peanut proteins are associated with allergies, questions have been raised as to the safety in consuming peanut products that do not contain proteins (such as oil). In a study by Hourihane *et al* (1997), 62 subjects allergic to peanuts were given a food challenge with refined and crude peanut oil. Crude peanut oil was differentiated as not including "degumming, refining, bleaching, and deodorisation." Although six subjects reacted to crude oil, none reacted to refined oil. The study also involved a peanut challenge at which 56 subjects had positive reactions to peanuts.

Although not all people who are documented as being allergic to peanuts

Figure 1 : Peanut structure (Woodroof, 1973)



will react to peanut products, the U.S. Food and Drug Administration is working with the Food Allergy Issues Alliance to prevent people from unknowingly ingesting foods containing even traces of allergens (U.S. Food and Drug Administration 2001a). Allergens are not always marked on the food label for several reasons. One reason is that they may be part of "Seasonings" or "Flavorings," which need not be spelled out on the label. Another reason is that they may be incorporated in the food as a result of adultery from packaging materials or machines used to make multiple different food products. Although debates still continue into the proper way to address this issue, some companies have taken to putting advisory labels on their products that alert people to the presence of such allergens as peanuts, soybeans, milk, eggs, fish, crustacea, tree nuts, and wheat.

Resveratrol and its medicinal properties

Resveratrol belong to a class of antibiotic compounds called phytoalexins. Phytoalexins are "low molecular mass natural products" made by plants for the purpose of defending the plant when it is injured or invaded (Celotti *et al*, 1996; Dixon, 2001). For example, in response to an invading fungus, resveratrol is synthesized from *p*-coumaroyl CoA and malonyl CoA (Soleas *et al*, 1997). In particular, resveratrol is classified as a stilbene (trans-3, 5, 4′-trihydroxystilbene) which is produced in a de novo process involving the addition of 4-coumaryl-CoA to 3 malonyl CoA and the use of the enzyme resveratrol synthase (Arora and Strange, 1991; Dixon, 2001).

Each ounce of peanuts contains 73 µg of resveratrol (compared to 160 µg per fluid ounce of red wine) (Lee, 1997). However, production of resveratrol and other phytoalexins vary within cultivars and stage of development. In a study by Arora and Strange (1991), peanut pods at different stages of development were sliced and subjected to normal microflora to stimulate resveratrol production. Using reverse phase high performance liquid chromatography (HPLC) separation, UV spectra, and mass spectrometry, the researchers found that resveratrol levels were higher in cultivars bred to have greater resistance to mould. Although resveratrol was not included in other tests, it was found that the production of other phytoalexins decreased, then increased halfway through development of the peanut pods.

In another study conducted by Sanders *et al* (2000) in USA cultivars and grades from three types of peanuts (Runner, Spanish, and Virginia) were stored for varying lengths of time, hand blanched or roasted, and then crushed into meal. Resveratrol was extracted from the different cultivars and from different parts of the peanuts. Overall, resveratrol amounts ranged from 0.022 µg/g in a Runner cultivar to 1.792 µg/g in a Spanish cultivar (Table 1).

Trans-resveratrol also varies with peanut processing. In research conducted by Sobolev and Cole (1999), trans-resveratrol content was compared for several types of peanut butters and other peanut products. The researchers found that roasted peanuts had the lowest readings with resveratrol concentrations from 0.018 to 0.080 µg/g while peanut

Table 1. Concentration of Resveratrol in Peanut Cultivars[a]

Peanut Type	Genotype Cultivar	Resveratrol (µg/g)	SD[b]
Spanish	Small White Spanish	1.792	0.616
Spanish	Spanette	0.126	0.107
Spanish	Pearl	0.112	0.090
Virginia	NC-18016	0.306	0.146
Virginia	Early Bunch	0.129	0.194
Runner	White's Runner	0.069	0.029
Runner	Florunner C1	0.067	0.072
Spanish	GA 207-3-4	0.057	0.066
Runner	GA 207-2	0.056	0.026
Virginia	NC-9	0.052	0.084
Runner	Florispan C1	0.049	0.087
Virginia	NC-17291	0.048	0.070
Runner	Dixie Runner	0.039	0.014
Spanish	PI-337396-FAV70	0.023	0.022
Runner	Florispan C3	0.022	0.014

