A review: *Stevia rebaudiana* Bertoni is non-caloric sugar for Diabetic patients.

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Abstract: *Stevia rebaudiana* Bertoni is an ancient South American plant with great potential as an agricultural crop for the production of a high-potency natural sweetener. It produces diterpene glycosides that are low calorie sweeteners, about 300 times sweeter than saccharose. Stevia extracts, besides having therapeutic properties, contain a high level of sweetening compounds, known as steviol glycosides, which are thought to possess antioxidant, antimicrobial and antifungal activity. S. rebaudiana leaves contain non-cariogenic and non-caloric sweeteners (steviol glycosides) whose consumption could exert beneficial effects on human health. Regular consumption of these compounds decreases the content of sugar, radionuclides, and cholesterol in the blood improves cell regeneration and blood coagulation, suppresses neoplastic growth and strengthens blood vessels. It is also a suitable raw material for the extraction and production of functional food ingredients. It is a good source of carbohydrates, protein, crude fibre, minerals, as well as dispensable and indispensable amino acids which are valuable for human nutrition. The sweetening compounds, found mainly in the leaves of the plant, are steviol glycosides, with stevioside being the most abundant, followed by rebaudioside A. Stevioside has a sweetening power comparable to that of artificial sweeteners presently marketed and consumed in several foods and beverages. Adverse effects of stevia have not really been observed. However, it is thought that stevia could provoke allergic reactions in people sensitive to plants of the Asteraceae family and it is also recommended that pregnant women should avoid consuming stevia.
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1. Introduction

Stevia is grown all across the world; it is known as stevia for its sweet leafs. It has been cultivated since long time in china and Southeast Asia and India has been one of the major cultivators of the stevia in international market. The leaves are the source of diterpene glycosides, stevioside and rebaudioside. Stevioside is non-caloric and is reported to be 30 times sweeter than sugar (Kolb et.al. 2001). In India diabetic patient are increasing day by day and according to world diabetic foundation it has the world's largest diabetes population, followed by China with 43.2 million and it has major concern among health experts and national and international healthcare. World health organization (WHO) has identified diabetes as an epidemic condition (King and Rewwers, 1991) and one of the major killer of the decade. Estimation by WHO, there will be about 250 million cases of diabetes mellitus throughout the world by 2025(Friedman, 2002). Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. According to World Health Organization Diabetes mellitus will become the seventh leading cause of death worldwide in 2030 (Mathers et al., 2006). Through proper diet, exercise and pharmacologic interventions, the incidence of diabetes can be overcome (Li et al., 2008). The pharmacological drugs used for the treatment of diabetes, are either too expensive or have certain adverse side effects. Therefore, for the treatment of diabetes mellitus many traditional plants have been preferred as natural source of drugs because they are considered to be safe, less toxic than synthetic ones (Dhasarathan et al., 2011) and have strong antioxidant activities due to which these plants become more effective against diabetes (Loew et al., 2006). *Stevia rebaudiana* Bertoni as a traditional plant is famous due to its sweet taste and beneficial effects in blood glucose regulation. *Stevia rebaudiana* Bertoni (family Asteraceae) popularly known as stevia, sweet weed, honey leaf and sweet herb of Paraguay (Anbazhagan et al., 2010). Stevia leaves contained complex mixture of diterpene glycosides including stevioside, steviolbioside, rebaudiosides (A, B, C, D, E) and dulcoside A but the major sweet constituents are stevioside and rebaudioside A (Lemus-Mondaca et al., 2012). Natural non-caloric sweetener stevioside (a

major component of stevia) is 100–300 times sweeter than sucrose and have been extensively used as a non-caloric sugar substitute in many kinds of foods, medicine, beverage, cosmetics, wine making, household chemical industry and other food industries (Stoyanova et al., 2011). It possesses anti-hyperglycaemic, anti-hypertensive, anti-oxidant, anti-tumor, anti-diarrheal, diuretic, gastro and renal-protective and immunomodulatory properties (Ferrazzano et al., 2016). The anti-hyperglycemic effect of *S. rebaudiana* was investigated in both rats and humans by (Thomas et al., 2010). They mentioned that stevioside demonstrates a positive effect on hyperglycemia through decreasing the absorption of glucose in duodenum, glycogenolysis and gluconeogenesis. As the synthetic drugs used for the treatment of diabetes result in many complications. Hence the use of natural source (*Stevia rebaudiana* Bertoni) for the treatment of diabetes is safe and non-carcinogenic (Lemus-Mondaca et al., 2012). Bernad is a scientist which told that this disease is occur due to the excessive production of glucose in the liver. It occurs all over the world but common in India. It is estimated that in 2025, about 57 million people will be affected from diabetes. For controlling this disease, different treatments are available, but they do not have a great success. Medicinal plants are important in medical field because the drugs obtained from these plants have fewer effects while the synthetic drugs are more effected for the human health. But now-a-days, wild plants and mostly those plants which are used for medicinal purpose has been affected by the man-made activities and world wild population status (Thiyagarajan and Venkatachalam, 2012).

