



Serum Lipid Profile of Adrenaline-induced Hypertensive Rats Administered with Aqueous Extract of *Arachis hypogea* Testa

**A. Y. Kabiru^{1*}, B. I. Muhammad², M. H. Garba³, M. M. Ndamitso⁴, Y. Garba⁵
and F. M. Madaki¹**

¹Department of Biochemistry, Malaria and Trypanosomiasis Research Unit, Federal University of Technology, P.M.B. 65, Minna, Niger State, Nigeria.

²Ibrahim Badamasi Babangida Specialist Hospital, Minna, Niger State, Nigeria.

³Department of Animal Production Technology, Federal College of Wildlife Management, P.M.B. 268, New Bussa, Niger State, Nigeria.

⁴Department of Chemistry, Federal University of Technology, P.M.B. 65, Minna, Niger State, Nigeria.

⁵Department of Biological Sciences, Federal College of Education, P.M.B. 39, Kontagora, Niger State, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Author AYK designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors BIM, MHG and FMM managed the literature searches and analyses of the result obtained. Authors MMN and AYK discussed the result citing relevant references. Author BIM also managed the experimental animals and process. Author YG identified the species of plant. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JOCAMR/2016/26861

Editor(s):

(1) Nawal Kishore Dubey, Centre for Advanced Studies in Botany, Banaras Hindu University, India.

Reviewers:

(1) Enyinnaya Anthony Ogbonnaya, University of Port Harcourt, Nigeria.

(2) Ntchapda Fidèle, University of Ngaoundéré, Cameroon.

Complete Peer review History: <http://www.sciencedomain.org/review-history/16446>

Original Research Article

Received 6th May 2016
Accepted 8th August 2016
Published 5th October 2016

ABSTRACT

Background: Hypertension is one of the leading causes of mortality and morbidity globally. Dyslipidemia is an index of hypertension that has also been identified as a risk factor in the development of coronary heart diseases.

Aim: This research set to investigate the potency; validate the traditional claim on the use *Arachis hypogea* testa in the management of hypertension in experimental rats.

*Corresponding author: E-mail: akabir63@yahoo.com;

Methodology: Thirty Albino Wister rats were grouped into six of five rats each. Hypertension was induced in Groups I to V animals by administering them with 0.1ml adrenaline intraperitoneally for six consecutive days. The rats in groups I to III were administered 400, 600 and 800 mg/kg body weight of *Arachis hypogea* testa extract respectively for seven days. Group IV was treated with a standard hypotensive drug – Propanolol, to serve as positive control, while rats in Group V were administered normal saline to serve as negative control and group VI rats were not induced with adrenaline but administered normal saline as placebo.

Results: The extract at a dose of 800 mg/kg body weight exhibited a significant effect on hypertensive rats compared to the standard drug-Propanolol in correcting the dyslipidemia caused by adrenaline - induced hypertension after seven days of treatment. There were significant increases in total cholesterol, HDL-Cholesterol, and Triglyceride levels in the group treated with 800 mg/kg body weight and the drug ($P = 0.05$), while the LDL-Cholesterol level for animals in the same groups were significantly lowered ($P= 0.05$) compared to the higher values obtained for the induced, untreated control group.

Conclusion: The results of this study demonstrated the ability of the aqueous extract of *A. hypogea* testa to significantly decrease LDL-cholesterol and increase HDL-cholesterol concomitantly in adrenaline-induced hypertensive rats, thus justifying its use in Nigerian traditional medical practice to manage hypertension.

Keywords: Hypertension; LDL-cholesterol; HDL-cholesterol; *Arachis hypogea*; dyslipidemia.

1. INTRODUCTION

Hypertension is one of the most common health challenges in the modern times. The prevalence is on the rise, particularly in the urban areas. Recent studies have shown that the prevalence of hypertension in Nigeria is 33%, and there is great possibility that this rate will rise in the nearest future [1,2].

Lipid profile is an index for determining the susceptibility of individuals to hypertension. The profile is used to determine the risk of coronary heart diseases. The concentration and relative ratio of lipids to one another are among the best indicators of whether an individual is susceptible to heart attack or stroke resulting from atherosclerosis or blockage of the blood vessels [3,4,5].

Lipid profile assay checks the concentration of Total cholesterol, Triglycerides, Low-Density Lipoprotein-Cholesterol (LDL-C) and High-Density Lipoprotein –Cholesterol (HDL-C). The LDL-C is often referred to as bad cholesterol, while HDL-C is often referred to as good cholesterol. Sometimes the profile may include Very-Low density Lipoprotein-Cholesterol (VLDL-C) and non-HDL-C [6].

