



Role of a vegetarian diet in the prevention of diabetes

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Abstract

Diabetes Mellitus is an alarming disease in the present day since there is no remedy for the same. All it can be done is to seek for prevention and arrest of the illness. Polyphenols are known to act as preventor of the disease. The objective of the investigation done here is to examine how the dietary phenolic acids and flavonoids could help in this goal. A vegetarian diet proposed earlier indicates that it can successfully prevent diabetes if taken regularly. Antidiabetic polyphenols have been estimated from the diet concerned by evaluating their presence in each element of the diet and the result is obtained by adding them up. The total amount of antidiabetic polyphenols is found to be approximately equal to the daily intake amount. So the diet can be thought to be an antidiabetic one and it can prevent diabetes.

Keywords: diabetes mellitus, polyphenols, insulin, p-cells, glucose level, antidiabetic phenolic acids and flavonoids

Introduction

Diabetes Mellitus (DM) is a burning problem of the day for human being. It is a metabolic disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action occurring singly or both [1,2&3]

Apart from gestational DM which occurs in women during pregnancy, there are mainly two types of diabetes viz. Type 1 which happens when the body fails to produce insulin and the person concerned is insulin dependent i.e. he has to get insulin from outside.

Type 2- This type of diabetes affects the mechanism of using the insulin secreted for lowering the blood sugar.

Actually Type 1 DM is due to an autoimmune disorder caused by autoaggressive T lymphocytes that infiltrate the pancreas and destroy insulin producing beta cells, leading to hypoinsulinemia consequently hyperglycemic condition [4].

Type 2 DM is characterized by altered lipid, glucose metabolism, impaired insulin secretion and increased insulin Resistance i.e. the resistance to insulin-mediated glucose disposal. Type2 DM accounts for about 90% of all diabetes and hence is the major causes of premature illness and death through the increased risk of cardiovascular disease.

While diabetes itself is manageable, its complications can severely affect the daily living some of which could be fatal [5]

Basically diabetes is known as an oxidative stress disorder which occurs due to an imbalance between free radical formation and the ability of the organism's natural antioxidant [6].

Antioxidants inhibit the activity of free radicals through destruction of free radicals, binding to metals that simulate the production of free radicals and inhibition of production of the same as well as acting as scavengers of free radicals.

Phenolic acids have been considered as ideal agents against oxidative stress and its complications [7].

Similarly, flavonoids, a group of hydroxylated phenolic substances have been known to be potent against free

Radical scavengers and hence attracted tremendous interest as possible therapeutics against free radical mediated diseases like diabetes mellitus [8&9].

After the success of a vegetarian diet [10] in so many aspects [11,12,13,14,15&16] it is now in order to investigate how the above diet helps an antidiabetic agent to combat diabetes, particularly Type 2 disease by the presence of polyphenols in the diet. If taken from very childhood, the proposed diet can act as preventive agent against diabetes because after all even children are affected by the above disease [17]

The phenolic acids present in the diet are: Salicylic Acid, Gallic Acid, Ellagic Acid, Caffeic Acid, Chlorogenic Acid, Sinapic Acid, Pcoumaric Acid, Ferulic Acid, Syringic Acid and Protocatechuic Acid.

The list of flavonoid in the diet is a big one which includes: Quercetin, Kaempferol, Isorhamnetin, Luteolin, Apigenin, Catechin, Isoflavones, Lycopene, Anthocyanin and Proanthocyanidin.

In this article, attention has been drawn to find the amount of polyphenols available from the proposed diet.

These polyphenols act as antidiabetic agents.

Materials and Methods

The diet in consideration involves variety of foods which contains legume, vegetables, cereal, dairy products fruits and refreshing items.

Estimation of the relevant polyphenols from each element of the diet have been calculated and added up to get the net result of the above. The result so obtained are believed to act as preventive doses and sometimes as medicinal doses against diabetes to arrest the disease.

