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Editorial

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Green papaya as a potential source for diabetic and diabetic-wound healing therapy

Editorial

According to a 2012 American Diabetes Association (ADA) report, about 30million Americans, or 9.3% of the population at the time, had diabetes. Its prevalence is highest (13-16%) among African-Americans and American Indians/Alaskan Natives, with more Americans diagnosed with diabetes every year. About 86 million Americans age 20 and older had prediabetes.[1] Furthermore, one major complication of diabetes is unmanageable wounds that lead to lower-limb amputation. About 73,000 non-traumatic lower-limb amputations were performed in diabetic adults aged 20years or older.[1] Diabetes and diabetes-related complications are an emerging serious local, regional, and national problem in America, particularly in the African- American population (Figure 1). The total cost in 2013 for diabetes management was about $245billion. It is important to reverse/decrease the occurrence of prediabetes and to treat diabetes and its complications with less expensive and less toxic therapies.

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The use of dietary antioxidants and nutraceuticals is one of the strategies often pursued as low cost remedies to reduce oxidative stress for preventing diabetes and its chronic complications.[2] Different parts of papaya (seeds, roots, leaves, barks, flowers, latex, and fruit) have been used in folk medicine to treat various diseases, including diabetes, cancer, and cardiovascular and infectious diseases.[3] Papaya (*Carica papaya*) is a perennial plant of tropical and subtropical regions, which requires temperatures between 21 and 33°C and cannot tolerate temperatures less than 15°C.[4,5] The papaya tree can grow to about 6-10 feet in high tunnels and produces unripe green papaya, which are harvested before the temperature drops below 15°C. Recent scientific studies have validated many of the traditional uses and reported antiviral, antibacterial, antiprotozoal, antifungal, anti-inflammatory, antitumor, antihypertensive, wound healing, neuroprotective, diuretic, abortifacient, antifertility, hypoglycemic, and hypolipidemic properties.[3,6–8] This wide range of biological activities from papaya is attributed to its content of a number of phytochemicals including, flavonoids, polyphenols, alkaloids, glycosides, triterpenes, lectins, saponins, polysaccharides, vitamins, minerals, enzymes, proteins, and oils.[3]

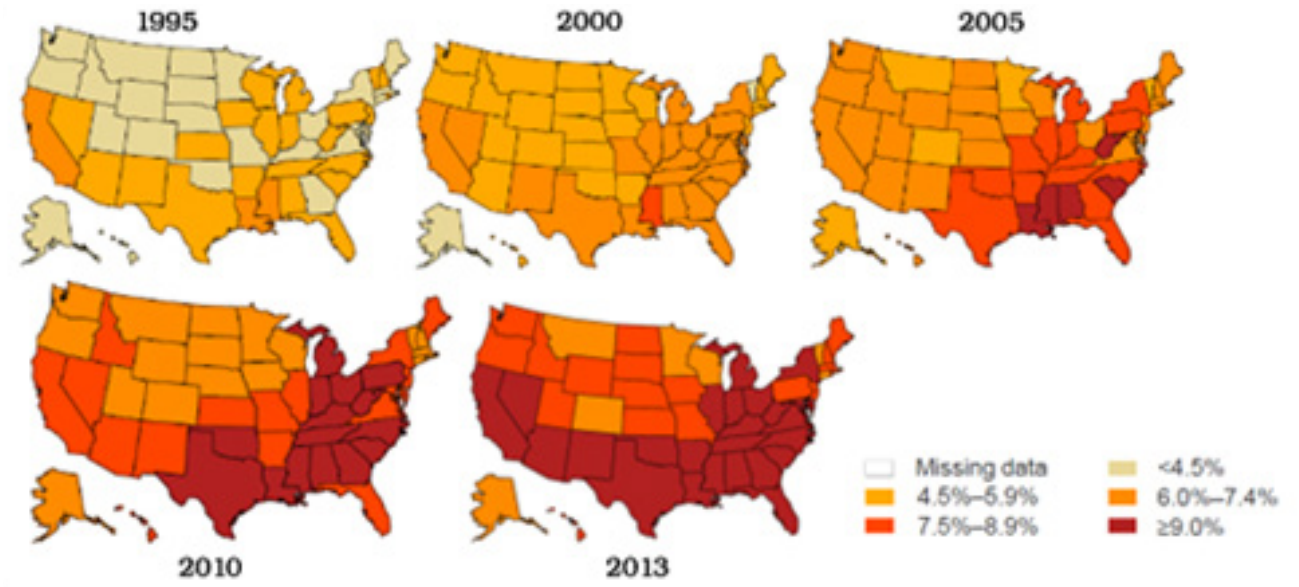

Figure 1 Progression of age-adjusted percentage of US adults diagnosed with diabetes.