Abnormalities in lipid profile have also been identified as an independent risk factor in essential hypertension by many researchers from various parts of the world [7,8,9,10,11,12]. Abnormalities in lipid profile in hypertensive

patients have been identified as a major risk factor in the development of Coronary Heart Diseases (CHD), Cerebro Vascular Accidents (CVA) and stroke [5]. It has been observed that various epidemiological studies and traditions suggest that there may be a connection between frequent nut consumption and a reduced incidence of Coronary heart disease [13].

In normal circumstances, circulating adrenaline plays an insignificant role in control of blood pressure in man and other animals such as rats. A small proportion of adrenaline secreted by the adrenal medulla is accumulated in sympathetic nerve endings and may be re-released by sympathetic nerve stimulation. Pharmacological studies recently conducted on animal models have revealed that adrenaline acts on a presynaptic beta-receptor on sympathetic nerve endings to facilitate noradrenaline release, and this observation led to the proposal that, adrenaline re-released from these nerve endings is therefore a functionally important "co-transmitter". Based on the aforementioned fact, it could be expected that Intermittently elevated secretion of adrenaline from the adrenal medulla could therefore lead indirectly to a sustained increase in neuronal release of noradrenaline and hence to hypertension [14].

Arachis hypogea (pea nut) is nutritionally rich and has several medicinal uses. It has been used locally to manage several abnormalities like diabetes, hypertension, and hemophilia. It has

also been shown to reduce the risk of cancer, cardiovascular diseases and ageing [15,16]. These health benefits in peanuts have been attributed to their composition of mono- and polyunsaturated fatty acids, phytosterols (plant sterols) and phenols like resveratrol among others [17,18,19].

Phytosterols, due to their structural similarity with cholesterol, inhibit its intestinal absorption, thereby lowering total plasma cholesterol and LDL levels [20]. Peanut sterols that have been identified are β -sitosterol, campesterol, stigmasterol and brassicasterol [21].

Peanuts contain significant amount of resveratrol, a phenol belonging to the stilbene group of phenolic compounds. This antioxidant compound was studied for potential anti-aging effects and also associated with reduced cardiovascular disease and reduced cancer risk. This compound is among the major constituents of the pea nut testa [22,23]. It has recently been found that the average amount of resveratrol in one ounce of commonly eaten peanuts (15 whole peanut kernels) is 73 μ g [24]. It also has several attributes that may provide protection from atherosclerosis, anti proliferative, and pro-apoptotic properties against breast, colon, prostatic, and leukemia cells [25,26].

Because of high incidence and morbidity associated with hypertension, various drugs and regimens have been suggested for its control in populations with high incidence rate. Many new drugs have been introduced which may demonstrate better efficacy but possess serious side effects. Current researches in the field of drug are focused towards herbal and mineral preparations which are traditionally used as potential therapeutic agents in the prevention and management of cardiovascular diseases [27].

2. MATERIALS AND METHODS

2.1 Collection of Seed Sample and Preparation of Extract

Arachis hypogea seeds were bought in Kure Market in Minna, North Central part of Nigeria in the month of November. The seeds were identified at the Biological Sciences Department of Federal University of Technology Minna.

The seeds were dried and the testa removed manually. It was then dried at room temperature,

pulverized to powdered form, and then stored in polythene bag and sealed until required for the study. One hundred grams (100 g) of the powdered groundnut testa was extracted in 1500 ml of distilled water sequentially for 72 hours (the extract was filtered after every 24 hours and replaced with distilled water of the same volume). The extract was filtered using a Muslin sieve cloth and concentrated by removing the solvent using a rotary evaporator and further dried on a water bath. The semi-solid filtrate was then stored in the refrigerator at 4°C.

2.2 Animal Model

Albino Wistar rats of average weight 160 ± 15 g were purchased at the College of Health Sciences, Benue State University, Makurdi, Nigeria. The rats were transported to Federal University of Technology, Minna, and allowed to acclimatize in the departmental laboratory for two weeks. The rats were fed with poultry feed (chick mash) purchased from *Vital feed* (Nasko feeds Nig. Ltd, Jos, Nigeria) and water was given *ad libitum*. The study was conducted in compliance with the internationally accepted principles of laboratory animal use and care as contained in the Canadian Council on Animal Care [28] guidelines for Animal use.

2.3 Animal Grouping and Induction of Hypertension

Thirty Albino Wister rats were grouped into six of five rats each. Groups I to V were induced with hypertension by administering 0.1 ml adrenaline into each animal intraperitoneally using 1 ml disposable syringe for six consecutive days until they were confirmed hypertensive using the procedure described by Omale and Ebiloma [29]. Subsequently, the rats in groups I to III were administered 400, 600 and 800 mg/kg body weight of *Arachis hypogea* testa extract respectively for seven days. Group IV was treated with a reference hypotensive drug – Propranolol. Group V was administered normal saline (Control) and group VI (Not induced with hypertension) was also administered normal saline as placebo.