In these plants, *Stevia rebaudiana* Bertoni is one which is best for the diabetic patients. Stevia is a shrub. It belongs to family Asteraceae. There are 150-300 species in this genus. It is known as Bertoni because in 1899 it was discovered by Moises Bertoni. Its seeds are infertile therefore it cannot be grown easily (Ibrahim et al., 2008).

This plant is also known as "Honey leaf" due to its sweet taste. It is three hundred times sweeter than the sugar cane. Its leaves contain rebaudioside, diterpene glycosides and stevioside. Due to the stevioside, it has a great importance and has a good taste. For nutrition and herbal purpose, it is cultivated in South America, Malaysia, Philippine, Taiwan, Hawaii and Europe. Its products are utilized in the food as a functional ingredient that are good for the diabetic and diet conscious person. (Ahmed et al., 2007).

Steviosides are three hundred times higher than common sugar. Therefore, it is required in low quantity. Rebaudioside-A is another glycoside in its leaves. Its sweetness is 400-times than sucrose (Sreedhar et al., 2008).

Rebaudioside A is organoleptic as well as it has physicochemical properties. Due to its solubility in water its formulation is easy. Rebaudioside A has unique properties due to which, it is considered as an important on industrial level for its utilization as an organic sweetener (Rajasekaran et al., 2007).

In addition to these, its leaf is a source of diterpene glycoside compounds which are sweeter than the sucrose. Its uses are safe for the diabetic patients because the above sweet compounds produced by its leaves can easily pass through the digestive process without any chemical breakdown. Diabetes is a major problem in India and other countries. Now, it is important to move the attention toward such natural sources which are acceptable for health. On the other hand, it also has some therapeutic properties like antihypertensive, anti-cancerous antihyperglycemic and has contraceptive properties. It is also beneficial for preventing the growth of fungi and bacteria. Now-a-days, stevia products are utilized by Israel, America, China, Korea, Japan, Argentina, Indonesia, Canada and Paraguay (Yadav et al., 2011). Annually 50 tons of stevioside are used in Japan with $220 million Canadian sales value. (Salim Uddin et al., 2006).

2. Review of literature:

Diabetes mellitus is a metabolic disorder because it affects all body organs. Therefore, health sector considers it as a nosological problem. It is a biochemical, physiological and anatomical disease which is caused by the disturbance of glucose level and low level of insulin production through the beta-cells in the pancreas. Long term disease create the vascular complication including large and small bood vessels such as ateriosclerosis, glomerulosclerosis and retinopathy. In Mexico, there is about 10% of the total population that are affected by diabetes. In 2012, NHNS (National Healthcare Safety Network) stated that approximately 6.4 million adults are affected by this disease. In 1995, the WHO (World Health Organization) observed that there are about 30 million people suffering from this disease in all over the world but in 2014 the WHO provided the data in which it told that about 347 million people are suffering in this disease. This institution estimated that in 2030 the infected people will be increased up to the 366 million worldwide (Carrera-Lanestosa et al., 2017).

In the India, the population is increaseing day by day due to which the sugar demand is also increasing along with the population but its production is very low. It is reported that in 2009-2010, sugar demand was 235 million tons but its production was 16 millions tons in India. In this country, about 70% sugar is consumed by sugar industries in the soft drinks, chocolates, candies and remaining sugar is

consumed by house purposes. In this country, a large proportion of the population is suffering from the diabates. So, they need such type of sugar which is free from the calories and chlorestrol. For fulfilling the demand of the people, researchers did many researches for increasing the sugar supply, then they focused on the stevia which is a sweetner and chloestrol free plant (Ranjan et al., 2011).