[a]Sanders *et al*, 2000; [b]Standard deviation

butter had higher amounts ranging from 0.148 to 0.504 µg/g and boiled peanuts kernels had the highest from 1.779 to 7.092 µg/g. Boiled peanut hulls had even higher ranges of resveratrol concentration from 2.415 µg/g to 7.873 µg/g. In the peanut butter products, natural peanut butters brands tended to be in the middle to high range for resveratrol content compared to more processed, blended brands. Sobolev and Cole (1999) also found that Runner peanuts that tend to be less mature are higher in resveratrol content (0.716 µg/g) compared to more mature Runner peanuts like Jumbos (0.070 µg/g). In addition, oil stock or Runner peanuts that were unacceptable for raw consumption, contained higher amounts of resveratrol ranging from 1.281µg/g to 7.092 µg/g. Ibern-Gómez *et al* (2000) similarly found that the resveratrol content of natural peanut butters was, on average, higher than the content of blended brands (0.652 µg/g compared to 0.409 µg/g) (Table 2).

As a natural chemical found in peanuts and peanut products, resveratrol content does not need to follow any regulation as of yet. However, in USA manufacturers and processors of peanut products cannot make such claims as "good source of resveratrol" and "resveratrol can help to prevent cancer and cardiovascular disease" because these health claims have yet to be defined and established. In addition, when resveratrol is extracted and touted as a dietary ingredient or supplement, it also must meet the approval of the U.S. Food and Drug Administration (USFDA). As defined by the U.S. Food and Drug Administration (2001b), a dietary ingredient is "a vitamin; a mineral; an herb or other botanical; an amino acid; a dietary substance for use by man to supplement the diet." For approval to produce and sell the dietary ingredient, a company seeking to produce this dietary ingredient in supplement form must assure that the supplement solely contains the dietary ingredient in an unadulterated form, and that the supplement has documented proof of safety. This documentation is to be submitted 75 days ahead of time. Although resveratrol may not be restricted in food, it still cannot be touted in supplemental form as a miracle phytochemical.

Table 2. Resveratrol content of peanut products

Kind of product/brand	Trans-resveratrol (µg/g) (Range of means)
Roasted peanuts[a]	0.056 ± 0.005
Examples: Planters, Staffs	(0.018 - 0.080)
Blended peanut butters[b]	0.409 ± 0.023
Examples: Jif, St. Michael, Sun-pat Nestlé	(0.265 - 0.671)
Natural peanut butters[b]	0.652 ± 0.020
Examples: Monki, Glaskbak, Jori, Adams	(0.534 - 0.753)
Boiled peanuts[a]	4.120 ± 0.971
Kernels	(1.779 - 7.092)
Hulls	4.316 ± 0.612 (2.415 - 7.873)
Liquids	0.543 ± 0.002 (0.048 - 0.064)

[a]Denotes average reading of trans-resveratrol in peanut products (Ibern-Gómez *et al*, 2000).
[b]Denotes average reading of trans-resveratrol in peanut butter (Sobolev and Cole, 1999).

Role of resveratrol in cardiovascular disease

Laboratory studies concerning the effectiveness of resveratrol in preventing cardiovascular disease have also been conducted. During studies (Juan *et al*, 1999), rats given oral supplements of resveratrol at 2 µg/kg were harvested at 15, 30, and 45 minutes after administration. Samples were taken from a cardiac puncture and examined for resveratrol using spectroscopic analysis with diode array UV detection and high-performance liquid chromatography. Even after only 15 minutes of administration, 0.175 mg/L were found in harvested samples.