Data is reproduced from http://www.cdc.gov/diabetes/statistics

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For medicinal purposes, seeds, leaves, and fruits are the most commonly used parts of the papaya. The primary components of papaya seeds are proteins, fatty acids, and phospholipids; as secondary metabolites, they also contain benzyl isothiocynate, benzyl glucosinolate, beta-sitosterol, caricin, carpaine, and enzyme myrosin.[9] The highest amount of polyphenol and flavonoid are contained in the papaya leaves, whereas the least amount of these secondary metabolites can be found in the seeds.[10] Papaya leaf extract have been used to treat cancer and infectious diseases.[11,12] Its vasodilating, anti-oxidation, hypoglycemic, and lipid-lowering properties are associated with lowering cardiovascular risk and treating diabetes.[13,14] The latex of papaya contains enzymes including papain, chymopapain, caricain, glycyl endopeptidase, and papaya lipase.[15] The latex preparations have been used to treat tissue burn and microbial/helmintic infection;[16,17] they have also been used for insecticidal/molluscicidal activity against various pests.[18,19] The flesh from both green and ripe papaya has also been shown to have anti-hyperglycemic and anti-cancer activity.[13,20,21] The fruit also shows antibacterial activity against *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli* and *Pseudomonas euroginosa*.[22,23] In addition, the proteolytic enzymatic activity and the antimicrobial activity in the pulp are effective in desloughing necrotic tissue and preventing wound infection.[24]

It is evident that compounds present in different parts of papaya are rich in a number of antioxidant, antimicrobial, and health-modulating activities, and papaya can be a potential therapeutic fruit for ameliorating diabetes and its associated complications.

Diabetes is a metabolic disorder of multiple etiologies. The diabetic onset is preceded by chronic hyperglycemia. Type 2 diabetes mellitus (DM 2) is caused by a relative deficit of insulin production and a combination of insulin resistance.[25,26] The defects in insulin secretion, insulin action or both, along with the associated hyperglycemia, lead to disturbances in the metabolism of carbohydrate, fat and protein, causing other chronic diseases such as metabolic syndrome, cardiovascular diseases, and cancer.[27] As mentioned above, the leaves of papaya have shown anti-hyperglycemic and hypolipidemic effects.[13,14] Furthermore, studies using fermented papaya have shown that this preparation is able to reduce both basal and postprandial glycemia and improves the lipid profile.[20,21] The papaya, therefore, has the potential to prevent or perhaps reverse the pre-diabetic condition in populations that are at a higher risk.

Another common complication in diabetic patients is infection of the foot, causing ulcers.[28] Diabetes progression leads to structural and functional changes within the arteriolar and capillary systems and also causes thickening of the basement membrane.[29] This thickened membrane impairs leukocyte migration and hampers the normal hyperglycemic or vasodilatory response to injury.[30] These diabetes-associated changes increase susceptibility to injury while at the same time blunting many of the typical manifestations of such an injury. Diabetic patients, therefore, are more susceptible to ensuing infection of the foot.

The use of papaya in traditional medicine for wound healing is believed to come from its papain content, an active principle, which exerts an ulcer protective effect.[23] The papaya-derived enzyme papain, when applied topically, may facilitate enzymatic wound debridement. Papain is a cysteine proteinase that digests necrotic tissue by liquefying eschar, thus facilitating the migration of viable cells from the wound edge into the wound cavity.[31] Papain is also useful in reducing the bacterial burden, decreasing exudates, and increasing granulation tissue formation.[32] The papain isolated from the latex of unripe papaya pulp is reported to be one of the earliest substances used in wound care and chronic skin ulcer therapy because of its anti-bacterial and fibrinolytic properties.[33,34]

The hypoglycemic and hypolipidemic activities of papaya fruit are important, yet unrecognized, resources in the dietary management of diabetes, and they deserve evaluation at the cellular and molecular level. It is important to conduct scientific studies and clinical trials to evaluate the potential antidiabetic and wound healing properties of green papaya. The data will provide us an opportunity to prevent and treat diabetes and diabetes-associated complications by using a low cost, non-toxic, and nutritious fruit. Once the active principle is identified, the information can also provide an opportunity for developing the papaya extract/bioactive compounds into an easy-to-use product, which will help thousands of people to manage diabetes and diabetes associated complications in a cost-effective manner.

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Conflict of interest

Author declares that there is no conflict of interest.

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