http://dx.doi.org/10.4314/ajtcam.v11i3.35 DIETARY SUPPLEMENTS IN THE MANAGEMENT OF HYPERTENSION AND DIABETES - A REVIEW

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Abstract

Background: The use of alternative therapies like herbs and dietary supplements is very common among hypertensive and diabetic patients all over the globe. Hypertension is a silent disease that causes increase in cardiovascular, cerebrovascular, renal morbidity and mortality whereas diabetic complications cause heart attack, stroke, blindness and kidney disease. These are serious and chronic metabolic disorders that have a significant impact on the health, quality of life, and life expectancy of patients, as well as on the health care systems. Orthodox drugs used for the treatment of hypertension and diabetes produce side effects such as headache, nausea, vomiting, stomach pain, constipation, diarrhea, weakness, fatigue and erectile dysfunction. The need for considering alternate therapies in the form of dietary supplements known to promote good health, having little or no side effects therefore arises.

Materials and methods: This review was carried out using comprehensive and systematic literature reports on the concurrent use of dietary supplements in the management of diabetes and hypertension. Empirical searches were conducted using Google scholar (http:// scholar. google.com), and Science Direct (http://www.science direct.com). In addition to these databases, the University database was also used. Searches were also undertaken using keyword combinations such as dietary supplements and the names of the diseases in question.

Result and Discussion: This review chronicled the therapeutic values of vitamins, minerals, amino acids, fruits, vegetables, herbs and other botanicals used as dietary supplements. Results show that these supplements provided better and safe substitutes to toxic and expensive conventional drugs. Generally dietary supplements are free from major side effects, readily available and affordable. It is envisaged that the use of dietary supplement will promote good health and improve the status of hypertensive and diabetic patients.

Conclusion: Medical doctors are therefore encouraged to incorporate dietary supplements into the regimen employed for hypertension and diabetes management.

Keywords: Blood pressure, blood glucose, botanicals, minerals, vitamins

Introduction

The practice of using nature as pharmacy dates back to antecedent/s and continues till date as many of the medications currently in use are derived from plants. Dietary supplements are food products, extracts or concentrates that are intended to supplement diets because they contain certain dietary ingredients such as vitamins, minerals, herbs, and amino acids (Halsad, 2003). They are usually found in many forms including tablet, capsule, powder, liquid, bar, soft-gel and gel-cap.

Dietary supplements are generally regarded as classes of foods not drugs. This is because like foods, most dietary supplements are not screened for safety and effectiveness following their removal from the regulatory authority of the Federal Food, Drug and Cosmetic Act of 1958. This prevents dietary supplements labels from assertions showing their intended ability to treat, diagnose, mitigate, prevent or cure diseases (DSHEA, 1994). The line between permissible and impermissible health claims for supplements is not always clear to the consumer, who naturally may misunderstand the apparent bounty of medicinal-sounding risk-free benefits. However, while many supplements may be beneficial, they are not without risks. Generally, several claims have been put forward regarding the beneficial attributes of dietary supplements including prevention of acne, reduction of fats, low cholesterol content, rich fibre content, and the promotion of healthy skin (DSHEA, 1994).

Dietary supplements occur in different forms ranging from vitamins, minerals, amino acids and botanicals. Vitamins are organic compounds that cannot be synthesized by the body, but are necessary for its proper functioning. There are two types of vitamins namely; fat soluble and water soluble vitamins. Fat soluble vitamins are A, D, E and K which can be stored in the body for future use. Vitamins B and C are water soluble that cannot be stored by the body and therefore need to be replenished regularly through diet in order to avoid deficiencies which can interfere with normal metabolic processes and cause severe illness (Bellow and More, 2012). For instance, pellagra and beriberi diseases result from niacin (vitamin B3), and thiamin (vitamin B1) deficiencies while scurvy is a disorder arising from ascorbic acid (vitamin C), deficiency (Beckman et al., 2001; Gaede et al., 2001; Pemberton, 2006).

Minerals are inorganic elements derived from soil and water which are absorbed by plants and eaten by animals. Some of these minerals are required in large amounts by the body e.g. calcium for bone development. Others like chromium, copper, iron, selenium and zinc often called trace minerals are needed in very small amounts. These minerals are chemical elements required by all living organisms along with carbon, hydrogen, nitrogen and oxygen for proper growth and development (Soetan et al., 2010).

Amino acids are the building blocks of proteins and they can be categorized into three groups namely indispensable (essential), conditionally indispensable and dispensable (non-essential). Indispensable amino acids must be consumed in the diet while conditionally indispensable amino acids can be synthesized by human body under most conditions but may require dietary supplementation under certain patho-physiological conditions such as catabolic stress or neonatal prematurity (Morris *et al.*, 2002). Five amino acids are dispensable, meaning that they can be synthesized from other amino acids or complex metabolites (Engelhart *et al.* 2002).

Other dietary supplements include metabolites and extracts. Metabolites are substances that are produced by metabolic actions or are necessary for metabolic processes while extracts are substances usually biologically active ingredients of plant or animal tissues prepared by the use of solvents to separate the substance from the original material. A herbal remedy is a plant or plant part (root, flower, leaf, and fruit), that is used for its medicinal or therapeutic properties (Awoyemi *et al.*, 2012). The potency of herbal products varies depending on each plant's growing conditions, level of maturity when harvested and the processes used to dry and store each ingredient.

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The popularity and increase in the use of dietary supplements have been reported by the media, government agencies and published studies in medical journals (De Smet, 2000; Litovitz *et al.*, 2001; Spencer, 2004; Wise, 2004). Reports showed significant difference/s in dietary supplement usage by age, with higher prevalence in older age groups for all supplements and for single ingredient vitamins/minerals. There is also a significant difference in supplement use by sex, with women having the upper hand than men for all supplements except herbs and botanicals. A significant difference also exists with respect to race/ethnicity, with higher use amongst whites than any other groups for all supplements including multivitamins/minerals. Household income as well as the level of education of users also shows some level of significance difference for all supplement, multivitamins/multi-minerals and herbs users (Timbo et al., 2006).

Methodology

This review was carried out by a comprehensive and systematic literature search on the concurrent use of dietary supplements in the management of diabetes and hypertension. Empirical researches were conducted using Google scholar (http:// scholar. google.com) and Science Direct (http://www.science direct.com). In addition to these databases, the University of Fort Hare's online database were also used. Significant inquiries were also made using keyword combinations such as dietary supplements and the names of the diseases in question.

Specific disease and types of dietary supplements used in its management

Dietary supplements used in the management of Hypertension includes cod liver oil, garlic, Co-enzyme Q10, beta glucan, lipoic acid, whole grains, vitamins E, B6, C, potassium, magnesium, sodium, polyphenol, botanicals and vanadium.

Dietary supplements used in the management of *Diabetes* includes Alpha-lipoic, chromium, omega 3 fatty acids, polyphenols, garlic, magnesium, coenzyme Q10, vanadium, folic acid, selenium, vitamins B6, C and E, zinc and copper.

Hypertension

Hypertension is a highly prevalent chronic medical condition in which blood pressure in the arteries is elevated (Tabassum and Ahmad, 2011). It is a global health burden affecting both developed and developing countries (Kearney et al., 2005). The condition is becoming an increasingly common problem and this may be attributed to the increasing longevity and prevalence of contributing factors such as obesity, physical inactivity and unhealthy diets (Singh et al., 2000; Yusuf et al., 2001). It is a silent disease, which if untreated or sub-optimally controlled, could lead to increase in cardiovascular, cerebrovascular as well as renal morbidity and mortality.

The proportion of global disease burden attributed to hypertension is substantially affecting 32% of men and 30% of women aged 16 and above in England (WHO, 2003; Huisman et al., 2004). The high prevalence of hypertension globally contributes to the present anticipated pandemic of cardiovascular diseases (CVD), which is of particular concern in developing countries (Kearney et al., 2005). The control of hypertension, together with other associated risk factors such as dyslipidemia and diabetes mellitus, constitute the ideal approach to primary prevention of atherosclerotic disease, and remains a major challenge for communities. The trend towards comprehensive cardiovascular risk factor management is the internationally accepted model of care (WHO, 2002).

