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Review

Reconsidering the properties of papaya fruit as anti-diabetes type 2

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Abstract

Diabetes mellitus (DM) is a condition that contributes to an impairment of the ability of the body to use food effectively triggered by the inability of the pancreas to generate insulin or body's dysfunction to adequately use insulin. Type 2 DM can induce oxidative stress leading to changes in endogenous antioxidant activity as well as a rise in biomolecular oxidative stress. This disease causes significant amounts of exogenous antioxidant supplementation to be prescribed in individuals with type 2 Diabetes to prevent oxidative damage in the body. Papaya (*Carica papaya* Linn) is one of the medicinal herbs which has anti-hyperglycemic activity as well as high antioxidants. Based on analysis of several studies it is noted that papaya supplies vitamin C, fiber saponins as well as flavonoids which can lower blood glucose levels. Nonetheless, to confirm this effect, even more, clinical studies are needed to be done.

Keywords: *Carica Papaya* Linn, Type 2 Diabetes Mellitus, Vitamin C, Flavonoids, Saponin.

Introduction

Diabetes mellitus (DM) is a condition rated as one of the world's biggest health issues [1]. Diabetes mellitus is triggered by a metabolic disorder in the body that is accompanied by irregularities in the metabolism of carbohydrates, fat, and proteins which is induced by abnormal insulin secretion, insulin deficiency, or both [2].

Uncontrolled diabetes mellitus which usually causes death can be avoided with the use of traditional medicines also by incorporating anti-hyperglycemic medicinal plants [3]. Oxidative stress that is marked by a discrepancy among oxidants and antioxidants in the body can be induced by the occurrence of type 2 diabetes mellitus. During oxidative stress conditions, endogenous antioxidant activity is reduced and the oxidative damage in biomolecules grows [4]. This possibly appears due to a rise in the regulation of elevated oxidative stress due to a glucose metabolism abnormality [5].

Research has also shown that oxidative damage plays a huge role in systemic inflammation, in impeding secretion of pancreatic β cells, impeding the use of glucose in peripheral tissues as well as endothelial dysfunction. Oxidative stress occurs in DM by three main mechanisms non-enzymatic protein glycation, sorbitol polyol pathways (aldosis reductase), including auto-glucose oxidation [4]. Excessive oxidative stress attributable due to irregularity in the production of glucose can be determined by controlling food intake, in particular antioxidant sources [4, 6]. Diabetes mellitus management in the presence of an integration of multiple medications as well as changes in lifestyle may help in preventing oxidative stress, vascular complications and also minimize mortality due to heart disease as well as other factors in people with DM [7, 8].

Increased oxidative stress induces significant quantities of exogenous antioxidant consumption in people with type 2 diabetes to prevent oxidative damage throughout the body [4, 6]. Papaya pharmacologically as well as its properties from so many past studies have shown that papaya extracts reduced blood glucose, which is believed to have vitamin C, fiber, flavonoid as well as saponin [9]. Besides being rich in nutrients guava and papaya fruits are inexpensive and nutritious fruits, conveniently available anywhere and fruit all year long. The authors were interested in doing a review of the impact of papaya fruit as an anti-diabetes type 2 based on this context.

Papaya Carica Papaya Linn

Carica papaya Linn (Caricaceae) is a tropical plant form and that is the only species in the Carica genus [9]. Tropical plants from tropical regions of America are now extensively grown in many other tropical regions of the world [10–15]. Papaya fruit can be eaten like a melon, available year-round [12]. The *Carica papaya* Linn tree is a straight tree that can grow up to 7–8 m high containing latex and also has a diameter of almost 20 cm [2]. The stem is cylindrical hollow which holds the leaves (like a parable) [13]. The leaves are soft, lobed and clumped close the top of the plant, approximately 80–90 cm in length [11–15].

The fruit is yellowish to orange in color, long to nearly rounded, about 7.5–45 cm thick, 2.5–5 cm thick, sweet and juicy [12]. Papaya has been one of the fruits abundant in nutrients such as vitamin, the cost is fairly cheap which can be used as a substitute for various health problems (i.e. constipation, overweight etc.). Certain study found that as much as 438 g of papaya fruit can substantially decrease blood glucose levels following consumption [13]. Diabetics should not avoid all fruits which contain sugar, one of them is papaya. Eating papaya in small amounts and preferably in the morning as energy feeder is safe for diabetics. Papaya has a glycemic index of 23 that could be graded as a low glycemic index. A low glycemic index can reduce the insulin and insulin sensitivity [13].