Results and Discussions

Before presenting the amount of phenolic acids and flavonoids obtained from the proposed diet, it may be relevant to discuss how the above phenolic acids and flavonoids take part to act as antidiabetic agents.

Table-1 below summarises the function of the phenolic acids and flavonoids [18] in relation to diabetes.

Table 1: The polyphenols and their functions towards prevention and arrest of diabetes.

Polyphenols(A)	Corresponding Antidiabetic Function(B)
1. Salicylic Acid	Phenolic acids are very much available in vegetables, fruits etc and if taken by human have demonstrated anti-diabetic effects ^[19] . Salicylic acid, one of the phenolic acids is present in the proposed diet ^[10] coming from guavas, tomatos, radish and mushrooms. Salicylic acid pharmacokinetic study achieved lower blood concentration of salicylic acid and subsequently incomplete inhibition of thromboxane A2 synthesis as measured with S-TxB2 concentrations and increased platelet reactivity in diabetes ^[20] .
Polyphenols(A)	Corresponding antidiabetic Function(B)
2. Gallic Acid	Gallic Acid, an endogenous plant phenol is found in black tea leaves, fruits, soybean, eggplant etc. It improves beta cell regeneration, insulin secretion, lipid profiles and could be used as a drug to bring about insulin secretagogue and hypolipidemic effects. Production of beta cells of the islets of Langerhan's thus stimulating the release of insulin and alleviating the oxidative stress through its antioxidant nature, Upregulation of PPAR expression and AKt activation. It enables glucose uptake through translocation and activation of glucose transporters (GLUT) 4 in phosphatidylinositol-3 Kinase path way. Gallic acid suppresses nuclear factor activity and cytokine release. It also reduces CREB-binding protein/ p-300(CBP/P300 a NF-K beta coactivator), gene expression, acetylation levels and CBP/ P300 histone acetyltransferase activity ^[1] .
Polyphenols(A)	Corresponding Antidiabetic Function(B)
3. Ellagic Acid	It is a natural phenol antioxidant found in cowpea, greenpea, Soybean, spinach, banana etc. Ellagic acid in EO exerts antidiabetic activity through the action on beta cells of pancreas that simulates insulin secretion and decreases glucose intolerance ^[2] . It reduces oxidative stress and improves histopathology in brain. It prevents lipid deposition and decreases vascular smooth muscle-cell proliferation. It suppresses oxidative stress and inflammation. Ellagic acid is believed to be most efficient in increasing the sexual function of diabetes. It attenuates the inflammatory processes by inhibition of NF-KB pathway ^[21] .
Polyphenols(A)	Corresponding Antidiabetic Function(B)
4. Caffeic Acid	It is present in apple, potato, mushroom, mango, guava etc. Caffeic acid is a good agent to treat diabetic patients. It suppresses the hepatic glucose output by enhancing hepatic glucose utilization and inhibiting glucose over production. It lowers triglyceride. It has anticoagulatory, antioxidative and anti-inflammatory protection for cardiac tissue of diabetes ^[22] . It inhibits nonenzymatic amino acid glycation in the living body which is associated with aging diabetic complications ^[23] .
Polyphenols(A)	Corresponding Antidiabetic Function (B)
5. Chlorogenic Acid	Chlorogenic acid, which is available from apple, peanut, moringa leaves, banana etc, reduces glycemia and the glycemic index of body, thereby lowering the intestinal absorption of glucose. It regulates glucose and lipid metabolism through the activation of AMPK. The mechanisms of the antinociceptive activity of chlorogenic acid may lower the blood glucose, and improve insulin sensitivity through an adiponectin receptor mediated signaling pathway ^[24] .
6. Sinapic Acid	This acid is present in Red Kidney bean, mushroom, peanut, cowpea, soybean. It improves hyperglycemia through phospholipase C-protein Kinase C signals to enhance the glucose utilization ^[25] .
Polyphenols(A)	Corresponding antidiabetic Function(B)
7. Pcoumaric Acid	The acid is found in apple, beans, potato, tomato mushroom etc. It modulates glucose and lipid metabolism via 5 AMPK activation in L6 skeletal muscle cells. Pcoumaric acid contents by high performance liquid chromatography, antioxidant activity as 1.1 diphenyl- 2picryl- hydrazyl- scavenging and porcine pancreatic amylase inhibitory activity ^[25] .
8. Ferulic Acid	Easily obtained from whole wheat, rice per boiled, banana, guava, potato, mung bean etc. It decreases blood glucose and glucose-6-phosphatase, phosphoenol pyruvate carboxykinase activities and higher glycogen and insulin. Reduces oxidative stress and inflammation pathway. Further, it decreases the glucose and lipid peroxidation. It exhibits significant protection against vascular endothelial dysfunction in diabetes ^[26] .
Polyphenols(A)	Corresponding antidiabetic Function (B)
	Ferulic acid treatment reduces the GLUT2 expression in diabetics by impairing the interaction between the transcription factors (SREBPIC, HNF1-alpha and HNF3-beta and GLUT2 genepromoter) ^[27] .
9. Syringic Acid	Available from fruits, blackbean, soybean, mungbean, mushroom, kidneybean syringic acid is a potential agent to secrete insulin from existing islet betacells. It exhibits lower HBAC1 and fasting plasma insulin levels and also improves glucose homeostatis in lever ^[28] .
Polyphenol(A)	Corresponding antidiabetic function (B)
10. Protocatechuic Acid	It is present in lentil, eggplant, peanut, mango, apple, brown rice etc which has tremendous effects in the treatment of diabetes. This acid normalizes hyperglycemia and reverses dyslipidemia associated with diabetes. It improves high density lipoprotein C and low density lipoprotein C levels in diabetes. The acid simulates the insulin signaling path way in human adipocytes increasing GLUT4 translocation and glucose uptake ^[29] .
11. Quercetin	Quercetin is available from redgram, eggplant, pumkin, tomato, spinach, various fruits etc and acts as antidiabetic agent. It improves hyperglycemia and oxidative stress. It downgrades glucose and blood HbA1C. It prevents beta cell death via the mitochondrial pathway and NFKB signaling.
Polyphenol(A)	Corresponding Antidiabetic Function (B)
12. Kaempferol	Available from apple, redspinach, potato etc. It inhibits cellular apoptosis and reduces caspase-3 activity in beta cells. Further it increases antioxidant and decreases lipid peroxidation markers. Enhances beta cell survival, improves CAMP signaling and increases GLUT4, AMPK ^[30&31] .
13. Isorhamnetin	This is a bioactive compound found from some elements like eggplant, tomato, pumkin, banana etc. It helps insulin secretion associated with increased GLUT2 and PPARY ^[23] . There is evidence that isorhamnetin glycosides possess antidiabetic effect and expression of enzymes regulating lipid metabolism ^[32] .
Polyphenol(A)	Corresponding anti-diabetic Function (B)
14. Luteolin	Luteolin is abundantly available in fruits and vegetables etc. It potentiates insulin action, inhibits NF-KB pathway,