Hypertension is more prevalent in men than in women and even more in those of low socio-economic status though menopause tends to decrease this difference (Carretero and Oparil, 2000). This gender disparity is common in hypertension (Du et al., 2006). Before menopause, blood pressure (BP) is significantly lower in women than in age-matched men. However, the incidence/s of hypertension increases dramatically in women following menopause, eventually approximating the incidence in men (Kotchen et al., 1982; Spence, 1996). Although the mechanism underlying this increase is unknown, the loss of oestrogen traditionally has been considered the primary factor (Kearney et al., 2005).

Dietary supplements used in the management of hypertension

Dietary interventions have been shown to reduce the occurrence of high blood pressure (Appel et al., 2006). In the United States, the combined use of herbal supplements as home remedies for the management of hypertension was put at 48% (Mansoor, 2001). Furthermore, in a survey performed within a primary care setting in Alabama, 41% of patients were taking nutritional supplements and 26% were taking herbal products (Phillips and Osborne, 2000). In another report by Winslow and Kroll (1998), up to 90% of hypertensive patients take either over-the-counter medications or supplements depending on the definitions used.

Studies in other patient populations including those suffering from hypertension have also shown a significant prevalence of supplements, herbs and other alternative therapy use (Gulla and Singer, 2000; Cappuccio et al., 2001). It is therefore a common practice among patients attending a medical care setting to use dietary supplements. Unfortunately, most patients do not reveal the use of such treatments to their health care providers (Gulla and Singer, 2000). Common dietary supplements used in the management of hypertension, their health benefits and limitations are presented in Table 1.

Dietary folate and plasma ascorbic acid have been found to be inversely associated with blood pressure in observational studies (Forman et al., 2005). However, intervention trials with vitamin C yielded inconsistent results (Ness et al., 1997). While in two small trials, folic acid was effective at lowering blood pressure, the finding of a lower risk of elevated blood pressure in the multiple supplement groups suggests that there was a relationship between these nutrients and blood pressure (van Dijk et al., 2001; Mangoni et al., 2002).

Some studies have reported the concurrent use of dietary supplements and conventional antihypertensive drugs. For example, Co-enzyme Q10 has been reported to exhibit significant reduction of systolic blood pressure (SBP), and diastolic blood pressure (DBP), when added to conventional antihypertensive drugs (Singh et al., 1999; Rasmussen et al., 2012). Similarly, the systolic blood pressure (SBP) and diastolic blood pressure (DBP) were reported to have decreased by 6 mm Hg and 5 mmHg respectively in a trial where hypertensive men received fish oil (eicosapentaenoic acid, docosahexaenoic acid) for 4 months followed by a 2 month reassessment period (Prisco et al., 1998).

Diabetes

Diabetes, borrowed from a Greek word meaning siphon, is a metabolic disorder marked by high levels of blood glucose resulting from

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defects in insulin production, insulin action or both which can lead to serious complications and premature death (Afolayan and Sunmonu, 2010). However, people with the condition, working together with their support network and their health care providers can take steps to control the disease and lower the risk of complications.

Diabetes mellitus is a serious disease that has a significant impact on the health, quality of life and life expectancy of patients as well as the health care system (Dey *et al.*, 2002). It is a disorder affecting the metabolism of carbohydrates, fats, proteins and electrolytes in the body leading to acute, sub-acute and chronic complications (Rang et al., 1991). Hyperglycemia, ketoacidosis and non ketotic syndromes are some of the complications of acute diabetes (Knentz and Nattras, 1991), while thirst, polyuria, visual blurriness, weight loss and lack of energy are experienced in sub-acute diabetes incidence (Kumar and Clark, 2002). Chronic hyperglycemia complication causes bonding of a protein or lipid molecules with a sugar molecule (glycation) which may eventually affect the eye, kidney, nerves and arteries (Sharma, 1993; Afolayan and Sunmonu, 2010).

Three main forms of diabetes were recognized by the world Health Organization; these are type 1, type 2, and gestational diabetes (WHO, 1999). These three forms of diabetes showed common symptoms but differs in their causes, diagnosis, population distribution and treatment. The causes of diabetes are due to the beta cells of the pancreas being unable to produce sufficient insulin to prevent hyperglycemia (Rother, 2007). Type 1, diabetes previously called insulin-dependent diabetes mellitus (IDDM), or juvenile-onset diabetes is usually due to auto-immune destruction of the pancreatic beta cells which produce insulin. It develops when the body's immune system destroys pancreatic beta cells, the only cells in the body that produce the hormone insulin that regulates blood glucose (Holt, 2004). People with type 1 diabetes must have insulin delivered by injection or a pump. It usually strikes children and young adults, although disease onset can occur at any age. Type 2 previously called non-insulin-dependent diabetes mellitus (NIDDM), usually begins as insulin resistance, a disorder in which the cells do not use insulin properly (Holt, 2004). It is characterized by tissue-wide insulin resistance and varies widely; it sometimes progresses to loss of beta cell function. As the need for insulin rises, the pancreas gradually loses its ability to produce insulin. Type 2, diabetes is associated with older age, obesity, family history of diabetes, history of gestational diabetes, impaired glucose metabolism, physical inactivity, and race/ethnicity. Gestational diabetes occurs during pregnancy, it is similar to type 2, diabetes, which involves insulin resistance. The hormones of pregnancy cause insulin resistance in those women genetically predisposed to developing this condition.

The World Health Organization (WHO) estimated diabetes in adults to be around 173 million, and about two-thirds of these patients live in developing countries (Wild et al., 2004; Sunmonu and Afolayan, 2013). The prevalence of diabetes is on the increase worldwide, and this is still expected to increase by 5.4% in 2025 (Moller and Flier, 1991; Sunmonu and Afolayan, 2013). Women suffer from diabetes in both developed and developing countries. Approximately, 2.1 million women die of diabetes each year in the world, making diabetes the ninth leading cause of death among women (IDF, 2011). Increase in sedentary lifestyle, consumption of energy-rich diet and obesity are some of the factors causing the rise in the number of diabetics. According to the American Diabetes Association (1997), Asia and Africa are regions with the greatest potential where diabetics could rise to two or threefold above the present level (Sunmonu and Afolayan, 2010).

Dietary supplements used in the management of diabetes

The management of diabetic condition has advanced considerably over the past 50 years. Today, people living with diabetes are able to use advanced equipment and treatments such as electronic monitors which gives accurate readings of their glucose levels. There are also insulin pumps about the size of a beeper, strapped to a belt which gives measured insulin injections under the skin. Despite this development, dietary supplements are still used to a very large extent in the management of diabetes (Table 2). Some dietary supplements that have been studied in clinical trials include alpha-lipoic acid, chromium and omega-3 fatty acids (Martin et al., 2006).

Alpha-lipoic acid (ALA), also known as lipoic acid or thioctic acid and acts as an antioxidant substance that protects against cell damage. ALA has been researched for its effect on insulin sensitivity, glucose metabolism and diabetic neuropathy (Jacob et al., 1996). Diabetic patients also take chromium in an effort to improve their blood glucose control. Chromium supplementation in diabetics has been researched but not with some controversies. While some researchers have found benefits, others have indicated little or no benefits (Cefalu and Hu, 2004). Therefore, additional high-quality research is needed to prove its efficacy. Omega-3 fatty acids are another class of compound that has been researched for their effect on controlling glucose and reducing heart disease risk in people with Type 2, diabetes. Studies showed that omega-3 fatty acids lower triglycerides, but do not affect blood glucose control, total cholesterol or HDL (good), cholesterol in people with diabetes (De Luis et al., 2009).

Complementary medicine is mostly used along with conventional medicine while alternative medicine is replacing conventional medicine (Egede et al., 2002). For example, ALA, Chromium supplements, cinnamon and host of other supplements have proved successful for quite some time in the treatment for peripheral neuropathy. ALA has been reported to lower blood glucose level even though; there is no evidence that the supplement prevents neuropathy (Ziegler et al., 1995; Reljanovic et al., 1999). However, chromium supplement on A1C, glucose, and insulin levels have shown little effect in a trial among diabetes and non diabetic patients, other studies have shown some benefit on these same markers in subjects who were chromium deficient (Althius et al., 2002). Similar reports was reported where participant received 1, 3, or 6 g of cinnamon daily for 40 days to have lowered the blood glucose levels of participants from 18 to 29%. There was further reduction in the glucose level for up to 20 days for the participants who consumed the least quantity (1g) of the supplement even after the discontinuation of its use (Khan et al., 2003). Despite insufficient data on supplement safety and effectiveness, the fact remains that people with diabetes do and will continue to use dietary supplements.