Vitamin C Advantages

Many research has also shown that papaya has a greater amount of vitamin C than soursop (*Annona muricata*), langsat including apple sugar [14]. Papaya contains 61 mg per 100 g of vitamin C [15, 16]. It has been stated in some publications that the levels of vitamin C each day for adults is 70–90 mg/dl, so that papaya could be used as an alternate choice for patients with type 2 diabetes mellitus [17]. Man cannot produce vitamin C in the body as they don't even have the enzyme L-gulonolactone oxidase which modulates the final step in ascorbic acid production so that they need a food sources from out of the body [18]. Vitamin C is an essential nutrient for humans that works as a reduction agent in free radical oxidation and can be assumed that vitamin C will function as an antioxidant [18]

The effects of vitamin C or ascorbic acid in diabetes is more of an inhibitor of the aldose reductase enzyme, and therefore reduced use of reduction equivalent [19] The presence of corresponding reducing agents is useful for oxidized glutathione conversion (GSSG) to lower glutathione (GSH). And that's what will then keep sorbitol from collecting in the system. Another advantage of using antioxidants is reducing the production of AGEs (advanced final components for glycosylation). This situation is similar to using vitamin C to mitigate the cycle of browning in fruit. The process of reducing AGEs formation is indistinguishable from the function of vitamin C in the sorbitol polyols (aldosis reductase) process [4, 19].

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Vitamin C is an essential micronutrient dissolving in water that cause a variety of enzyme reactions. Vitamin C is an antioxidant that inhibits reactive oxygen species from causing oxidative damage and protects tissues against oxidative stress. One of the functions of antioxidant properties is minimizing oxidant stress [20]. Vitamin C is a non-enzymatic antioxidant that plays an important role in protecting free radicals from cell damage. By enhancing endothelial function, and reducing oxidative stress, vitamin C will improve insulin resistance. Vitamin C reduces the toxicity of glucose which helps prevent a reduction in β-cell mass as well as blood sugar. An enhanced insulin-mediate vitamin C function is primarily due to an increase in non-oxidative glucose metabolism [21].

Advantages of Fiber

Dietary fiber is a component of plants that can be ingested and is made up of carbohydrates which is resistant to digestion and absorption by the small intestine [22]. Dietary fiber has indeed been reported to decrease blood sugar levels since the mid-1970s, as demonstrated by a 6-week long-term clinical trial that showed diets rich in soluble fiber could decrease blood sugar levels. Dietary fiber is graded into two fibers called soluble and insoluble. The advantage of soluble fiber it slows down gastric emptying so that post-prandial blood sugar reaction can be minimized [23]. Many studies have demonstrated that 7.5 g of soluble fiber can improve postprandial glycaemia, which is involved with delaying gastric emptying. Complicated diabetes or severe hyperglycemia showed a considerable pause in gastric emptying by soluble fiber [24].

A further study, the therapeutic effect of water-soluble fiber on patients with type 2 diabetes in 120 respondents in China, revealed that soluble fiber with a volume of 20 g could boost postprandial 2-hour blood sugar, fasting insulin levels, insulin resistance index as well as maintain successful glycemic control without disturbing the functional secretion of the Langerhans islets [25]. Eating high-fiber foods can regulate blood glucose and reduce insulin demands. Fiber consumption, especially insoluble fiber found in grains and some plants, can help prevent diabetes from occurring by increasing the supply and role of the hormone insulin to regulate blood glucose in the body, Insoluble fiber will move via the entire digestive system and will provide a better more satisfying taste that helps regulate appetite [26]. A further advantage of insoluble fiber is that it might decrease the risk of type 2 diabetes but also enhance the sensitivity to insulin [27]. The results of other studies have obtained the same findings, namely the discovery of a beneficial association of fiber consumption and blood sugar concentrations of type 2 diabetics, which implies lower fiber intake, elevated blood sugar levels of diabetics and its strength of the association in a broad category [28].