Group I: *Arachis hypogea* extract (400 mg/kg body weight)

Group II: *Arachis hypogea* extract (600 mg/kg body weight)

Group III: *Arachis hypogea* extract (800 mg/kg body weight)

Group IV: Positive control group treated with propranolol (80 mg/kg body weight)

Group V: Hypertensive rats (negative control) - administered normal saline

Group VI: Normal rats (not induced) - administered normal saline as placebo.

2.4 Dose Preparation of Hypotensive Drug (Propranolol)

The daily dose of Propranolol for human is 80 mg/70 kg body weight. The average body weight of hypertensive rats were determined and based on this, the daily dose was calculated. The drug was dissolved in normal saline and administered intraperitoneally using 1 ml syringe for six days.

2.5 Dose Preparation of the Plant Extract

A measured weight (1 g) of the extract was dissolved in a given volume of normal saline (10 ml) to obtain a concentration of 100 mg/ml stock solution. From this, dosages of 400, 600 and 800 mg/kg body weight/day were measured and administered by cannulation to groups I- III for seven days.

2.6 Analyses of the Biochemical Parameters

After seven days of treatment, the animals were sacrificed based on the method described by Omale and Ebiloma [29]. The blood was collected in a tube pre coated with Ethylenediaminetriacetate (EDTA) and centrifuged at 2000 g, the clear serum from the centrifuged blood was collected. Subsequently, blood glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides were determined using commercial reagent kits developed by DIALAB, Austria.

3. RESULTS

The result in Table 1 shows the effect of the extract on glucose level of rats administered different doses. The level of glucose after seven days of administration of extract was not significantly different in the groups administered 800 mg/Kg bodyweight/day and Propranolol, compared to normal rats thus indicating that the effect of the extract at the highest dose and the standard drug was same.

The results in Tables 2, 3, 4 and 5 show the effect of the extract on the lipid profiles of rats administered different doses. The aqueous extract demonstrated appreciable hypotensive potential in a dose-dependent pattern. The extract administered at 800 mg/kg bw demonstrated a significant hypolipidemic activity that was comparable to that exhibited by the reference drug – Propranolol. In both cases, the dyslipidemia caused by adrenaline - induced hypertension in the animals was reversed after seven days of treatment. There was significant increase in Total Cholesterol, HDL-Cholesterol, and Triglyceride values in the group treated with 800 mg/kg body weight/day and the standard drug ($P = 0.05$), while the LDL-Cholesterol level was significantly lowered ($P = 0.05$). However, LDL - Cholesterol level was higher in the induced but untreated control group.

Table 1. Effect of the extract on the blood glucose levels of the animals

Group	Dosage of the extract (mg/Kg)	Glucose conc. (mg/dl)
1	400	116.40 ± 6.37 ^c
2	600	50.20 ± 10.46 ^a
3	800	105.0 ± 9.67 ^{bc}
4 Propranolol	80	103.00 ± 8.01 ^{bc}
5 Control	-	88.60 ± 3.32 ^b
6 Normal rats	-	105.60 ± 10.62 ^{bc}

The data are expressed as mean ± Standard Error of mean (SEM). Values carrying different superscripts differ significantly at $P < 0.05$

Table 2. Effect of the extract on the serum triglyceride levels of the animals

Group	Dosage of the extract (mg/Kg)	Triglyceride conc. (mg/dl)
1	400	31.81 ± 6.21 ^a
2	600	38.18 ± 5.01 ^a
3	800	105.76 ± 5.72 ^b
4 Propranolol	80	104.24 ± 7.42 ^b
5 Control	-	44.24 ± 7.43 ^a
6 Normal Rats	-	126.59 ± 15.05 ^b

The data are expressed as mean ± Standard Error of mean (SEM). Values carrying different superscripts differ significantly at $P < 0.05$

4. DISCUSSION

Peanuts contain high amounts of both mono- and polyunsaturated fats which have been generally shown to lower total cholesterol and the

incidence of heart diseases [30]. Hypertension and dyslipidaemia are well known to frequently co-exist. Cardiovascular disease (CVD) risk is synergistically enhanced when there is dyslipidaemia and for this reason, both conditions should be treated together [31,32,33].

Table 3. Effect of the extract on the serum cholesterol levels of the animals

Group	Dosage of the extract (mg/Kg)	Cholesterol conc. (mg/dl)
1	400	32.76 ± 5.57 ^a
2	600	81.64 ± 8.48 ^d
3	800	56.51 ± 5.70 ^{bc}
4 Propanolol	80	69.14 ± 9.52 ^{cd}
5 Control	-	41.54 ± 3.80 ^{ab}
6 Normal rats	-	78.00 ± 10.04 ^{cd}

The data are expressed as mean ± Standard Error of mean (SEM). Values carrying different superscripts differ significantly at $P < 0.05$