	consequently increases iNOS, elevates antioxidants and increases in uptake of FFAS. It reduces mast cell and macrophage infiltrations and inflammatory cytokine levels ^[33&34] .
15. Apigenin	Apigenin is found in fruits, vegetables, nuts etc. It decreases glucose and increases antioxidant enzymes. It helps in the antioxidant and mitochondrial protection while decreasing apoptosis. It is insulin secretagogue ^[35,36&37] .
16. Catechin	Catechins are abundant in green tea. It is also found in black tea, apple, mango, banana etc. Studies suggest ^[38] that catechins can be used in the treatment for controlling blood sugar and risk factors associated with type 2 diabetes like obesity, dyslipidemia and oxidative stress.
Polyphenols(A)	Corresponding antidiabetic Function(B)
17. Isoflavones	Soybean, kidneybeans, peas and peanut are the sources of isoflavones in the proposed diet ^[10] of which soybeans are major contributor to the isoflavones. Soy isoflavones contain 12 different isoform in four chemical forms containing genistein. Over the years various studies show that genistein possesses antidiabetic properties like direct effect on beta cell proliferation, glucose simulated insulin secretion and protection against apoptosis ^[39] . The soy isoflavone genistein reverses oxidative and inflammatory state ^[40] .
Polyphenol(A)	Corresponding antidiabetic Function(B)
18. Lycopene	Lycopene is available from tomato, mango, guava and carrot etc. Diabetes is a chronic metabolic disorder. The most commonly accepted cause of diabetes is the oxidative damage caused by free radicals. It is believed that the oxidative damage and low insulin levels associated with diabetes are improved with application of lycopene. Lycopene can act in the prevention of diabetic disorders like body weight loss, decreased insulin levels and decreased plasma glucose level also ^[41] .
19. Anthocyanin	This flavonoid is available from apples, eggplant and radishes etc. It helps in the protection against the development of type2 diabetes. It is conjectured that a lower risk of type2 diabetes was associated with higher anthocyanin content in the diet ^[42] .
Polyphenol (A)	Corresponding antidiabetic Function(B)
	Considering the impact of anthocyanin on the regulation of glycemia and reduction of insulin resistance, it appears that the consumption of foods rich in anthocyanins may support the prevention and treatment of type2 diabetes ^[43] .
20. Proanthocyanidin	Proanthocyanidin is available from apple, mango, banana, red kidney bean etc. Diabetes is a chronic metabolic disease where glucose metabolism is impaired due to toxicity on pancreas gland and deficit in insulin level. Its therapy requires the inhibition of excess digestive enzymes and formation of advanced glycation end product (AGE). Proanthocyanidin increases normal insulin content and decreases the apoptotic cells in diabetic pancreatic islet.
Polyphenol (A)	Corresponding antidiabetic function (B)
	Endoplasmic reticulum(ER) stress is switched on during diabetic stress. Proanthocyanidin partially improves ER stress. It attenuates oxidative stress through inhibition of lipid peroxidation and reduces the risk of vascular disease in diabetes. It also controls hyperglycemia. Proanthocyanidins may slow the progression of diabetic retinopathy ^[44]