Reasons for the use of dietary supplements in the management of hypertension and diabetes

Several reasons can be attributed to the upsurge in the use of dietary supplements for the management of diseases. Diabetes and hypertension represent huge financial cost to the government and affected individuals, which is predicted to increase over the next 20 years. Not everyone can afford the latest technology and advancements in the treatment of these diseases; dietary supplements and pharmacological interventions are therefore necessary (Bastaki, 2005).

Another important factor is lack of response and unwanted side effects arising from the use of conventional treatments which have forced many patients to explore dietary supplements as alternative therapy (Halat and Dennehy, 2003). The properties of dietary supplements used to treat hypertension and diabetic neuropathy are well described (Halat and Dennehy, 2003; Gupta and Guptha, 2010) Comparisons of these supplements with regard to dosages, frequencies and adverse effects described in medical literatures help with selection of the most appropriate supplements for individual patient. Majority of hypertensive patients (especially those with mild elevated blood pressure), claim they obtained little or no benefit from drug therapy and that the risks of some orthodox drugs far outweigh the benefits (Mansoor, 2001). Therefore, diet and other non-pharmacological approaches represent a safer approach to treating diabetes and hypertension with the added benefit of reduced cost (Halat and Dennehy, 2003).

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S/no	Dietary supplement	Nutrients/ food sources	Form found	Target organ/cell	Health benefits	Limitations	Reference
1.	Cod liver oil	Vitamin A, D, and omega-3 fatty acids. Fish oils, flax seed, primrose, borage and flaxseed oils.	Herring haddock, Atlantic salmon, trout, tuna, cod and mackerel.	Cardiovascular system.	Reduces cardio metabolic risk factors, protects sudden cardiac death after myocardial infraction, reduces raised plasma triglycerides, reduces blood pressure and ameliorates atherogenic effects.	High doses required for reduction of blood pressure may have side effects.	Warner, 2000; Marchioli <i>et al.</i> , 2002; Hooper <i>et al.</i> , 2006; Apel <i>et al.</i> , 2006; Abeywardena and Patten, 2011; Trofimiuk and Braszko, 2011.
2.	Garlic	Gamma glutamyl peptides, flavonol magnesium, ajoenes phosphorus, adenosine, allicin and sulphur	Allium sativum, aglio, ail, Da-suan, Knoblauch, La-juan, rustic treacle, stinking rose	Cardiovascular system.	Reduces cardiovascular diseases by lowering blood pressure and increases levels of antioxidant enzymes.	Inhibits platelet aggregation which may prolong bleeding time.	Mohamadi <i>et al.</i> , 2000; Weiss, 2000; Mansoor, 2001.
3.	Coenzyme Q- 10	B vitamins; B6, B12, niacin and folic acid. Fatty fish, organ meats and peanut.	Reduced or oxidized form of CoQ10 in dry powder capsules dispersed in oil, surfactants and emulsifiers such as lecithin and polysorbate 80 to improve absorption.	Heart, lung and liver	Strengthens heart muscle and improves a variety of heart conditions.	Low level compromises myocardial energy generation leading to "energy starvation" of the myocardium, considered to be a pathogenic mechanism of chronic heart failure (CHF).	Mohamadi <i>et al.</i> , 2000; Weiss, 2000; Mansoor, 2001.
4.	Beta glucan	Sorghum, rye, maize, triticale, wheat, rice, seaweed and mushrooms.	Oat and barley bran.	Heart	Immune enhancer and cholesterol-lowering effect.	Delay stomach emptying.	Mohamadi <i>et al.</i> , 2000; Weiss, 2000; Mansoor, 2001.
5.	Lipoic acid	Liver, spinach, broccoli and potato.	Lipoic acid in tablet and capsule.	Nerve cell, kidney, heart and liver.	Lowers blood pressure in persons with hypertension.	Pregnant women or nursing mothers should avoid lipoic acid supplements at pharmacologic doses.	Mohamadi <i>et al.</i> , 2000; Weiss, 2000; Mansoor, 2001.
6.	Whole grains	Brown rice, wheat, barley, rye, maize.	Oat meal, polenta, wheat pasta, wheat bread, corn meal.	Heart and liver	Reduces systolic and diastolic pressures along with mean arterial pressure (MAP).	Intake of three servings a day must be ensured for positive result.	Anderson et al., 2000.
7.	(i) Potassium	Fruits and vegetables such as apricots,	Citrate and chloride.	Cell membranes.	Reduces blood pressure.	Potassium depletion in normal individuals causes sodium retention and	Kotchen and McCarron, 1998.

Table 1: Common dietary supplements used in the management of hypertension

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		bananas, tomatoes and carrots.				increased blood pressure.	
	(ii) Magnesium	Fat or fibre (from fruits, vegetables and cereal grains.	Citrate, stearate and sulphate forms.	Heart and kidney.	Inhibits platelet dependent thrombosis.	lequate levels may se loose stool in sitive individuals.	Touyz, 1991; Burgess et al., 1999.
	(iii) Sodium	Fat or fibre from fruits, vegetables and cereal grains.	Additive in commercial processed foods.	Heart and blood vessels.	Moderate intake reduces mean arterial pressure as well as morbidity and mortality.	Excess sodium in the diet can lead to or complicate high blood pressure.	McCarron, 1997 Burgess et al., 1999; Kotchen and McCarron, 1998.
8.	Vitamin E	Vegetable oil, sunflower nuts, avocado, carrot, peanut, almonds, hazelnuts.	Alpha – Tocopherol	Heart, brain, lung, and muscle	Reduces elevated blood pressure caused by excess endogenous aldehydes in insulin resistance hypertension.	Large doses of α- tocopherol inhibits normal blood coagulation.	Jiang <i>et al.</i> , 2001; Vasdev <i>et al.</i> , 2002.
9.	Vitamin B6	Brown rice, oats, wheat germ, molasses, cereals, potato, banana, plum and salmon fish.	Pyridoxine	Jejunum, ileum, heart.	Prevents heart attacks and nerve damage.	Excess doses over long period of time result into painful and ultimately irreversible neurological problem.	Schaumburg <i>et al.</i> , 1983; Bendich and Cohen, 1990; McCormick, 2006.
10.	Vitamin C	Fruits and vegetables.	Ascorbic acid	Blood plasma, brain, spleen, lung, liver, kidney and pancreas.	Lowers blood pressure in persons with hypertension, helpful for long term health maintenance of arteries.	Causes diuretic effect which gets rid of fluids.	Ness <i>et al.</i> , 1997; Vasdev <i>et al.</i> , 2002.
11.	Polyphenol	Fruits and vegetables, nuts and their products.	Catechin and epicatechin.	Heart	Inhibits oxidation of low density lipoprotein (LDL), inhibits platelet aggregation and vascular relaxation through the production of nitric oxide.	Safety should be carefully tested in relation to the disease status of potential users.	Frankel <i>et al.</i> , 1993; McCarron, 1997; Dubick and Omaye, 2001; Halsad, 2003; Carlson <i>et al.</i> , 2008.
12.	Botanicals	Prickly pear, cactus, Coccinea indica, Aloe vera, fenugreek, bitter melon, Ginseng.	Herbs	Liver, bones, skin and heart.	Prevents hypertension and ulcerative colitis.	Lack of dose regimen and limited research on the efficacy of these botanicals.	Merchant and Andre, 2001; Van Breemen <i>et</i> <i>al.</i> , 2007.
13.	Vanadium	Black pepper, mushroom, shell fish parsley, fresh fruits and vegetables.	Chelate and sulphates.	Muscles, liver, heart and body fluids.	Lowers blood pressure.	GI irritation and tissue accumulation, uncertain long term safety profile.	Bhanot <i>et al.</i> , 1994a; Bhanot <i>et al.</i> , 1994b Cohen <i>et al.</i> , 1995; Goldfine <i>et al.</i> , 1995; Boden <i>et al.</i> , 1996;; Preuss <i>et al.</i> , 1998.