Table 4. Effect of the extract on the serum LDL-C levels of the animals

Group	Dosage of the extract (mg/Kg)	LDL conc. (mg/dl)
1	400	19.33 ± 0.78 ^{ab}
2	600	20.11 ± 0.59 ^{ab}
3	800	13.67 ± 1.16 ^a
4 Propanolol	80	23.00 ± 1.34 ^b
5 Control	-	30.45 ± 4.55 ^c
6 Normal Rats	-	24.84 ± 2.80 ^{bc}

The data are expressed as mean ± Standard Error of mean (SEM). Values carrying different superscripts differ significantly at $P < 0.05$

In this study, the glucose level of the group administered the highest dose of the extract (800 mg/kg bodyweight/day) was not significantly different from the normal (un-induced, un-treated group) and the standard drug treated group (Table 1). This is an indication that the extract and the standard drug may be acting in the same way in their effect on serum glucose. However, the serum glucose level in the group administered 600 mg/kg body weight of the extract was found to be significantly lower (50.20 ± 10.46 mg/ml) compared to other treated groups, implying that at this dose the extract hypoglycemic, thus reversing the effect of adrenaline (used to induce hypertension) which naturally raises the serum glucose level.

Table 5. Effect of the extract on the serum HDL levels of the animals

Group	Dosage of the extract (mg/Kg)	HDL conc. (mg/dl)
1	400	8.00 ± 5.11 ^a
2	600	53.89 ± 8.50 ^c
3	800	21.73 ± 5.51 ^{ab}
4 (Propanolol)	80	25.30 ± 7.57 ^{ab}
5 Control	-	4.27 ± 7.38 ^a
6 Normal rats	-	36.00 ± 8.14 ^{bc}

The data are expressed as mean ± Standard Error of mean (SEM). Columns carrying different superscripts differ significantly at $P < 0.05$

The effect of the extract on serum triglycerides was observed to be dose-dependent with the highest dose, 800 mg/kg bodyweight/day, producing a significantly high serum triglycerides level ($P = 0.05$) comparable to that of the standard drug – treated group and the normal group (un-induced, untreated) (Table 2), while lower doses of the extract produced significantly lower levels of serum triglycerides comparable to the induced but untreated group. The results obtained in this study regarding the effect of the extract on glucose and triglycerides does not agree with the results from previous studies [23,34,35,36]. They all reported that *A. hypogea* extract elicited hypolipidemic and hypoglycemic effect in alloxan - induced diabetic rats. Mona et al. [37] and Ramesh et al. [38] also reported that dietary pea nut oil decreased serum glucose and triglyceride in streptozotocin - induced diabetic rats. Possible reasons for variations in the result obtained in this study could be attributed to the fact that since adrenaline facilitates the breakdown of glycogen to glucose, the adrenaline - induced rats became hyperglycemic and hyperlipidemic as a result of the increase in the activity of adrenaline on the system, and the extract did not reverse the trend.

Studies have shown that elevation in serum total cholesterol, LDL-C, and Triglycerides are among the salient anomalies that are observable in hypertensive humans. More so, high levels of LDL have been identified as the major factor in obesity, atherosclerosis and other related diseases [39,40,41,42,43,44].

The level of total cholesterol was not consistent in the extract-treated groups because the lowest dose used (400 mg/kg bodyweight) caused a decrease in total cholesterol level that was

significantly different from all other groups. The effect was therefore not dose-dependent.

This increase in the total cholesterol is attributable to the rise ($P < 0.05$) in the HDL-cholesterol in Table 5 because total cholesterol is the sum of HDL and LDL cholesterols. Similarly, Table 5 shows that the extract significantly lowers LDL-cholesterol at 800 mg/kg body weight much more than the reference drug. This is plausible because concomitant reduction of LDL-cholesterol and increase in HDL-cholesterol have been identified as good indicators in reducing cardiovascular diseases. Several researches in the past have shown that low level of HDL cholesterol is an important indicator of increased cardiovascular risk. There is also strong epidemiological evidence that low HDL-C is an independent risk factor for CVD with strong suggestions that interventions to increase HDL-cholesterol will yield clinically significant outcome benefits [45,46,47].

The Multiple Risk Factor Intervention Trial [48] showed that each decrease in HDL-cholesterol of 1 mg/dL (0.03 mmol/L) was associated with an increase in the risk of coronary heart disease of 2% in men and 3% in women. It has been shown that a 1% reduction in HDL-C is associated with a 2-3% increase in CHD risk. Clinical and experimental evidence show that HDL-Cs exert multiple anti-atherogenic and antithrombotic effects that together are consistent with a marked reduction in the risk of a morbid cardiovascular event, supporting an anti-atherogenic role for HDL-cholesterol [49,50].

The exact mechanisms by which a low HDL-C increases CVD risk has however not been fully elucidated, though experimental studies suggest a direct role for HDL-C in promoting cholesterol efflux (reverse cholesterol transport) from foam cells in the atherosclerotic plaque depots in blood vessels to the liver for excretion. HDL-C also exhibits potent anti-inflammatory and antioxidant effects that inhibit the atherogenic process [51,52,53].