In the world, there are two types of sugar are present. One is natural sugar and other is synthetic sugar. Synthetic sugar has harmful effects on the human health. Now-a-days, due to the higher utilization of chemical sugar, many people are suffering in the chronic diseases such as diabetes, obesity, cardiac disease, blood pressure etc. For controlling these diseases, the scientists conducted numerous researches for the innovation of sweeteners which contain less calories and no side effects. Later, the scientists achieved their goal and introduced 'Stevia' which is natural non-caloric sweetener (Priya et al., 2011).

The botanical name of stevia is "*Stevia rebaudiana* bertoni". It belongs to the "Asteraceae" family. It is perennial shrub which cultivated in semi-humid subtropical areas. It is a wild plant of Paraguay and Brazil. The other name of this plant is "sweet herb of Paraguay". This plant can be cultivated up to the height of about 26 to 72 inches. The fertile and sandy soil is more suitable for its growth (Ahmed et al., 2011).

For the first time, it came under the observation in European region when its unique characters were studied by the M.S. Bertoni from the Paraguayan Indians and Mestizos. Then it was cultivated in England in 1942 but gave the unsatisfactory yield. It is reported that first time it was cultivated on the economical level in paragay in 1964. Sumida was a scientist which did many efforts for the introduction of stevia in the Japan. After that, it was cultivated as a crop in many countries including Brazil, Brazil, Korea, Mexico, United States.

Indonesia, Tanzania and Canada. China is the largest producer than the other countries (Brandle et al., 1998).

It has a woody stem above the ground which contain the paired leaf with the size of about 3-4 cm. It has axillary branches from nodes. It is a short-day plant, so its flowers are developed by increasing the length of dark period. Along with the day length, other factors which affect the floral development are plant genotypes, nutrients, heat and water stress. It has a compound inflorescence with the five tubular flowers having white colour. Its single stem has all reproductive stages because it has non-uniformity in the flowers. It has one seeded fruit which known as achene having feathery pappus. It has both vegetative and reproductive stages. (Carneiro, 2007). For the improvement of its yield and rebaudioside-A, different methods of conventional breeding has been utilized (Madan et al., 2010).

It can be cultivated by the seed or vegetative propagation but its rate of gernmination is not so high. On a commercial level, it can not be grown due to its high cost but on the small level it can be cultivated by clonal propagation method. It is perennial plant but in Canada it is cultivated as an annual plant. It can be cultiavetd in Feb or March and haversted in late summer. After the transplation of crop, its floral development should be completed between 54-104 days if long day length provided. For its cultivation, 23^0C is suitable temperature. During its pollination and seed fillling, if excessive rainfall occurs, its viability and production can be affected. If its seed is not stored at 0^oC then its rate of germination can be reduced to about 50% over the 3 years (Brandle et al., 1998).

Through the seed, its germination rate is approximately 50%. So, it can be cultivated through the stem cutting but it is very diffcult method because it needs a large number of cuttings. Therefore, tissue culturing is an alternative method for its good cultivation (Yadav and Guleria., 2012).

Its growth is affected by the moisture content in soil, wind, photoperiod, intensity of temperature, day length and radiation. Its yield depends upon the genetic characteristic. However, there are some factors of environment and climate which affect its growth like the terpenes synthesis is affected by the both factors. However, stevia gives better growth in semi-humid climate and the suitable temperature for its growth should be from -6.0 to 43°C and the average is 23°C. The duration of sun light is an important factor because in long days the area of leaf, its dry weight and the length of internodes increase as compared to short days. Long days also increase contents of glycoside in leaves, but flowering decreased its content. In short nights, when flowering of its plant is delayed, glycoside starts to accumulate in its leaves (Yadav et al., 2011).

It is good source of carbohydrates, minerals, protein and crude fibre. According to the recommended value of FAO and WHO for the adults, it contains the higher amount of essential amino acid (Esmat Abou-Arab et al.,2010). The chemical morphology of this plant is not completely studied but for its chemical composition different species has been studied. Then the scientists observed that leaf is an important part of this plant. Because its leaves contain those compounds which are the sources of sweetness. Only 18 species have these compounds out of 110 (Goyal et al., 2010).