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S/no	Dietary supplement	Nutrients/ food source	Form found	Target organ/cell	Health benefits	Limitations	Reference
1.	Alpha-lipoic acid	Liver, spinach, broccoli and potato.	lipoic acid in tablet and capsule.	Nerve cell, kidney and liver.	Prevents cell damage, improves the body's ability to use insulin.	May lower blood sugar too much.	Jacob <i>et al.</i> , 1995; 1996; Konrad <i>et al.</i> , 1999.
2.	Chromium	Trace element, meat, whole grain products, some fruits, vegetables and spices.	Capsule and tablets sold as chromium picolinate, chromium chloride, chromium nicotinate.	Pancreas	Keeps pancreas working well and lowers blood sugar levels.	Lower doses are safer as high doses can cause kidney problem.	McCarty, 1999; Althuis <i>et al.</i> , 2002; Cefalu and He, 2004; Balk <i>et al.</i> , 2007; Jellin and Gregory, 2007.
3.	Omega- 3fatty acids	Poly unsaturated fatty acids. Oil, vegetable oil (canola and soybean), walnuts, and wheat germ.	Capsule or oil.	Liver and heart.	Maintains blood glucose levels.	Safer at low to moderate doses, may interfere with certain medications.	Hartweg <i>et al.</i> , 2007; Hartweg <i>et al.</i> , 2008.
4.	Polyphenols	Tea and dark chocolate.	Green tea	Vascular tissue	Lowers blood glucose levels by enhancing insulin action.	Contains caffeine, which can cause, in some people, insomnia, anxiety, or irritability. Green tea also has small amounts of vitamin K, which can make anticoagulant drugs, such as warfarin, less effective.	ino <i>et al.</i> , 2005; 1 <i>et al.</i> , 2006 Collins <i>et al.</i> , 2007; Kim <i>et al.</i> , 2007; Mackenzie <i>et al.</i> , 2007; Potenza <i>et al.</i> , 2007.
5.	Garlic	Allium sativum	S-ally cysteine sulphoxide (SACS).	creas	Reduces fasting blood glucose and lower serum cholesterol levels.	ibits platelet gregation and / prolong eding time.	Sheela and Augusti, 1992; Kaczmar, 1998. Banerjee and Maulik, 2002.
6.	Magnissium	Fat or fibre from fruits, vegetables, cereals and grain.	Citrate, chloride, sulphate and stearate.	Heart, kidney and muscle.	Improves insulin response and glucose handling in the elderly and in type 2 diabetics.	Causes loose stool in sensitive individuals.	Begon <i>et al.</i> , 2000; Larsson and Wolk, 2007; Schulze <i>et al.</i> , 2007.
7.	Coenzyme Q10	B vitamins i.e. niacin and folic acid. Fatty fish, organ meat, peanuts, spinach.	Oil	Heart, liver and lungs.	Improves long-term glycemic control in type 2 diabetics.	Body stores of Co- Q10 can be reduced when used alongside prescribed diabetic medications such as glyburide.	Anderson <i>et al</i> , 2001; Hodgson <i>et al.</i> , 2002; Bonadkdar and Guarneri, 2005.
8.	Vanadium	Black pepper, mushroom, shell fish parsley, fresh fruits and vegetables.	Chelate and sulphates.	Muscles, liver and body fluids.	Helps cells of both the liver and muscles use insulin more effectively, controls glucose and insulin sensitizers.	Adverse reactions of diarrhea, green Tongue, nausea, vomiting and cramps are reported.	Cusi <i>et al.</i> , 2001.
9.	Folic Acid	Vitamin B9, spinach	Oxidized synthetic	Liver and kidney	Along with B12, folic acid	High dosages cause	Salardi <i>et al.</i> , 2000.

 Table 2: Common dietary supplements used in the management of diabetes

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		broccoli, avocado, oranges, tomatoes, banana.	folate tablet form.		prevents strokes and loss of limbs due to diabetic complications.	neural damage.	
10.	Selenium	Broccoli, raddish, cabbage, onion, garlic, cereals, meat, mushroom, fish, nuts and egg.	Chelate	Small intestine, kidney	Helps take blood sugar into cells, protects against blood vessel and nerve damage from elevated blood sugars.	Low blood selenium predisposes to cancer, coronary heart disease and diabetes.	Mukherjee <i>et al.</i> , 1998; Stapleton, 2000.
11.	Vitamin B6	All bran, brown rice, oats, molasses, wheat germ, banana, plum, fish and salmon.	Pyridoxine	Jejunum, ileum	Pyridoxine with folic acid, B12 and B6 helps prevent diabetic blindness and vision loss.	Excessive vitamin B6 produces painful, disfiguring dermatological lesions.	Bendich and Cohen, 1990; Ellis <i>et al.</i> , 1991; McCormick, 2006.
12.	Vitamin C	Fruit and vegetables	Ascorbic acid	Endothelial cells	Improves insulin stimulated glucose metabolism.	May raise blood sugar level.	Paolisso <i>et al.</i> , 1994; 1995.
13.	Vitamin E	Vegetable oil, sunflower, nuts, whole grain, green leafy avocado, carrot, peanuts, almond, hazelnuts.	Tocopherol	Kidney, brain, muscles, heart and lung.	Produces a significant improvement in insulin mediated glucose utilization in healthy people and type-2 diabetics.	Large doses of α- tocopherol are known to deplete plasma and tissue γ- tocopherol.	Paolisso <i>et al.</i> , 1993; Barbagallo <i>et al.</i> , 1999; Jiang <i>et al.</i> , 2001.
14.	Zinc	Minerals	Zinc (picolinate)	Immune and metabolic cells.	Assists normal production, storage and secretion of insulin, necessary for the conformational integrity of insulin, helps blood sugar get into cells.	Significantly higher doses may cause nausea, vomiting, headache and drowsiness.	Paolisso <i>et al.</i> , 1993; Barbagallo <i>et al.</i> , 1999; Jiang <i>et al.</i> , 2001.
15.	Copper	Oat, bran, apple, almond.	Copper picolinate	Pancreas, blood vessels and nerves.	Protects pancreatic cells, prevents diabetes-related damage to blood vessels and nerves and lowers blood sugar levels.	Health benefits impaired by high intake of zinc.	Johnson <i>et al.</i> , 1998; Sitasawad <i>et al.</i> , 2001.

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Shortcomings of dietary supplements

Notwithstanding the popularity and widespread use of dietary supplements, a number of shortcomings have been recorded against them. Some of the risks involved include allergic reactions, competitive inhibition for absorption of other nutrients and drug-nutrient interactions resulting in long-term adverse effects. (Palmer and Howland, 2001; Palmer and Betz, 2002). Most of the dietary supplements including herbs and botanicals do not undergo the same stringent regulatory approval process as drugs. Food and drug laws do not require demonstration of safety and efficacy to support legal marketing of dietary supplements. There is lack of standardization among brands of supplements and the bioactive ingredients in products can vary widely (van Breemen *et al.*, 2007). For instance, few clinical trial reports are available to support the use of herbal and botanical supplements in the prevention or treatment of high blood pressure or heart disease. At a minimum, health care professionals should ask their patients about the use of herbal products and educate them on the possibility of herb-drug interactions. The active compound of a particular herb may not be known or if known may not be on the label. Furthermore, the amount of the active substance stated may not be accurate. Quality control measures vary from company to company and from product to product. Consumers should consider buying from manufacturers that have obtained Pharmacopeia standards for product purity and content reliability, thus at least ensuring some standards are followed during manufacture.