It may now be interesting to note the amount of the relevant phenolic acids and flavonoids obtainable from the proposed diet. This has been presented in Table-2 below.

Table 2: The amount of polyphenols evaluated from the proposed diet

Polyphenols(a)	Amount of minimum value in mgm/day (b)	Amount of maximum value in mgm/day (c)
1. Salicylic Acid	3.71	4.15
2. Gallic Acid	37.81	40.41
3. Ellagic Acid	13.26	17.45
4. Caffeic Acid	33.38	41.85
5. Chlorogenic Acid	24.78	32.12
6. Sinapic Acid	18.37	21.25
7. Pcoumaric Acid	16.98	22.80
8. Ferulic Acid	29.34	32.07
9. Syringic Acid	12.36	21.45
10. Protocatechuic Acid	19.54	24.89
11. Quercetin	12	15
12. Kaempferol	12.25	13.22
13. Isorhamnetin	14.74	21.19
14. Luteolin	13.60	24.83
15. Apigenin	8.32	9.32
16. Catechin	7.72	12.07
17. Isoflavones	130.65	178.81
18. Lycopene	10.46	17.50
19. Anthocyanin	54	100
20. Proanthocyanidin	670	715

We are now in a position to calculate the mean values of the polyphenols obtained per day from the proposed diet and

compare them with the daily intake amounts. They are presented in Table-3.

Table 3: The mean values of the polyphenols obtained from the proposed diet per day and the daily intake amount.