Several studies have demonstrated that resveratrol is an effective antioxidant (Frankel *et al*, 1993; Chanvitayapongs *et al*, 1997; Belguendouz *et al*, 1998). It inhibits lipid peroxidation of low-density lipoprotein (LDL) (Chanvitayapongs *et al*, 1997; Belguendouz *et al*, 1998), prevents the cytotoxicity of oxidized LDL (Chanvitayapongs *et al*, 1997), and protects cells against lipid peroxidation (Chanvitayapongs *et al*, 1997). It is thought that because it contains highly hydrophilic and lipophilic properties, it can provide more effective protection than other well-known antioxidants, such as vitamins C and E (Chanvitayapongs *et al*, 1997).

Reduced platelet aggregation has also been demonstrated in studies on resveratrol, further contributing to its prevention of atherosclerosis (Soleas *et al*, 1997, Rotondo *et al*, 1998). In addition to testing the relative transfer of resveratrol to the cardiovascular system, studies have also looked at the mechanisms that resveratrol uses to protect the cardiovascular system. Ferrero *et al* (1998) found that resveratrol had an effect on granulocyte and monocyte adhesion to arterial cell walls, important factors in the beginning of atherogenesis. The researchers found that even small amounts of resveratrol (1µmol/L and 100 nmol/L) effectively counteracted chemicals that stimulated vascular cell adhesion (VCAM-1) and intracellular adhesion molecules (ICAM-1) in human umbilical vein endothelial cells. Resveratrol also inhibited the adhesion of monoclonal antibodies and neutrophils to stimulated cells.

Bruder *et al* (2001) reported that resveratrol may affect the actual shape of the arterial endothelial cells, making them less susceptible to tearing from arterial stress and activating chemicals which would aid in endothelial resilience during arterial stress. Bovine pulmonary arterial endothelial cells were applied to plastic coverslips and were treated with up to 100 µM of resveratrol or left untreated. The coverslips were examined for changes in the cells. The researchers found that the cells treated with resveratrol changed from a "cobblestone to elongated and ellipsoidal" shape with as little as 25 µM. The coverslips were then subjected to simulated arterial stress and tested at two and five minutes to see how many cells remained on the coverslip. While the control did not have any remaining cells after five minutes, the treated cells did have some cells remaining after five minutes. Resveratrol also stabilized the level of chemicals activated in times of shear stress (ERK ½-P) and stimulated the release of chemicals that help to minimize oxidant damage (enzyme nitric oxide synthase).

Role of resveratrol in cancer prevention

Although few, if any, studies have been conducted on the epidemiological relationship between cancer prevention and resveratrol in peanuts, several laboratory studies have found that resveratrol may play an active role in the prevention of tumour cell growth. It has been shown to act as an antioxidant by inhibiting free radical formation, and as an anti-mutagen in rat. Jang *et al* (1997) studied the effect of resveratrol on cancerous lesions in mouse mammary glands, tumour incidence, and number of tumours in mouse mammary glands and skin cells. Resveratrol was found to decrease the per cent of lesions in mouse mammary glands. It also decreased skin cell tumour incidence by 50-88% and the number of tumours by 68-90%. The researchers also examined the specific effect of resveratrol on two of the three stages of carcinogenesis, promotion and progression. They found that resveratrol may prevent cyclooxygenase and hydroxyperoxidase activity, which play a role in the promotion of tumour cell growth through inflammation and activation of carcinogens. In addition, resveratrol may control the reproduction of "unlimited proliferative" HL-60 (proliferative) cells by prohibiting thymidine incorporation through granulocyte and macrophage formation.

Wolter *et al* (2001) studied the effect of resveratrol on the cell cycle of colon adenocarcinoma cells. The researchers found that resveratrol interfered with cell cycle growth at certain

points in the cycle, particularly the S → G2/M phase. Resveratrol also controlled levels of proteins used to imbibe impaired cell growth and tumorogenesis. In addition increased administration of resveratrol led to increased capase-3 activity, which was a marker for apoptosis of cells (a part of the normal cell cycle).