Conclusion

Dietary supplements used presently occur in a variety of forms including vitamins, minerals, herbals, botanicals, amino acids and enzymes. Deficiency in the consumption of some recommended foods requires the use of supplements. This may help ensure adequate amounts of essential nutrients and help promote optimal health and performance. Scientific evidence supporting the benefits of some dietary supplements is well established for certain health conditions like hypertension and diabetes. In affected individuals, inadequate nutritional intake of essential vitamins and minerals may worsen their conditions. Therefore, additional nutrients from supplements can help patients meet their medical needs and requirements. We envisage that the application of dietary supplements in the management of hypertension and diabetes is an opportunity for health care professionals to work in partnership with patients to educate and support beneficial self-care behaviors.

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References

1. Abeywardena, M.Y., and Patten, G.S. (2011). Role of omega 3 Long chain polyunsaturated fatty acids in reducing cardio-metabolic risk factors. End. Metabol. and Immune Disorder-Drug Target., 11 (3):232-246.

Afolayan, A.J., and Sunmonu, T O. (2010). In vivo studies on Antidiabetic plants used in South Africa Herbal medicine. J. Clin. Biochem. Nutri., 47: 98-106.
 Althuis, M.D., Jordan, N.E., Ludington, E.A. and Wittes, J.T. (2002). Glucose and insulin responses to dietary chromium supplements: A meta-analysis. Am. J. Clin. Nutr., 76(1):148-155.

4. American Diabetes Association, "Standards of medical care for patients with diabetes mellitus (position statement)," Diabetes Care, vol. 20, no. 1, pp. 518–520, 1997.

Anderson, J.W., Hanna, T.J., Xuejun, Peng B.S., and Kryscio, R.J. (2000). Whole grain food and heart disease risk. J Ame College of Nutri., 19 (3): 291-299.
 Anderson, R.A., Evans, M.L., Ellis, G.R., Graham, J., Morris, K., Jackson, S.K., Lewis, M.J., Rees, A., and Frenneaux M.P. (2001). The relationships

between post-prandial lipaemia, endothelial function and oxidative stress in healthy individuals and patients with type 2 diabetes. Atherosclerosis., 154: 475-483. 7. Appel, L.J., Brands, M.W., Daniels, S.R., Karanja, N., Elmer, P.J., and Sacks, F.M. (2006). Dietary approaches to prevent and treat hypertension. A scientific statement from the American Heart Association. Hypertension, 47:296-308.

8. Awoyemi, O.K., Ewa, E.E., Abdulkarim, I.A., and Adepoju AR. (2012). Ethnobotanical assessment of herbal plants in South-Western Nigeria. Acad. Res. Intern., 2 (3): 50-57.

9. Balk, E.M., Tatsioni, A., Lichtenstein, A.H., Lau, J., and Pittas, A.G. (2007). Effect of chromium supplementation on glucose metabolism and lipids: a systematic review of randomized controlled trials. Diabetes Care., 30(8):2154-2163.

10. Banerjee, S.K., and Maulik, S.K. (2002). Effect of garlic on cardiovascular disorders: A review. Nutri. Journal., 1: (1):4.

11. Barbagallo, M., Dominguez, L.J., Tagliamonte, M.R., Resnick, L.M., and Paolisso, G. (1999). Effect of vitamin E and glutathione on glucose metabolism: Role of magnesium. Hyper., 34: 1002-1006.

12. Bastaki, S. (2005). Review: Diabetes mellitus and its treatments. Int. J. Dia Metabol., 13: 111-134.

13. Beckman, J.A., Goldfine, A.B., Gordon, M.B., and Craeger, M.A. (2001). Ascorbate restores endothelium-dependent vasodilation impaired by acute hyperglycemia in humans. Circulation., 103:1618-1623.

14. Begon, S., Pickering, G., Eschalier, A., and Dubray, C. (2000). Magnesium and MK-801 have a similar effect in two experimental models of neuropathic pain. Brain. Res., 887:436-439.

15. Bellows, I., and Moore, R. (2012). Water-soluble vitamins: B- complex and vitamin C. Colorado State University, Cooperative Extension fact sheet No. 9.312.

16. Bendich, A., and Cohen, M. (1990). Vitamin B6 safety issues. Annals of New York Academy of Sci., 585:321-30.

17. Bhanot, S., Bryer-Ash, M., Cheung, A., and McNeill, J.H. (1994a). Bis (maltolato) oxovanadium (IV) attenuates hyperinsulinemia and hypertension in spontaneously hypertensive rats. Diabetes., 43:857-861.

 Bhanot, S., McNeill, J.H., and Bryer-Ash, M. (1994b) Vanadyl sulfate prevent fructose-induced hyperinsulinemia and hypertension in rats. Hyperten., 23:308-312.

19. Boden, G., Chen, X., Ruiz, J., van Rossum, G.D.V., and Turco, S. (1996). Effects of vanadyl sulfate on carbohydrate and lipid metabolism in patients with non-insulin-dependent diabetes mellitus. Metabol., 45:1130-1135.

20. Bonadkdar, R.A., and Guarneri, E. (2005). Coenzyme Q10. American Family Physician, 72(6):1065-1069.

http://dx.doi.org/10.4314/ajtcam.v11i3.35

21. Burgess, E., Lewanczuk, R., Bolli, P., Chockalingam, A., Cutler, H., Taylor, G., and Hamet P. (1999). Recommendations on potassium, magnesium, and calcium. Can. Med. Ass., 160: (9) 35-45.

22. Cappuccio, F.P., Duneclift, S.M., Atkinson, R.W., and Cook, D.G. (2001). Use of alternative medicines in a multi-ethnic population. Ethnic and Dis., 11:11-18.

23. Carlson, S., Peng, N., Prasain, J.K., and Wyss, J.M. (2008). Effects of Botanical dietary supplements on cardiovascular, cognitive and metabolic function in males and females. Gender Med., 5: 76-90.

24. Carretero, O.A., and Oparil S. (2000). "Essential hypertension. Part I: definition and etiology". Circulation., 101 (3): 329–35.

25. Cefalu, W.T., and Hu, F.B. (2004). Role of chromium in human health and in diabetes. Diabetes Care, 27:2741-2751.

26. Cohen, N., Halberstasm, M., Slimovitch, P., Shammon, H., and Rosetti, L. (1995). Oral vanadyl sulfate improves hepatic and peripheral insulin sensitivity in patients with non-insulin-dependent diabetes mellitus. J. Clin. Invest., 95:2501-2509.

27. Collins, Q.F., Liu, H.Y., Pi, J., Liu, Z., Quon, M.J., and Cao, W. (2007). Epigallocatechin-3-gallate (EGCG), a green tea polyphenol, suppresses hepatic gluconeogenesis through 5-AMP activated protein kinase. J. Bio. Chem., 282(41):30143-30149.

28. Cusi, K., Cukier, S., DeFronzo, R.A., Torres, M., Puchulu, F.M., and Redondo, J.C. (2001). Vanadyl sulfate improves hepatic and muscle insulin sensitivity in type 2 diabetes. J. Clin. Endocrinol, Metab., 86: 1410-1417.

29. De Luis, D.A., Conde, R., Aller, R., Izaola, O., Gonzalez Sagrado, M., Perez Castrillon, J.L., Duenas A., and Romero, E. (2009). Effect of omega-3 fatty acids on cardiovascular risk factors in patients with type 2 diabetes mellitus and hypertriglyceridemia: an open study. Eur. Rev. Med. Pharmacol. Sci., 13: 51-55.

30. De Smet, P.A. (2000). Herbal remedies. New Engl. J. Med., 347:2046-2056.

31. Dey, L., Attele, A.S., and SuYuan, C. (2002). Alternative therapies for type 2 diabetes. Alt. Med. Rev., 7 (1): 45-48.

32. DSHEA. (1994). Dietery supplements Health and Education Act. <u>www.wikipedia</u> accessed on 11/04/2013.

33. Du, X.J., Fang, L., and Kiriazis, H. (2006). Sex dimorphism in cardiac pathophysiology: Experimental findings, hormonal mechanisms, and molecular mechanisms. Pharmacol. Ther., 111:434-475.

34. Dubick, M., and Omaye, S.T. (2001). Modification of atherogenesis and heart disease by grape wine and tea polyphenols. In: Wildman REC, ed. Handbook of nutraceuticals and functional foods. Boca Raton, FL: CRC Press, 235-260.