Advantages of Flavonoids

Flavonoids are phenyl-propanoid substances with a C6-C3-C6 carbon base. Flavonoids are a source of secondary metabolites commonly derived from plants, mostly the Leguminosae family. Generally, flavonoids are associated or known to bind with sugar compounds. Flavonoid compounds have several functions like anti-hyperglycemic activity. Flavonoids works to lower blood sugar levels by regenerating pancreatic beta cells thereby increasing insulin secretion, and also increasing cell insulin sensitivity. A further function of flavonoids that exhibits hypoglycemic activity is to minimize glucose uptake and also to control the expression activity of enzymes engaged in carbohydrate metabolism [29].

Flavonoids are beneficial as exogenous antioxidants that can cure beta-cells in the pancreas as well as increase insulin sensitivity by decreasing oxidative stress and reducing oxidative stress. The process specifically lessens free radicals by contributing atoms of hydrogen. Radicals can oxidize flavonoids to form quite stable and much less reactive components [30]. Flavonoids block GLUT-2 also from the mucosa of the intestines. This inhibitory mechanism is non-competitive and can reduce the uptake of carbohydrates which lowers blood glucose levels [31].

Flavonoids also can suppress phosphodiesterase, such that the pancreatic beta cells can induce insulin secretion. Flavonoids are antagonists of alpha-glucosidase that impede the alpha-glucosidase enzyme necessary for carbohydrate degradation before even being absorbed as monosaccharides. The above process of activity results in reduced blood glucose [32]. For the α-glucosidase enzyme, the inhibitory mechanism of flavonoids is through hydroxylation bonds as well as the β ring substitution. This inhibition is based on the theory of delaying carbohydrate hydrolysis and glucose absorption and preventing sucrose metabolism into glucose [33]. A study of the anti-hyperglycemic effect of papaya fruit, with a dosage of 100–400 mg/kg, was also performed intra-peritonially during 21 days. The test results indicated a drop in glucose levels [34].

Flavonoids are believed to play a significant role in enhancing the function of antioxidant enzymes in the healing process of diabetes and are capable of regenerating damaged β-pancreatic cells in order to resolve insulin deficiency. Plant-containing flavonoids are also expected to promote insulin receptor sensitivity [35]. Flavonoids can prevent β-cell damage on the pancreatic island of Langerhans, which releases insulin which induces insulin secretion into the blood of pancreatic β cells. Flavonoids also can restore cell sensitivity to insulin receptors [36].

Advantages of Saponin

Saponins are existing glycosides attaching to steroids or to triterpene. Saponins have actions like insulin, can impede lipolysis, can improve the absorption of glucose by adipose cells. One data suggests that saponin substances can increase the production of insulin [37]. The saponins act as α glucosidase enzyme inhibitors. The enzyme plays an important role in transforming carbohydrates into glucose, but if this enzyme is impaired, the level of blood glucose in the body reduces [38]. Saponins have been shown to decrease blood glucose levels by promoting insulin release [39]. Saponin works by blocking blood glucose absorption by blocking the movement of glucose to the intestinal boundary brush in the gastrointestinal tract, which is really the location where glucose is absorbed. The mechanism that saponin is also believed to help reduce blood glucose levels [40].

The saponin acts with the occurrence of pancreatic regeneration that produces a growth in the number of pancreatic β cells including islands of langerhans, so that the production of insulin can increase. Improved release of insulin can help lower blood glucose levels. Pancreatic β cells are regenerated due to the presence of quiescent cells in the pancreas [41]. Findings from other researchers have said that the papaya extract had a significant reduction in blood glucose levels. The outcomes of the papaya leaf extract's bioactive compounds study are considered to possess flavonoids, saponins, most of which have anti-hyperglycemic effects [15]. It was shown to reduce blood glucose levels by a dose of 5000 mg/kg BW. Due to the active substance content of saponins and alkaloids in papaya which induced hypoglycemia, a decrease in blood glucose levels in Wistar rats has been demonstrated. Additionally, the bioactive compounds in papaya also played a significant role in triggering the production of insulin from pancreatic beta cells as well as somatostatin, however, inhibited glucose release [42].

Conclusion

Papaya provides nutrients that are effective for controlling diabetes mellitus. But to confirm such results, further clinical studies will have to be undertaken.

Conflict of Interest

The authors declare no conflict of interest.