The amount of steviol glycosides compounds depends upon plant organs, age of plant and developmental stages. The upper shoot section (leaves) contain the highiest amount of steviol glycosids while the lower section contain the lowest glycoside compounds. Every organs contain different proportion of SGs compounds and its proportion is decrease according to this order: leaves, flower, stem, seed and root. In the leaves, the concentration of SGs compounds can be change according to the age of plant and stages of the plant development. It observed that the concentration of glycoside compounds enhanced during the ontogeny in both mature leaves and stem upto the budding phase and flowering stage (Bondarev et al., 2003). Nitrogen fertilizer is important for the yield, plant heigh, leaf gases exchange as well as steviol glycoside compounds. The amount of steviol glycoside compounds are postively corelated to the nitrogen fertilizer. If the nitrogen fertilizer dose is decreases then the amount of SGs compounds also decreases and vice virsa. Due to the deficiency of nitrogen, the metabolic activities is distrubed in the stevia plant (Tavarini et al., 2016).

Its leaf has a sweet taste due to the presence of diterpenoid glycosides compounds. Along with these compounds, it also consists of diferent types and numbers of sugars which are attached with the C-13 and C-19. The *Stevia rebaudiana* bertoni consists of large amount of steviol glycoside that contains the steviosides and rebaudiosides-A (Philippe et al., 2014).

In these compounds, stevioside is a source of sweetness in its leaves. Its chemical structure was discovered by Mosettig, Fletcher and their colleagues, in 1963. In addition to these, there are four additional compounds which cause the sweetness in its leaves, rebaudiosides -A, -B, -C and -D which belong to the diterpenoids glycoside family. In case of taste, rebaudiosides are sweeter and less bitter than the steviosides. It is reported that its flower-buds contain these glycosides compounds but not exist in its roots (Tanaka, 1982).

From these glycoside compounds, rebaudiosides-A is a significant compound which is more sweeter than the other compounds. Along this, it is more stable and less bitter in taste than the stevioside. In 1987, Pederson has been reported that stevioside is a white crystalline powder which is obtained from its leaves. In 2006, it is reported that its fresh leaves contain 80-85% water. In addition to these glycosides, its leaves contain other substances such as ascorbic acid, b-carotene, chromium, cobalt, magnesium, iron, potassium, phosphorous, riboflavin, thiamine, tin and zinc (Goyal et al., 2010).

Stevioside is a stable compound which does not show the mutation and toxic effect on the human health. Therefore, it is used as a taste modifer and sugar substitute through out the world. It has an ability to stimulate the secretion of insulin from the pancrease for maintaning the glucose level in blood (Puri et al., 2012).

In case of medicinal, its importance has been introduced by the Kinghorn and Soejarto. They told that this plant is a source of non-caloric sugar that is beneficial for the diabetic patients. After the investigation, they observed that glucose level in blood can be maintained by these compounds. Stevioside has a property to stimulate the insulin secretion. Due to this property, stevioside is one which reduces the sugar level in both types of diabetes (Seema, 2010).

There are many methods for the extraction of steviol glycosides, but Ultrasound assisted-extraction method is suitable than the conventional method. Through this process, higher amount of steviol glycoside is obtained than the conventional method. This method takes less time for the extraction as compared to the conventional method. In this method, water is used as a solvent (Zlabur et al., 2015). Few years ago in India, its leaves were directly used as a sweetening agent in the tea and this tea were taken several times in a day without any side effect. In America, stevia products were banned because that time there was no any report about the safety of its utilization. But after investigation by Doug Kinghorn of the Herb Research Foundation and other researchers, it proved that stevia has no side effects. It is a natural sugar with no calories. Now its products are used throughout the European countries. (Ahmed et al., 2011).

Its products can be utilized throughout the world. In Japan, it is utilized in different diets, soft drinks, teas, coffees etc. In South America, its leaves are used in drinks, drinks, soju, soy sauce, yogurt and other foods. In Bangladesh, it is used in the tea for the diabetic patients. In the different European countries, it is used as a supplement. In addition to this, it is used as an antihyperglycemic, antihypertensive and antiviral (Hossain et al., 2010). There is no any attack of insects on this crop because it has the inherent sweetner which acts as a repellent. But different fungal diseases are identified such as root rot, leaf spot, powdery mildew, damping off, alternaria leaf spot and septoria leaf spot. So, the resistance sources are needed for making the resistance varieties against these disease (Yadav et al., 2011).

Conclusion

Stevia is having low calorie as compared to sugar. Chlogenic acids reduce conversion of glycogen to glucose and reduces absorption of glucose and reduce blood sugar level. It is used as a flavour

enhancer, taste enhancer and anti-bacterial effect. It is heat stable at high temperature can be cooked with tea and food. Stevia can be used widely in Jams, Sauces, Jelly, Confections, Beverages, and Pharmaceuticals and in Alcoholic beverages and in dental products. It is used in tea, coffee and dairy products.

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