

## Review Article

### Stevia (Madhu Patra) – A natural low calorie sweetener with more promising benefits.

BM Sattigeri

Department of Pharmacology, Sumandeep Vidyapeeth's SBKS Medical Institute and Research Center, Piparia, Tal: Waghodia Vadodara, Gujarat, India.

#### Abstract:

Sedentary life styles that we all tend to lead in present days facilitate increase in the incidence of disease conditions like obesity, diabetes and hypertension. Of all diabetes is most alarming especially in India which is labeled as "Diabetes Capital of world".

Several sweeteners are available that provide sweet taste for food and beverages, However natural sweeteners like honey and corn syrup are of threat as they precipitate diabetes, but non nutritive low calorie sweeteners are available. Ex Saccharin, Sucralose, Aspartame etc. The long term threatening effects reported with the use of these artificial sweeteners has made a way for introduction of an almost zero calorie natural sweetener Stevia with additional health benefits.

Stevia is a herb with medicinal values. Glycosides (stevioside, rebaudioside) obtained by the leaves of stevia are 250- 300 times as sweet as Sucrose. It is steadily gaining greater patronage in the growing global natural food market.

**Key Words:** Low calorie sweetener, Rebaudioside, Stevia, Stevioside.

#### INTRODUCTION

Obesity and its related health problems like diabetes, dislipidemia, heart disease, hypertension stroke etc are the results of a great advancement in life style, poor dietary habits, lack of exercise and stress, apart from genetic contribution.

Of all, the most alarming related health problem is diabetes. Consumption of sugar sweetened beverages is a major cause of obesity and diabetes. There is an alarming increase in the incidence of diabetes in India and with world's largest population being noted, India is labeled as "Diabetic capital of world". Therefore, substituting sugar with low calorie sweeteners may be efficacious in reducing the weight and its related health

problems. So, sugar substitutes like saccharin, sucralose and aspartame gained importance in reducing calorie intake. However they are artificial substitutes. Recently, it has been evident that prolonged use of artificially sweetened beverages / or prolonged use of aspartame lead to an increase in frequency of brain tumors in humans which is a major concern [1].

Stevia, commonly known in Sanskrit as *madhu patra*, meaning sweet leaf is natural and healthy alternative to sugar and artificial sweeteners. It is a famous perennial shrub, belongs to the family asteraceae, genus stevia and species rebaudiana. It is extensively grown in the subtropical regions, and has been available since decades for its

wide use as a sweetener in beverages and to mask the bitter taste of certain herbal medicinal plants in several countries like Brazil, Japan, and Paraguay etc [2].

The herb was for the first time researched by Spanish Botanist and Physician, Peter Jacob Stevius, from whose surname originates the Latinized word Stevia. There are 240 species of which *S.rebaudiana* is used in humans as sweetener. Leaves of this plant have 30-45 times the sweetness of sucrose. The plant has long history of its medicinal use in Paraguay and Brazil [3, 4].

In 1899, Moises Santiago Bertoni first described the plant and its sweet taste. Later with limited research in the field the topic remained dormant until 1931 while the French Chemist identified and isolated the glycoside that gives stevia its taste. The glycosides were named as stevioside and rebaudioside being 250-300 times as sweet as sucrose, heat stable, pH stable and non fermentable [5,6].

In 1970's while cyclamate and saccharin were suspected as carcinogens, Japan began cultivating stevia as an alternative which soon gained popularity and got commercialized. As it possesses flavor enhancing property it is used in food products and soft drinks like Coco-cola, Pepsi etc [7]. Today it is widely cultivated in countries like China, Korea, Thailand, Brazil, Peru, Paraguay and Isreal etc.

Apart from its sweetness stevioside along with related compounds which include rebaudioside A and steviol offer many therapeutic benefits that include antihypertensive, antidiabetic, anti-inflammatory, anti tumor, antioxidant, antidiarrhoeal, diuretic and immunomodulatory actions. Steviol interacts with the drug transporters and for this property of its, Steviol is proposed as drug modulator [6, 8, 9].

#### **Mechanism of action:**

The taste buds on the tongue react to the glucose in the glycoside. Those glycosides with more glucose (rebaudioside) taste sweeter than (stevioside) that tastes less sweet. Some of the taste buds react to the bitter taste of aglycone [5, 6].

#### **Pharmacokinetics:**

Gardana et al in their study show that, in the gut, rebaudioside and stevioside are hydrolyzed to steviol and glucose. The glucose released in the process is used by bacteria in colon and not absorbed into blood stream. Steviol was absorbed and conjugated to glucuronide. The half life ( $t_{1/2}$ ) for both glycosides is approximately 14hrs. It is excreted as steviol glucuronide through urine and feces [10, 11, 12].