35. Egede, L.E., Ye, X., Zheng, D., and Silverstein, M.D. (2002). The prevalence and pattern of complementary and alternative medicine use in individuals with diabetes. Dia. Care., 25:324-329.

36. Ellis, J.M., Folkers, K., Minadeo, M., Vanbuskirk, R., Xia, L.J., and Tamagawa H. (1991). A deficiency of vitamin B6 is a plausible molecular basis of the retinopathy of patients with diabetes mellitus. Biochem. Biophy. Res. Comm., 179: 615-619.

37. Engelhart, M.J., Geerlings, M.I., Ruitenberg, A., van Swieten, J.C., Hofman, A., Witteman, J.C., and Breteler, M.M. (2002). Dietary intake of antioxidants and risk of Alzheimer disease. J. Am. Med. Ass., 287: 3223-3229.

 Forman, J.P., Rimm, E.B., Stampfer, M.J., and Curhan, G.C. (2005). Folate intake and the risk of incident hypertension among US women. JAMA., 293:320-329.

39. Frankel, E.N., Kanner, J., German, J.B., Parks, E., and Kinsella, J.E. (1993). Inhibition of oxidation of human low-density lipoprotein by phenolic substances in red wine. Lancet., 341:454-457.

40. Fukino, Y., Shimbo, M., Aoki, N., Okubo, T., and Iso, H. (2005). Randomized controlled trial for an effect of green tea consumption on insulin resistance and inflammation markers. J. Nutr. Sci. Vitaminol., 51(5):335–342.

41. Gaede, P., Poulson, H.E., Parving, H.H., and Pederson, O. (2001). Double-blind, randomised study of the effect of combined treatment with vitamin C and E on albuminuria in Type 2 diabetic patients. Diabet Med.; 18:756-760.

42. Goldfine, A.B., Simonson, D.C., Folli, F., Patti, M.E., and Kahn, C.R. (1995). Metabolic effects of sodium metavanadate in humans with insulin-dependent and non-insulin-dependent diabetes mellitus. J. Clin. Endocrinol. Metabol., 80:3311-20.

43. Gulla, J., and Singer, A.J. (2000). Use of alternative therapies among emergency department patients. Ann. Emerge. Med. 35: 226 -228.

44. Gupta, R., and Guptha, S. (2010). Strategies for initial management of hypertension. Indian. J. Med. Res., 132: 531-542.

45. Halat, K.M., and Dennehy, C.E. (2003). Botanicals and dietary supplements in diabetic peripheral neuropathy. J. Am. Board. Family Pract., 16: 47-57.

46. Halsad, C.H. (2003). Dietary supplements and functional foods: 2 sides of a coin. American J. Clinic. Nutri., 77:1001-1007.

47. Hartweg, J., Farmer, A.J., Perera, R., Holman, R. R, and Neil, H.A. (2007). Meta-analysis of the effects of n-3 polyunsaturated fatty acids on lipoproteins and other emerging lipid cardiovascular risk markers in patients with type 2 diabetes. Diabetologia., 50(8):1593-1602.

48. Hartweg, J., Perera, R., Montori, V.M., Dinneen, S.F., Neil, A.H.A.W.N., and Farmer, A.J. (2008). Omega-3 polyunsaturated fatty acids (PUFA) for type 2 diabetes mellitus. Cochrane Database of Systematic Reviews; 2008. doi:10.1002/14651858.CD003205.pub2. Issue 1.Art. No.: CD003205.

49. Hodgson, J.M., Watts, G.F., Playford, D.A., Burke, V., and Croft, K.D. (2002). Coenzyme Q10 improves blood pressure and glycemic control: A controlled trial in subjects with type 2 diabetes. Eur. J. Clinic. Nutri., 56; 1137-1142.

50. Holt, R.I.G. (2004). Diagnosis, epidemiology and pathogenesis of diabetes mellitus: an update for psychiatrists. The British Journal of Psychiatry 184: 47-55 doi: 10.1192/bjp.

51. Hooper, L., Thompson, R.L., Harrison, R.A., Summerbell, C.D., Ness, A.R., Moore, H.J., Worthington, H.V., Durrington, P.N, Higgins, J.P.T., Capps, N.E., Riemersma, R.A., Ebrahim, S.B.J., and Davey Smith, G. (2006). Risks and benefits of omega-3 fats for mortality, cardiovascular disease and cancer: a systematic review. Achieves of British Med. Journal., 332:752-760.

52. Huisman, M., Kunst, A.E., Andersen, O., Bopp, M., Borgan, J.K., Borrell, C., Costa, G., Deboosere, P., Desplanques, G., Donkin, A., Gadeyne, S., Minder, C., Regidor, E., Spadea, T., Valkonen, T., and Mackenbach, J.P. (2004). Socio-economic inequalities in mortality among the elderly in 11 European populations. J. Epidemiol. Comm. Health., 58:468–475. International Diabetes Federation (2011).

53. Jacob, S., Henriksen, E.J., Schiemann, A.L., Simon, I., Clancy, D.E., Tritschler, H.J., Jung, W.I., Augustin, H.J., and Dietze, G.J. (1995). Enhancement of glucose disposal in patients with type 2 diabetes by alpha-lipoic acid. Arzneimittel-Forschung., 45(8): 872-874.

54. Jacob, S., Henriksen, E.J., Tritschler, H.J., Augustin, H.J., and Dietze, G.J. (1996). Improvement of insulin-stimulated glucose-disposal in type 2 diabetes after repeated parenteral administration of thioctic acid. Exp. Clin. Endocrinol. Diabetes., 104 (3): 284-288.

55. Jellin, J.M., and Gregory, P.J. (2007). Pharmacist's Letter/Prescriber's Letter Natural Medicines Comprehensive Database. 9th ed. Stockton, CA: Therapeutic Research Faculty.

56. Jiang, Q., Chrieten, S., Shigenaga, M.K., and Ames, B.N. (2001). γ- Tocopherol, the major form of Vitamin E in the US diet deserves more attention. Ame. Soc. Clinic. Nutri., 74 (6): 714-722.

57. Johnson, M.A., Smith, M.M., and Edmonds, J.T. (1998). Copper, iron, zinc, and manganese in Dietary supplements, infant formulas, and ready-to-eat breakfast cereals. Ame. J. Clinic. Nutri., 1035-1040.

58. Kaczmar, T. (1998). Herbal support for diabetes management. Clinical Nutrition Insights CNI608 5/98, Vol. 6, No.8.

59. Kearney, P.M., Whelton, M., Reynolds, K., Muntner, P., Whelton, P.K., and He, J. (2005). Global burden of hypertension: analysis of worldwide data. Lancet., 365:217-223.

60. Khan, A., Safdar, M., Ali Khan, M.M., Khattak, K.N., and Anderson, R.A. 2003. Cinnamon improves glucose and lipids of people with type 2 diabetes. Diabetes Care 26:3215-3218.

61. Kim, J.A., Formoso, G., Li, Y., Potenza, M.A., Marasciulo, F.L., Montagnani, M., and Quon, M.J. (2007). Epigallocatechin gallate, a green tea polyphenol, mediates NO-dependent vasodilation using signaling pathways in vascular endothelium requiring reactive oxygen species and Fyn. J. Bio. Chem., 282(18):13736-13745.

http://dx.doi.org/10.4314/ajtcam.v11i3.35

62. Knentz, A.J., and Nattras, M. (1991). Diabetic ketoacidosis, non ketotic hyperosmolar coma and lactic Acidosis. In: Handbook of diabetes (Pickup JC and Williams, G,eds) (2nd edition). Blackwell Science, pp.479-494.

63. Konrad, T., Vicini, P., Kusterer, K., Hoflich, A., Assadkhani, A., Bohles, H.J., Sewell, A., Tritschler, H.J., Cobelli, C., and Usadel, K.H. (1999) α-Lipoic acid treatment decreases serum lactate and pyruvate concentrations and improves glucose effectiveness in lean and obese patients with type 2 diabetes. Dia Care., 22:280–287.

64. Kotchen, T.A., and McCarron, D.A. (1998). Dietary electrolytes and blood pressure: A statement For Healthcare Professionals from the American Heart Association Nutrition Committee. Circulation., 98:613-617.