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References

1. Tabish, S. A. (2007). Is diabetes becoming the biggest epidemic of the twenty-first century? *Int J Health Sci (Qassim)* 1(2): 5–8.
2. American Diabetes Association. (2009). Diagnosis and classification of diabetes mellitus. *Diabetes Care* 32(1): 62–67.
3. Choudhury, H., Pandey, M., Hua, C. K., et al. (2017). An update on natural compounds in the remedy of diabetes mellitus: A systematic review. *J Tradit Complement Med*. 8(3): 361–376.
4. Tan, B. L., Norhaizan, M. E., Liew, W. P., Sulaiman, R. H. (2018). Antioxidant and oxidative stress: A mutual interplay in age-related diseases. *Front Pharmacol*. 9: 1162.
5. Rabiee, M. R., Babajafari, S. Probiotics and diabetes: A review. *Int J Nutr Sci*. 3: 73–81.
6. Kurutas, E. B. (2016). The importance of antioxidants which play the role in cellular response against oxidative/nitrosative stress: current state. *Nutr J*. 15(1): 71.
7. Lastra, G., Syed, S., Kurukulasuriya, L. R., Manrique, C., Sowers, J. R. (2014). Type 2 diabetes mellitus and hypertension: An update. *Endocrinol Metab Clin North Am*. 43(1): 103–122.
8. Fowler, M. J. (2008). Microvascular and macrovascular complications of diabetes. *Clin Diabetes*. 26(2): 77–82.
9. Sarala, N., Paknikar, S. S. (2014). Papaya extract to treat dengue: A novel therapeutic option? *Ann Med Health Sci Res*. 4(3): 320–324.
10. Tarun, V., Yash, P. (2015). A review on medicinal properties of carica papaya linn. *Asian Pac J Trop Dis*. 5: 1–6.
11. Hickman, I. J., Macdonald, G. A. (2007). Impact of diabetes on the severity of liver disease. *Am J Med*. 120: 829–834.
12. Weickert, M. O., Pfeiffer, A. (2018). Impact of dietary fiber consumption on insulin resistance and the prevention of type 2 diabetes. *J Nutr*. 148(1): 7–12.
13. Fatema, K., Rahma, F., Sumi, N., et al. (2011). Glycemic and insulinemic responses to pumpkin and unripe papaya in type 2 diabetic subjects. *Int J Nutr Metab*. 3: 1–6.
14. Coria-Telluz, A. V., Gonzalez, E. M., Yakia, E. M., Vazquez, E. N. (2018). Annona muricata: A comprehensive review on its traditional medicinal uses, phytochemicals, pharmacological activities, mechanisms of action and toxicity. *Arabian J Chem*. 11(5): 662–669.
15. Saidu, A. N., Nweri, C. G. (2013). Phytochemical screening and effects of methanol extract of carica papaya stem bark in alloxan induced diabetic rats. *J Emerg Trends Engineer Apl Sci*. 4: 819–822.
16. Maisarah, A. M., Amira, B.N., Asmah, R., et al. (2013). Antioxidant analysis of different parts of carica papaya. *Int Food Res J*. 20: 1043–1048.
17. Montonen, J., Knekt, P., Järvinen, R. (2004). Dietary antioxidant intake and risk of type 2 diabetes. *Diabetes Care*. 27(2): 362–366.
18. Henriques, S. F., Duque, P., Fernández, H. L., Vázquez, N., Fdez-Riverola, F., Reboiro-Jato, M. (2019). Multiple independent L-gulonolactone oxidase (GULO) gene losses and vitamin C synthesis reacquisition events in non-Deuterostomian animal species. *BMC Evolut Biol*. 19(126).
19. Dakhale, G. N., Chaudhari, H. V., Shrivastava, M. (2011). Supplementation of vitamin C reduces blood glucose and improves glycosylated hemoglobin in type 2 diabetes mellitus: A randomized, double-blind study. *Adv Pharmacol Sci*.
20. Ilhami, G. (2020). Antioxidants and antioxidant methods: an updated overview. *Arch Toxicol*. 94: 651–715.
21. Lauer, A. C. (2013). Dose-dependent vitamin C uptake and radical scavenging activity in human skin measured with in vivo electron paramagnetic resonance spectroscopy. *Skin Pharmacol Physiol*. 26(3): 147–154.