A study by Kimura and Okuda (2001) found similar results to those of Wolter *et al* (2001) with cells in Lewis lung carcinoma-bearing mice. Treatment with resveratrol led to increased apoptosis and decreased DNA synthesis. In addition, Kimura and Okuda (2001) also studied the formation of tumours on human umbilical vein endothelial cells subjected to Lewis lung carcinoma tumours. They found that resveratrol did not prevent tumour adhesion to the cells, but did prevent neovascularization (a vital part in promoting tumour growth and spread) to areas affected by the Lewis lung carninoma cells.

Health studies involving peanut consumption

Within the past few years the benefits of peanuts and the benefits of resveratrol have been discussed in association with cardiac protection and cancer prevention (Sanders and McMichael, 1998). Several studies have looked at the health benefits of regular consumption of nuts, like peanuts. In a study by Fraser *et al* (1992), researchers compared the food consumption and lifestyle habits of a group of California Seventh Day Adventists to their risk of coronary heart disease. Nut consumption options were defined as less than once a week, one to four times a week, and five or more times a week. Researchers found that the people in this population who had higher levels of nut consumption tended to have a lower risk of coronary heart disease (1.00, 0.78, 0.49, respectively with increased consumption), even in old age (1.00, 0.71, 0.46). Common nut selection for people in this population included peanuts, almonds, walnuts, and other nuts.

A similar study conducted by Hu *et al* (1998) involved the Nurses Health Study. As with the Seventh Day Adventist study, the Nurses Health Study involved a survey of incidences of coronary heart disease and compared these incidences to the dietary and lifestyle practices of the subjects. Consumption of nuts were grouped into almost never, one to three times per month to once per week, two to four times per week, and five or more times per week. When adjusted for other factors, consumption of nuts at least five times a week led to lower risk (0.71). Peanut and peanut butter were also assigned separate categories in this study. Peanut consumption resulted in a similar reduced risk of 0.66 at two to four times per week. Peanut butter consumption was only slightly associated with lower coronary heart disease risk at 0.92 (Table 3).

Table 3. Risk[a] of Coronary Heart Disease (CHD) events compared to nut consumption

Cardiac Event (Study)	Nut Consumption (Peanut Consumption – Hu *et al*. 1998 only)			
	Almost never	-3/month to 1/week[b]	At least 2-4 times/week[c]	≥5 times/week
Fatal CHD				
(Hu *et al*. 1998)	1.0	0.76	0.60	0.60
(Fraser *et al*. 1992)	N/A	1.00	0.76	0.52
Non-Fatal Myocardial Infarcation (CHD)				
(Hu *et al*, 1998)	1.00 (1.00)	1.00 (0.96)	0.89(0.66)	0.71 (N/A)
(Fraser *et al*, 1992)	N/A	1.00	0.78	0.49

[a]Risk has been adjusted for other factors such as age, dietary pattern, exercise, sex, etc.

[b]Defined as < 1 time/week in Fraser *et al*, 1992.

[c]Defined as 1-4 times/week in Fraser *et al*, 1992.

Conclusion

Peanuts have long been referred to as health foods for their high protein content. Several processing techniques allow peanuts to be made into a wide variety of products to suit many people's needs. However, with rising concerns over allergies due to peanuts, steps are being taken to ensure that even minute levels of peanuts are reported on consumer packaging. Peanuts, in addition to being high in protein, also contain resveratrol (a cardioprotective and chemopreventive substance). Studies continue into the role of resveratrol in inhibiting crucial steps in cardiovascular disease and cancer formation, as well as physiological steps (arterial endothelial cell formation and neovascularization to tumours). Although resveratrol has more often been associated with red wine grape skins in the past, its link to other foods such as peanuts, poses a new potential for increased consumption. As rising numbers of studies continue to support the role of resveratrol in preventing cancer and cardiovascular disease, as well as investigate the resveratrol content of peanut products, the reputation of peanuts as a nutritionally important food may be enhanced by its non-nutritional, functional role in the body.

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