5. CONCLUSION

Findings from this research clearly showed that aqueous extract of *A. hypogea* testa has significantly decreased and increased LDL-cholesterol and HDL-cholesterol respectively in adrenaline induced hypertensive rats, and therefore gives credence and scientific justification to the use of *A. hypogea* testa by

trado-medical practitioners to treat hypertension. Since peanuts are among the common diet of humans all over the world, the above scientific appraisals further prove the nutraceutical significance. Phytosterols are among the functional components of peanuts that are responsible for reduction of blood cholesterol, particularly LDL-cholesterol [54,55,56,57]. The mechanism of action for phytosterols is still unclear. One of the suggested mechanisms is that phytosterols, being more hydrophobic than cholesterol, have a higher affinity for micelles and may compete with cholesterol for incorporation into mixed micelles in the intestinal tract, thus resulting in reduced cholesterol absorption and higher fecal excretion of cholesterol. Another mechanism is that phytosterols increase cholesterol efflux out of the intestinal enterocytes back into the lumen; therefore, less cholesterol is incorporated into chylomicrons for entry into circulation. A lower level of intestinal-derived cholesterol prompts cells to restore cellular cholesterol homeostasis by other mechanisms. These alternative mechanisms include increasing the expression of total LDL receptors that in turn decreases LDL formation along the apolipoprotein B cascade and increase in cholesterol synthesis. The resulting effect of reduced serum LDL cholesterol has been suggested as a reason for the role of phytosterols in decreasing atherosclerosis through decreased plaque formation [58,59,60, 61,62] of *A. hypogea* seeds and it can also be packaged as phytomedicine against this dreaded disease of both developed and under developed countries.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical approval was obtained from the research and ethical committee of the Federal University of Technology, Minna, Nigeria for the conduct of this work. The authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- Okechukwu SO, Ikechi O, Innocent IC, Joshua OA, Basden JCO, Ayodele OF, Simon S, Karen S. Blood pressure, prevalence of hypertension and hypertension related complications in Nigerian Africans: A review. *World J Card.* 2012;4(12):327-340.
- Asekun-Olarinmoye EO, Akinwusi PO, Adebimpe WO, Isawumi MA, Hassan MB, Olowe OA, Makanjuola OB, Alebiosu CO, Adewole TA. Prevalence of hypertension in the rural adult population of Osun State, southwestern Nigeria. *International Journal on Gender Management.* 2013;6:317-322. DOI:<http://dx.doi.org/10.2147/IJGM.S42905>
- Davidson MH, Ballantyne CM, Jacobson TA, Bittner VA, Braun LT, McKenny JM. Clinical utility of inflammatory markers and advanced lipoprotein testing; 2011.
- Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III); 2002.
- Aclan Ozder. Lipid profile abnormalities seen in T2DM patients in primary healthcare in Turkey: A cross-sectional study. *Lipids Health Dis.* 2014;13:183. DOI: 10.1186/1476-511X-13-183
PMCID: PMC4271485
- Assmann G, Schulte H, Von Eckardstein A, Huang Y. High-density lipoprotein cholesterol as a predictor of coronary heart disease risk. The PROCAM experience and pathophysiological implications for reverse cholesterol transport. *Atherosclerosis.* 1996;124:S11–S20.
- Marta Guasch-Ferré, Mònica Bulló, Miguel Ángel Martínez-González, Emilio Ros, Dolores Corella, Ramon Estruch, Montserrat Fitó, Fernando Arós, Julia Wärnberg, Miquel Fiol, José Lapetra, Ernest Vinyoles, Rosa Maria Lamuela-Raventós, Lluís Serra-Majem, Xavier Pintó, Valentina Ruiz-Gutiérrez, Josep Basora, Jordi Salas-Salvadó. Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial. *BMC Med.* 2013;11:164. DOI: 10.1186/1741-7015-11-164
PMCID: PMC3738153
- Charles UO, Emeka GO, Emmanuel IO, Gladys IA. Serum lipid profile of newly diagnosed hypertensive patients in Nnewi, South-East Nigeria. *International Journal of Hypertension.* Hindawi Publishing Corporation; 2012.
- Peela J, Abdalla MJ. Lipid profile in essential hypertension. *Egyptian Journal Biochemistry and Molecular Biology.* 2012;Special Issue. ISSN 1687-1502.
- Lakshmana KN, Deepthi J, Rao YN, Kiran DM. Study of lipid profile, serum magnesium and blood glucose in hypertension. *Biology and Medicine.* 2010;2(1):6-16. Available:www.biolmedonline.com
- Sarkar D, Latif SA, Uddin MM, Aich J, Sutradhar SR, Ferdousi S, Ganguly KC, Wahed F. Studies on serum lipid profile in hypertensive patient. *Mymensingh Med Journal.* 2007;16(1):70-6.
- Saha MS, Sana NK, Ranajit KS. Serum lipid profile of hypertensive patients in the Northern Region of Bangladesh. *Journal of Biological Science.* 2006;14:93-98.
- Kornsteiner M, Wanger KH, Elmadfa I. Tocopherols and total phenolics in 10 different nut types. *Food Chemistry.* 2006;98:381-387.
- Brown MJ, Dollery CT. Adrenaline and hypertension. *Clin Exp Hypertens.* 1984;6(1-2):539-49.
- Settaluri VS, Kandala CVK, Puppala N, Sundaram J. Peanuts and their nutritional aspects — A review. *Food and Nutrition Sciences.* 2012;3:1644-1650. DOI:<http://dx.doi.org/10.4236/fns.2012.312215>
Available:<http://www.SciRP.org/journal/fns>
- Azadmard-Damirchi S, Emami SH, Hesari J, Peighambari SH, Nemati M. Nuts composition and their health benefits. *World Academy of Science, Engineering and Technology.* 2011;5:508-512.
- Prabhu R, Divyadharsini R, Gopikrishnan P, Manivannan N, Mothilal A, Ibrahim SM, Vanniarajan C, Yesuraja I, Balakrishnan K. Variability studies in F3 population of groundnut (*Arachis hypogaea* L.). National Seminar on: Challenges and Innovative Approaches in Crop Improvement. On the eve of Golden Jubilee Celebration Agricultural College and Research Institute, Madurai, Tamil Nadu Agricultural University Programme; 2014.
- Bhimana Gautami, Daniel Foncéka, Manish K Pandey, Márcio C Moretzsohn, Venkataswamy Sujay, Hongde Qin, Yanbin Hong, Issa Faye, Xiaoping Chen, Amindala BhanuPrakash, Trushar M Shah,