Polyphenols(a)	Mean values of proposed diet in mg/day(b)	Mean values of intake amount in mg/day(c)
1. Salicylic Acid	3.93	10
2. Gallic Acid	39.11	97.2
3. Ellagic Acid	15.355	30
4. Caffeic Acid	37.615	70
5. Chlorogenic Acid	28.45	300
6. Sinapic Acid	19.81	10
7. Pcoumaric Acid	19.89	17.9
8. Ferulic Acid	30.705	250
9. Syringic Acid	16.905	4.82
10. Protocate-chuic Acid	22.215	17
11. Polyphenols (a)	Mean values of proposed diet in mg/day(b)	Mean values of intake amount in mg/day(c)
12. Quercetin	13.5	40
13. Kaempferol	12.735	13.3
14. Isorhamnetin	17.965	20.7
15. Luteolin	19.215	0.20
16. Apigenin	8.82	6.5
17. Catechin	9.895	11.1
18. Isoflavones	154.73	50
19. Lycopene	13.98	21
20. Anthocya-nin	77	64.4
21. Proantho-cyanidin	692.5	189
22. Total:-	1248.325	1223.12

From the above data it is clear that of the antidiabetic polyphenols some like luteolin, isoflavones and proanthocyanidin are higher contributor to the antidiabetic effects from the proposed diet while gallic acid, caffeic acid, chlorogenic acid and ferulic acid take the leading role as obtained from the daily intake amount. Graphical presentation of the mean values of the polyphenols from the proposed diet and the daily intake amount are shown in Fig-1 and Fig-2.

From the above graphs it is evident that the various elements of the polyphenols in two sets have no correlation between each other. However one interesting point that occurs in the two sets of data is that the total amount of antidiabetic polyphenols in the two cases are almost same. Thus it can be inferred that they contribute equally to the prevention of diabetes. However, since the elements of antidiabetic polyphenols in the above two sets contribute differently it may be interesting to study in detail how they act and which set could be more effective in relation to diabetes, and that investigation could be done elsewhere.

Conclusion

Diabetes is a leading problem of the day and the number of diabetic patients are increasing alarmingly day by day. So, scientists and doctors are engaged to investigate the ways for prevention and remedy of the disease. To get remedy, it may prove fatal due to side complications. Prevention and arrest of the disease could be wise to search for. As there are many polyphenols which act as antidiabetic, attention has been drawn in this article to the availability of the above polyphenols from a proposed diet. It has been shown that the diet in consideration supply phenolic acids and flavonoids in sufficient amount per day to prevent diabetes. The amount of polyphenols evaluated from the diet differ from the daily intake amount and the amount of various elements from the diet and the daily intake amount have no one-to-one correspondence. But the net amount of antidiabetic polyphenols from the diet match quite successfully with the daily intake amount. Hence it may be concluded that the diet presented here could be successful as a preventor of diabetes.

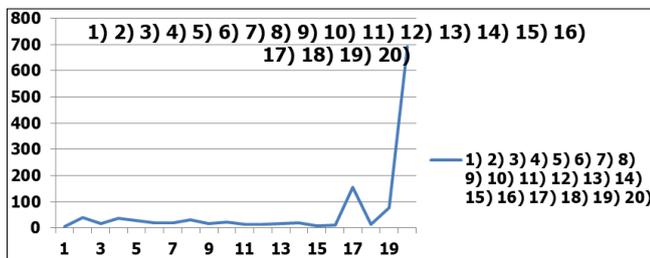


Fig 1: Mean values of the antidiabetic polyphenols per day from the proposed diet

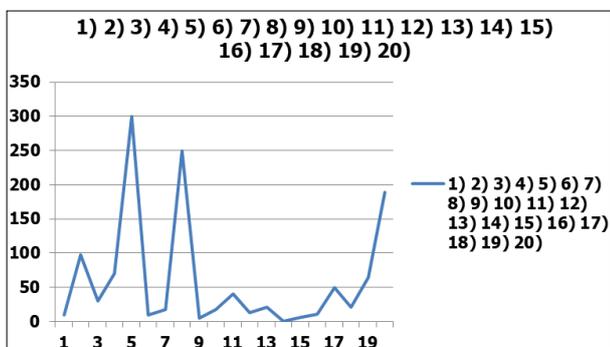


Fig 2: Mean values of the antidiabetic polyphenols intake per day

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