65. Kotchen, J.M., McKean, H.E., and Kotchen, T.A. (1982). Blood pressure trends with aging. Hypertension., 4:128-134.

66. Kumar, P.J., and Clark, M. (2002). Textbook of clinical medicine. Saunders, London, pp 1099-1121.

67. Larsson, S.C., and Wolk, A. (2007). Magnesium intake and risk of type 2 diabetes: a meta-analysis. J. Intern. Med., 262(2):208-214.

68. Litovitz, T.L., Klein-Schwartz, W., White, S., Cobaugh, D.J., Youniss, J., Omslaer, J.C., Drab A., and Benson, B.E. (2001). 2000 Annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Ame J. Emergency Med., 19:337-395.

69. Mackenzie, T., Leary, L., and Brooks, W.B. (2007). The effect of an extract of green and black tea on glucose control in adults with type 2 diabetes mellitus: double-blind randomized study. Metabol., 56(10):1340-1344.

70. Mangoni, A.A., Sherwood, R.A., Swift, C.G., and Jackson, S.H. (2002). Folic acid enhances endothelial function and reduces blood pressure in smokers: a randomized controlled trial. J. Internal Med., 252:497-503.

71. Mansoor, G.A. (2001). Herbs and alternative therapies in the hypertension clinic. American J. Hyperten., 14: 971-975.

72. Marchioli, R., Barzi, F., Bomba, E., Chieffo, C., Di Gregorio, D., Di Mascio, R., Franzosi, M.G., Geraci, E., Levantesi, G., Maggioni, A.P., Mantini, L., Marfisi, R.M., Mastrogiuseppe, G., Mininni, N., Nicolosi, G.L., Santini, M., Schweiger, C., Tavazzi, L., Tognoni, G., Tucci, C., Valagussa, F., and GISSI-Prevenzione Investigators. (2002). Early Protection against death by n-3 polyunsaturated fatty acid after myocardial infarction: time-course analysis of the results of the Gruppo Italiano per lo studio della Sopravvienza nell'Infarto Miocardico (GISSI)-Prevenzione. Circulation, 105: 1897-1903.

73. Martin, J., Wang, Z.Q., Zhang, X.H., Wachtel, D., Volaufova, J., Mathews, D.E., and Cefalu, W.T. (2006). Chromium picolinate supplementation attenuates body weight gain and Increases insulin sensitivity in subjects with type 2 diabetes. Dia Care., 29 (8):1826-1832.

74. McCarron, D.A. (1997). Role of adequate dietary calcium intake in the prevention and management of salt-sensitive hypertension. Am. J. Clinic Nutri., 65:712-716.

75. McCarty, M.F. (1999). High-dose biotin, an inducer of glucokinase expression, may synergize With chromium picolinate to enable a definitive nutritional therapy for type II diabetes. Med. Hypotheses., 52: 401-406.

76. McCormick, D. (2006). Vitamin B6. In: Bowman B, Russell R, eds. Present Knowledge in Nutrition. 9th ed. Washington, DC: International Life Sciences Institute.

77. Merchant, R.E., and Andre, C.A. (2001). Nutritional supplement Chlorella pyrenoidosa in the treatment of fibromyalgia, hypertension and ulcerative colitis. Alternative Therapies in Health and Medicine., 7(3): 79-91.

78. Mohamadi, A., Jarrell, S.T., Shi, S.J., Andrawis, N.S., Myers, A., Clouatre, D., and Preuss, H.G. (2000). Effects of wild versus cultivated garlic on blood pressure and other parameters in hypertensive rats. Heart Dis., 2:3-9.

Moller, D. E. and Flier, J. S. (1991). "Insulin resistance-mechanisms, syndromes, and implications," The New England J. Med., 325 (13): 938–948, 1991.
 Morris, M.C., Evans, D.A., Bienias, J.L., Tangney, C.C., Bennett, C.C., and Aggarwal, N. (2002). Dietary intake of antioxidant nutrients and the risk of

incident Alzheimer disease in a biracial community study. J. Am. Med. Ass., 287:3230-3237.

81. Mukherjee, B., Anbazhagan, S., Roy, A., Ghosh, R., and Chatterjee, M. (1998). Novel implications of the potential role of selenium on antioxidant status in streptozotocin induced diabetic mice. Biomed. Pharmacother., 52(2):89-95.

82. Ness, A.R., Chee, D., and Elliott, P. (1997). Vitamin C and blood pressure: an overview. J. Human Hyperten., 11:343-350. National Institutes of Health Office of Dietary Supplements: Dietary supplement fact sheet: chromium[article online]. Available fromhttp://ods.od.nih.gov/factsheets/chromium.asp#en35. Accessed 19 February 2013.

Palmer, M.E., and Howland, M.A. (2001). Herbals and dietary supplements. In: Ford M et al, eds. Clinical toxicology. Philadelphia: WB Saunders: 316–31.
Palmer, M., and Betz, J. Plants. (2002). In: Goldfrank LR, Flomenbaum NE, Lewin NA, et al, eds. Goldfrank's toxicologic emergencies 7th edn. New York: McGraw-Hill: 1150–82.

85. Paolisso, G., D'Amore, A., Giugliano, D., Ceriello, A., Varricchio, M., and D'Onofrio, F. (1993). Pharmacologic doses of vitamin E improve insulin action in healthy subjects and non-insulin dependent diabetic patients. Am. J. Clinic. Nutri., 57: 650-656.

86. Paolisso, G., D'Amore, A., Balbi, V., Volpe, C., Galzerano, D., Giugliano, D., Sgambato, S., Varricchio, M., and D'Onofrio, F. (1994). Plasma vitamin C affects glucose homeostasis in healthy subjects and in non-insulin dependent diabetes. Am J. Physiol., 266: 261-268.

87. Paolisso, G., Balbi, V., Volpe, C., Varricchio, G., Gambardella, A., Saccomanno, F., Ammendola, S., Varricchio, M., and D'Onofrio, F. (1995). Metabolic benefits deriving from chronic vitamin C supplementation in aged non-insulin dependent diabetics. J. Am. Coll. Nutr., 14:387–392.

88. Pemberton, J. (2006). "Medical experiments carried out in Sheffield on conscientious objectors to military service during the 1939–45 war". Int. J. Epidemiol., 35 (3): 556-558.

89. Phillips, A.W., and Osborne, J.A. (2000). Survey of alternative and nonprescription therapy use. Am. J. Health Syst. Pharm., 57:1361–1362.

90. Potenza, M.A., Marasciulo, F.L., Tarquinio, M., Tiravanti, E., Colantuono, G., Federici, A., Kim, J.A., Quon, M.J., and Montagnani, M. (2007). EGCG, a green tea polyphenol, improves endothelial function and insulin sensitivity, reduces blood pressure, and protects against myocardial I/R injury in SHR. Am. J. Physiol. Endocrinol. Metab., 292:1378–1387.

91. Preuss, H.G., Jarrell, S.T., Scheckenbach, R., Lieberman, S., and Anderson, R.A. (1998). Comparative Effects of Chromium, Vanadium and Gymnema Sylvestre on Sugar Induced Blood Pressure Elevations in SHR. J. Am. College Nutri., 17 (2): 116-123.

92. Prisco, D., Paniccia, R., Bandinelli, B., Filippini, M., Francalanci, I., Giusti, B., Giuriani L., Gensini G.F., Abbate R., and Neri Serneri G.G. (1998). Effect of medium-term supplementation with a moderate dose of n-3 polyunsaturated fatty acids on blood pressure in mild hypertensive patients. Thromb Res., 91:105–112.

93. Rang, H.P., Dale, M.M., and Ritters, J.M. (1991). The endocrine pancreas and the control of blood glucose, in pharmacology, Simmons, B. and Beasley, S. eds, Longman Group Ltd., UK, pp 403-410.

94. Rasmussen, C.B., Glisson, J.K., and Minor, D.S. (2012). Dietary Supplements and HypertensionPot ential Benefits and Precautions - A review. The J. Clinical. Hyperten., 14(7):467-471.