- Makanahally VC, Gowda, Shyam N, Nigam, Rajeev K, Varshney. An International reference consensus genetic map with 897 marker loci based on 11 mapping populations for tetraploid groundnut (*Arachis hypogaea* L.). PlosOne Journal; 2012.
DOI: 10.1371/journal.pone.0041213
19. Chen C-YO, Blumberg J. Phytochemical composition of nuts. *Asia Pac J Clin Nutr*. 2008;17:329-332.
 20. Brauner R, Johannes C, Ploessl F, Bracher F, Lorenz RL. Phytosterols reduce cholesterol absorption by inhibition of 27-hydroxycholesterol generation, liver X receptor α activation, and expression of the basolateral sterol exporter ATP-binding cassette A1 in Caco-2 enterocytes. *J Nutr*. 2012;142(6):981-9.
DOI: 10.3945/jn.111.157198
Epub 2012 Apr 25.
 21. Marzena Gawrysiak-Witulska, Magdalena Rudzińska. Degradation of phytosterols during near-ambient drying of rapeseeds in a thick immobile layer. *J Am Oil Chem Soc*. 2012;89(9):1681-1689.
DOI: 10.1007/s11746-012-2065-3
PMCID: PMC342357
 22. Rahul Venugopal, Rui Hai Liu. Phytochemicals in diets for breast cancer prevention: The importance of resveratrol and ursolic acid. *Food Science and Human Wellness*. 2012;1(1):1-13.
DOI: 10.1016/J.FSHW.2012.12.001
 23. Athar M, Back JH, Tang X. Resveratrol: A review of preclinical studies for human cancer prevention. *Toxicology and Applied Pharmacology*. 2007;224(3):274-83.
 24. Sanders TH, McMichael Jr RW, Hendrix KW. Occurrence of resveratrol in edible peanuts. *Journal of Agricultural and Food Chemistry*. 2000;48(4):1243-6.
 25. Toshiya Kuno, Testuya Tsukamoto, Akira Hara, Takuji Tanaka. Cancer chemoprevention through the induction of apoptosis by natural compounds. *Journal of Biophysical Chemistry*. 2012;3(2):156-173.
DOI:http://dx.doi.org/10.4236/jbpc.2012.32_018
 26. Francisco MLDL, Resurreccion AVA. Functional components in peanuts. *Critical Reviews in Food Science and Nutrition*. 2008;48:715-746.
 27. Suzanne J Grant, Yu Sun Bin, Hosen Kiat, Dennis Hsu-Tung Chang. The use of complementary and alternative medicine by people with cardiovascular disease: A systematic review. *MC Public Health*. 2012;12:299.
DOI: 10.1186/1471-2458-12-299
Available:<http://www.biomedcentral.com/1471-2458/12/299>
 28. CCAC. Canadian Council on Animal Care guidelines on: Annual use and protocol review; 1997.
 29. Omale J, Etubi AF, Ebiloma GU. Antihypertensive effect of methanol extract of *Napoleona imperialis* (p. beauv) in adrenaline induced hypertensive albino rats. *International Journal of Biochemistry*. 2011;1(2):47-57.
 30. The Peanut Institute. Food for thought good fat, bad fat, and trans fat: The facts about fat in peanut butter. 2014;4(2).
 31. Alessandra Saldanha de Mattos Matheus, Lucianne Righeti Monteiro Tannus, Roberta Arnoldi Cobas, Catia C. Sousa Palma, Carlos Antonio Negrato, Marilia de Brito Gomes. Impact of diabetes on cardiovascular disease: An update, review article. *International Journal of Hypertension*. 2013;15. Article ID 653789.
DOI:<http://dx.doi.org/10.1155/2013/653789>
 32. Jamshed J Dalal, Padmanabhan TNC, Piyush Jain, Shiva Patil, Hardik Vasawala, Ashish Gulati. LIPITENSION: Interplay between dyslipidemia and hypertension. *Indian J Endocrinol Metab*. 2012;16(2):240-245.
DOI: 10.4103/2230-8210.93742
PMCID: PMC3313742
 33. Okpechi IG, Chukwuonye II, Tiffin N, Madukwe OO, Onyeonoro UU, Umezudike TI, Ogah. Blood pressure gradients and cardiovascular risk factors in urban and rural populations in Abia State South Eastern Nigeria using the WHO STEPwise approach. *PLoS One*. 2013;8(9):e73403. Epub 2013 Sep 5
 34. Ezekwe Ahamefula Sunday, Elekwa Ify, Osuocha Kelechi Uzoma. Hypoglycemic, hypolipidemic and body weight effects of unripe pulp of *Carica papaya* using diabetic Albino rat model. *Journal of Pharmacognosy and Phytochemistry*; 2015.
Available:www.phytojournal.com
(Accessed on 9/06/2015)
 35. Jiang S, Ma SY, Yan D. Antioxidant and antimicrobial properties of water soluble polysaccharides from *Arachis hypogaea* Seeds. *Journal of Food Science and*