22. Sherafatmanesh, S., Ekramzadeh, M., Moosavi, L. (2017). The role of carbohydrate related factors in pathogenesis of nonalcoholic fatty liver disease: a review. *Int J Nutr Sci*. 2: 52–57.
23. Mihai, B. M. (2018). Bidirectional relationship between gastric emptying and plasma glucose control in normoglycemic individuals and diabetic patients. *J Diabetes Res*.
24. Marathe, C. S. (2013). Relationships between gastric emptying, postprandial glycemia, and incretin hormones. *Diabetes Care*. 36(5): 1396–1405.
25. Chen, C., Zeng, Y., Xu, J., et al. (2016). Therapeutic effects of soluble dietary fiber consumption on type 2 diabetes mellitus. *Exp Ther Med*. 12(2): 1232–1242.
26. Yu, K., Ke, M., Li, W., et al. (2018). The impact of soluble dietary fibre on gastric emptying, postprandial blood glucose and insulin in patients with type 2 diabetes. *Asia Pac J Clin Nutr*. 2014; 23.
27. Weickert, M. O., Andreas, F. H. (2018). Impact of dietary fiber consumption on insulin resistance and the prevention of type 2 diabetes. *J Nutr*.148(1): 7–12.
28. Hussain, A. (2007). Prevention of type 2 diabetes: A review. *Diabetes Res Clin Pract*. 76(3): 317–326.
29. Vinayagam, R., Xu, B. (2015). Antidiabetic properties of dietary flavonoids: a cellular mechanism review. *Nutr Metab*. 12: 60.
30. Grassi, D., Desideri, G., Ferri, C. (2010). Flavonoids: Antioxidants against atherosclerosis. *Nutrients* 2(8): 889–902.
31. Testa, R., Bonfigli, A. R., Genovessa, S. (2016). The possible role of flavonoids in the prevention of diabetic complications. *Nutrients* 8(5): 310.
32. Hosseini, S. E., Rezaei, E., Mehrabani, D., et al. (2013). Effect of pomegranate juice on lipid profile in streptozotocin-induced diabetic adult male rats. *J Exp Anim Biol*. 2: 13–20.
33. He, C., Liu, X., Jiang, Z., Geng, S., Ma, H., Liu, B. (2019). Interaction mechanism of flavonoids and α-glucosidase: Experimental and molecular modelling studies. *Foods* 8(9): 355.
34. Russo, B., Picconi, F., Malandrucco, I., Frontoni, S. (2019). Flavonoids and insulin-resistance: From molecular evidences to clinical trials. *Int J Mol Sci*. 20(9): 2061.
35. Hosseini, S. E., Mehrabani, D., Ghaedi, H. R. (2013). The effect of pomegranate juice on hemogram and weight profile in streptozotocin-induced diabetic adult male rats. *Damghan J Zool*. 6: 1–8.
36. AL-Ishaq, R. K., Abotaleb, M., Kubatka, P., Kajo, K., Büsselberg, D. (2019). Flavonoids and their anti-diabetic effects: Cellular mechanisms and effects to improve blood sugar levels. *Biomolecules* 9(9): 430.
37. Beecher, G. R. (2003). Overview of dietary flavonoids: Nomenclature, occurrence and intake. *J Nutr*. 133: 3248S–3254S.
38. Elekofehinti, O. O., Ejelonu, O. C., Kamdem, J. P., Akinlosotu, O. B., Gbadura, I. (2017). Saponins as adipokines modulator:

A possible therapeutic intervention for type 2 diabetes. *World J Diabetes*. 8(7): 337–345.

39. Dunmore, S. J., Brown, J. E. (2013). The role of adipokines in β-cell failure of type 2 diabetes. *J Endocrinol*. 216: T37–T45.
40. Elekofehinti, O. O. (2015). Saponins: Anti-diabetic principles from medicinal plants - A review. *Pathophysiology* 22: 95–103.
41. Singh, S., Farswan, M., Ali, S., Afzal, M., Al-Abbasi, F. A., Kazmi, I., Anwar, F. (2014). Antidiabetic potential of triterpenoid saponin isolated from Primula denticulate. *Pharm Biol*. 52(6): 750–755.
42. Juarez, I. E., Juan, C. D. Z., Jorge, L. B. C., et al. (2012). Hypoglycemic effect of Carica papaya leaves in streptozotocin-induced diabetic rats. *BMC Complement Altern Med*. 12: 1–12.

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