95. Reljanovic, M., Reichel, G., Rett, K., Lobisch, M., Schuette, K., Moller, W., Tritschler, H.J., and Mehnert, H. (1999). Treatment of diabetic polyneuropathy with the antioxidantthioctic acid (alpha-lipoic acid): a two year multicenter randomized double blind placebo controlled trial. Free. Radic. Biol. Med., 31:171-179.

96. Rother, K.I. (2007). "Diabetes Treatment- Bridging the Divide". N. Engl. J. Med., 356 (15): 1499-1501.

97. Ryu, O.H., Lee, J., Lee, K.W., Kim, H.Y., Seo, J.A., Kim, S.G., Kim, N.H., Baik, S.H., Choi, D.S., and Choi, K.M. (2006). Effects of green tea consumption on inflammation, insulin resistance and pulse wave velocity in type 2 diabetes patients. Diabetes. Res. Clinic. Practice., 71(3):356-358.

98. Salardi, S., Cacciari, E., Sassi, S., Grossi, G., Mainetti, B., Casa, C.D., Pirazzoli, P., Cicognani, A., and Gualandi, S. (2000). Homocysteinemia, serum folate and vitamin B12 in very young patients with diabetes mellitus type 1. J. Pediatr. Endocrinol. Metab., 13:1621-1627.

99. Schaumburg, H., Kaplan, J., Windebank, A., Vick, N., Rasmus, S., Pleasure, D., and Brown, M.J. (1983). Sensory neuropathy from pyridoxine abuse. A new megavitamin syndrome. New Engl. J. Med., 309: 445-448.

http://dx.doi.org/10.4314/ajtcam.v11i3.35

100. Schulze, M.B., Schulz, M., Heidemann, C., Schienkiewitz, A., Hoffmann, K., and Boeing, H. (2007). Fiber and magnesium intake and incidence of type 2 diabetes: a prospective study and meta-analysis, Archives Intern. Med., 167 (9): 956–965.

101. Sharma, A.K. (1993). Diabetes mellitus and its complications: An update. Galadari EO, Behara I, Manchandra M, Abdulrazzaq SK, Mehra MK (eds) Macmillian, New Delhi.

102. Sheela, C.G., and Augusti, K.T. (1992). Antidiabetic effects of S-ally cysteine sulphoxide isolated from garlic Allium sativum Linn. Ind. J. Experiment. Bio., 30:523-526.

103. Singh, R.B., Sul, I.L., Singh, V.P., Chaithiraphan, S., Laothavorn, P., Sy, R.G., Babilonia, N.A., Rahman, A.R.A., Sheikh, S., Tomlinson, B., and Sarraf-

Zadigan, N. (2000). Hypertension and stroke in Asia: prevalence, control and strategies in developing countries for prevention. J. Human Hyperten., 14: 749-763.

104. Singh, R.B., Niaz, M.A., Rastogi, S.S., Shukla P.K., and Thakur A.S. (1999). Effect of hydrosoluble coenzyme Q10 on blood pressures and insulin resistance in hypertensive patients with coronary artery disease. J. Hum. Hypertens., 13:203–208.

105. Sitasawad, S., Deshpande, M., Katdare, M., Tirth, S., and Parab, P. (2001). Beneficial effect of supplementation with copper sulfate on STZ-diabetic mice (IDDM). Diabetes. Res. Clin. Pract., 52: 77-84.

106. Soetan, K.O., Olaiya, C.O. and Oyewole, O.E. (2010). The importance of mineral elements for humans, domestic animals and plants; A review. Afr. J. Food. Sci., 4 (5): 200-222.

107. Spence, J.D. (1996). Cerebral consequences of hypertension: Where do they lead? J. Hypertens. Suppl.14: S139–S145.

108. Spencer, J. (2004). The risk of mixing drugs and herbs. Wall Street Journal June 22, 2004:D1.

109. Stapleton, S.R. (2000). Selenium: an insulin-mimetic. Cell. Mol. Life. Sci., 57:1874-1879.

110. Sunmonu, T.O., and Afolayan, A.J. (2013). Evaluation of Antidiabetic Activity and Associated Toxicity of Artemisia afra Aqueous Extract in Wistar Rats. Evidence-Based. Complementary and Alternative Medicine. Volume 2013 Article ID 929074, 8 pages

111. Tabassum, N. and Ahmad, F. (2011). Role of natural herbs in the treatment of hypertension. Pharmacog. Rev., 5:30-40.

112. Timbo, B.B., Ross, M.P., McCarthy, P.V., and Lin, C.J. (2006). Dietary supplements in a National Survey: Prevalence of Use and Reports of Adverse Events. J. Am. Diet. Ass., 106:1966-1974.

113. Touyz, R.M. (1991). Magnesium supplementation as an adjuvant to synthetic calcium channel antagonists in the treatment of hypertension. Med. Hypotheses., 36: 140-141.

114. Trofiniuk, E, Braszko, J.J. (2011). Long-term administration of cod liver oil ameliorates cognitive impairment induced by chronic stress in rats. Lipids., 46(5): 417-423.

115. Van Breemen, R.B., Fong, H.H., and Farnsworth, N.R. (2007). The role of quality assurance and standardization in the safety of botanical dietary supplements. Chem. Res. Toxicol., 20:577-582.

116. Van Dijk, R.A., Rauwerda, J.A., Steyn, M., Twisk, J.W., and Stehouwer. C.D. (2001). Long-term homocysteine-lowering treatment with folic acid plus pyridoxine is associated with decreased blood pressure but not with improved brachial artery endothelium-dependent vasodilation or carotid artery stiffness: a 2-year, randomized, placebo-controlled trial. Arteriole. Thrombo. Vas. Bio., 21: 2072-2079.

117. Vasdev, S., Longerich, L., Gill, V., and Singal, P. (2002). Dietary management of hypertension. Kuwait Med. Journ., 34 (1) 2-11.

118. Warner, M.G. (2000). Complementary and alternative therapies for hypertension. Complementary Health Practice Review 6:11-19.

119. Weiss, D. (2000). Cardiovascular disease: risk factors and fundamental nutrition. International J. Integra. Med., 2: 6-12.

120. World Health Organization Department of Non-communicable Disease Surveillance (1999). Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications (PDF).

121. World Health Organization. (2002). Integrated management of cardiovascular risk. Geneva:

122. WHO, (2002). http://whqlibdoc.who.int/publications/9241562242.pdf (accessed 20 June, 2012).

123. World Health Organisation. (2003). The world health report 2003. International Society of Hypertension (ISH) statement on management of hypertension. J. Hyper., 21: 1983-1992

124. Wild, S., Roglic, G. Green, Sicree, R., and King, H. (2004). "Global prevalence of diabetes: estimates for the year 2000 and projections for 2030," Diabetes Care, vol. 27, no. 5, pp. 1047-1053.

125. Winslow, L.C., and Kroll, D.J. (1998). Herbs as medicine. Arch. Intern. Med., 158: 2192-2199.

126. Wise, E. (2004). Twelve dangerous dietary supplements identified by 'Consumer Reports' widely used herbs linked to several serious ailments. USA Today, April 8, 9D.

127. www.wikipedia.org . Dietery supplement Retrieved 14/102/2014.

128. Yosefy, C., Viskoper, J.R., Laszt, A, Priluk R., Guita E., Varon D., Illan Z., Berry E.M., Savion N., Adan, Y., Lugassy, G., Schneider R., and Raz, A. (1999). The effects of fish oil on hypertension, plasma lipids and hemostatis in hypertensive, obese yslipidemic patients with and without diabetes mellitus. Prostaglandins Leukot Essent Fatty Acids., 61:83-87.

129. Yusuf, S., Reddy, S., Ounpuu, S., and Anand, S. (2001). Global burden of cardiovascular diseases. Part 1: General considerations, the epidemiologic transition risk factors and impact of urbanization. Circulation., 104: 2746-2753.

130. Ziegler, D., Hanefeld, M., Ruhnau, K.J., Meibner, H.P., Lobisch, M., Schuette, K., and Gries, F.A. (1995). Treatment of symptomatic diabetic peripheral neuropathy with the anti-oxidant "lipoic acid": a 3 week multicentre randomized controlled trial (ALADIN Study I). Diabetologia 38:1425-1433.