- Technology-Mysore. 2014;51(10):2839-2844
36. Bilbis LS, Shehu RA, Abubakar MG. Hypoglycemic and hypolipidemic effects of aqueous extract of *Arachis hypogaea* in normal and alloxan-induced diabetic rats. *Int Journal of Phytotherapy and Phytopharmacology*. 2002;9(6):553-5.
37. Mona Anwara, Wafaa Ghoneim Shoushab, Hatem A El-mezayenb, Raafat A Wadallaha, Maha El-Wassef A, Naglaa M Nazif, Mona A El-banaa Antiatherogenic effect of almond oil in streptozotocin induced diabetic rats. *Journal of Applied Pharmaceutical Science*. 2013;3(10):059-065.
Available:<http://www.japsonline.com>
DOI: 10.7324/JAPS.2013.31010
ISSN 2231-3354
38. Ramesh B, Saravanan R, Pugalendi KV. Effect of dietary substitution of groundnut oil on blood glucose, lipid profile, and redox status in streptozotocin-diabetic rats. *Yale Journal of Biology and Medicine*. 2006;79:9-17.
39. Motazacker MM, Peter J, Treskes M, Shoulders CC, Kuivenhoven JA, Hovingh GK. Evidence of a polygenic origin of extreme high-density lipoprotein cholesterol levels. *Arterioscler Thromb Vasc Biol*. 2013;33(7):1521-8.
DOI: 10.1161/ATVBAHA.113.301505
Epub 2013 May 16.
40. Stitzel NO, Fouchier SW, Sjouke B, Peloso GM, Moscoso AM, Auer PL, Goel A, Gigante B, Barnes TA, Melander O, et al. Exome sequencing and directed clinical phenotyping diagnose cholesterol ester storage disease presenting as autosomal recessive hypercholesterolemia. *Arterioscler Thromb Vasc Biol*. 2013; 33(12):2909-14. Epub 2013 Sep 26.
41. Hoarse CL, Frikke-Schmidt R, Nordestgaard BG, Tybjaerg-Hansen A. Population-based resequencing of APOA1 in 10,330 individuals: Spectrum of genetic variation, phenotype, and comparison with extreme phenotype approach. *PLoS Genet*. 2012;8(11):e1003063. Epub 2012 Nov 29.
42. Daphna Weissglas-kov, Paivi Pajukanta. Genetic causes of high and low serum HDL- cholesterol. *Journal of Lipids Research*. 201051(8):2032-2057.
DOI: 101194/jlr.R004739
43. Ukoh VA, Oforofuo IAO. Plasma lipid profiles in Nigerians with normal blood pressure, hypertension and other acquired cardiac conditions. *East African Medical Journal*. 2007;84(6):264–270.
44. Oghagbon EK, Okesina AB. Pattern of some risk factors for cardiovascular disease in untreated Nigerian hypertensive patients. *West African Journal of Medicine*. 2006;25(3):190–194.
45. Gene ID: 348,2015.
Available:www.nlm.nih.gov/guidelines/cholesterol/atp3full.pdf
(Accessed October 2015)
46. Hajjar I, et al. Apolipoprotein E, carbon dioxide vasoreactivity, and cognition in older adults: Effect of hypertension. *J Am Geriatr Soc*; 2015.
PMID 25688603
47. Terry A Jacobson. Lipoprotein(a), cardiovascular disease, and contemporary management. Office of Health Promotion and Disease Prevention, Department of Medicine, Emory University School of Medicine, Atlanta, GA; 2013.
DOI:<http://dx.doi.org/10.1016/j.mayocp.2013.09.003>
48. Is it good to eat peanut?
Available:www.healthwomen.org/content/blog
(21/05/2015)
49. Andrew J Murphy, Marit Westerterp, Laurent Yvan-Charvet, Alan R Tall. Anti-atherogenic mechanisms of high density lipoprotein: Effects on myeloid cells (Areview). *Biochimica et Biophysica Acta (BBA) - Molecular and Cell Biology of Lipids*. 2012;1821(3):513–521.
50. Alan Chait, Katherine Lewis, Lisa Tannock, Kevin O'Brien, Barbara Retzlaff, Steven Kahn, Robert Knopp, Thomas Wight. Nutrition and inflammation: Role of dietary cholesterol. *International Congress Series*. 2004;1262:313–316. *Atherosclerosis XIII*. Proceedings of the 13th International Atherosclerosis Symposium.
51. Otis JP, Zeituni EM, Thierer JH, Anderson JL, Brown AC, Boehm ED, Cerchione DM, Ceasrine AM, Avraham-Davidi I, Tempelhof H, Yaniv K, Farber SA. Zebrafish as a model for apolipoprotein biology: Comprehensive expression analysis and a role for ApoA-IV in regulating food intake. *Dis Model Mech*. 2015;8(3):295–309.
DOI: 10.1242/dmm.018754
PMCID: PMC4348566

52. Prashant Shukla, Madhava Rao G, Gitu Pandey, Shweta Sharma, Naresh Mittapelly, Ranjita Shegokar, Prabhat Ranjan Mishra. Therapeutic interventions in sepsis: Current and anticipated pharmacological agents. *Br J Pharmacol*. 2014;171(22):5011–5031. Published online 2014 September 5. DOI: 10.1111/bph.12829
PMCID: PMC4253453
53. Kenneth R Feingold, Carl Grunfeld. The role of HDL in innate immunity. *J Lipid Res*. 2011;52(1):1–3. DOI: 10.1194/jlr.E012138
PMCID: PMC2999920
54. Phillips KM, Ruggio DM, Ashraf-Khorasani M. Phytosterol composition of nuts and seeds commonly consumed in the United States. *Journ. Agric. Food Chem*. 2005;53: 9436-9445.
55. Richard E Ostlund Jr. Phytosterols, cholesterol absorption and healthy diets. *Lipids*. 2007;42(1):41-45.
56. Gupta AK, Savopoulos CG, Ahuja J, Hatzitolios AI. Role of phytosterols in lipid-lowering: Current perspectives. *International Journal of Medicine*. 2011;104(4):301-308. DOI:<http://dx.doi.org/10.1093/qjmed/hcr007> 301-308 (First published online: 16 February 2011)
Available:www.pharmacytimes.com (Accessed on 2/12/2015)
58. Azadmard-Damirchi S, Emami SH, Hesari J, Peighambaroust SH, Nemati M. Nuts composition and their health benefits. *World Academy of Science, Engineering and Technology. International Journal of Biological, Food, Veterinary and Agricultural Engineering*. 2011;5(9).
59. Prabhjot S Nijjar, Frances M Burke, Annette Bloesch RD, Daniel J Rader. Role of dietary supplements in lowering low-density lipoprotein cholesterol: A review. *Journal of Clinical Lipidology*. 2010;4(4): 248–258.
60. Sathe Sh K, Monaghan EK, Kshirsagar HH, Venkatachalam M. Chemical composition of edible nut seeds and its implications in human health. In: *Tree nuts composition, phytochemicals, and health effects*, Alasalvar C, Shahidi F, Eds. Taylor & Francis Group. 2008;11-35.
61. Sharrett AR, Ballantyne CM, Coady SA. Coronary heart disease prediction from lipoprotein cholesterol levels, triglycerides, lipoprotein(a), apolipoproteins A-I and B, and HDL density subfractions: The atherosclerosis risk in communities (ARIC) study. *Circulation*. 2001;104(10):1108–1113.
62. The role of phytosterols in cholesterol management. Published Online: Friday, December 13, 2013. Available:www.pharmacytimes.com (12/06/2015)

© 2016 Kabiru et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

*The peer review history for this paper can be accessed here:
<http://sciencedomain.org/review-history/16446>*