#### **Therapeutic Benefits:**

**1. Anti hyperglycemic effect:** Animal studies have shown that stevia has a revitalizing effect on the beta cells of pancreas, also improves insulin sensitivity and promotes additional insulin production. Chen TH and co-workers found that stevioside was able to regulate blood glucose levels by enhancing not only insulin secretion but also insulin utilization in insulin deficit rats. The later was due to decreased phosphoenol pyruvate carboxykinase gene expression in rat liver by stevioside's action of slowing down glucogenesis. Stevioside reduces the postprandial blood glucose levels. Several human trials conducted in normal healthy volunteers have shown that extracts of stevia rebaudiana leaves could increase glucose tolerance in humans. Therefore stevia may be advantageous in the treatment of type 2 diabetes [13, 14, 15, 16, 17].

**2. Antihypertensive effect:** Physiological and Pharmacological experiments have suggested that stevioside from the leaves of stevia act as a typical systemic vasodilator. Melis MS et al in their studies have demonstrated that stevioside from stevia rebaudiana leaves provoked hypotension, diuresis and natriuresis in both normal and hypertensive rats. An increase in the renal plasma flow and glomerular filtration in rats had been observed in normal rats and the effect was attributed to the vasodilatation of afferent and efferent arterioles [18, 19].

Human studies have also suggested its beneficial role in hypertension for its vasodilator property. It was suggested that 750 – 1500 mg/ day of stevioside, reduces systolic blood pressure by 10 – 11 mmHg and diastolic blood pressure by 6 -14 mmHg within one week of starting the treatment [20,21].It is found that stevioside causes vasorelaxation by inhibition of  $Ca^{++}$  influx into the blood vessels [22]. Therefore stevia could prove to be beneficial in hypertensive patients.

**3. Anti oxidant effect:** Being natural stevia is potential source of natural antioxidants. Varieties of antioxidants were obtained from the extracts of stevia rebaudiana, they include, opigenin, kaempferol and quereitrin that inhibited DNA strand damage. Isosteviol, a derivative of stevioside inhibits angiotensin II induced cell proliferation and endothelin I secretion while attenuation of reactive oxygen species generation [23, 24]. Hence it could be beneficial in a variety of diseases like cancer, reproductive problems and developmental defects.

**4. Anti Cancer effect:** Although limited evidence are available, animal studies by Yasukawa et al indicate that the four isolates of steviol glycoside - stevioside,

rebaudiosides A & C and ducloside A from stevia rebaudiana have a strong inhibitory effect on 12- O- tetradecanoylphorbol-13-acetate (TPA) induced inflammation in mice which is suggestive of its anticancer effect [ 25,26].

**5. Antimicrobial effect:** Evidential research reports indicate that derivatives prepared by stevia isolates which included octa - acetylombuoside, ombuine and retusine were found to have antimicrobial action against few types of gram positive bacteria [27].

**6. Anti-inflammatory and immunomodulatory effect:** Stevia has been found to attenuate synthesis of the inflammatory mediators in LPS stimulated THP-1 cells by interfering with the I Kappa B kinases (IKKbeta) and Kappa B signaling pathway thus beneficial as anti inflammatory and immunomodulatory substance[28].

**7. Miscellaneous:** Stevia is also rich in beta carotene, ascorbic acid, protein, calcium, iron, magnesium, phosphorus and numerous other phytochemicals. Hence the herbal derivative apart from its sweetening property also is beneficial with its nutritive value. Other proposed uses include alcohol abuse, anti inflammatory, anti mutagenic, antitumor, diuretic, digestive aid, food additive, immunomodulation and obesity [9].

#### Advantages of Stevia:

In comparison to the artificial sweeteners Stevia posses several advantageous properties that include;

- 1.Appetite regulation / suppression.
- 2.Being zero calorie sweeteners, assists in weight management / weight loss (as it reduces craving for sweets).

- 3.No major safety concerns.
- 4.Ideal for cooking and baking as it is non fermentable and heat stable up to 200°C.
- 5.Calorie value is 2.7kcal/gm.
- 6.Intense in its sweetening property.
- 7.Cheaper as compared to other sweeteners.
- 8.Safe and beneficial in management of diabetes and obesity.

**Drug Interactions:**

1. It has diuretic effect so it decreases the excretion of lithium with resultant increase in plasma lithium concentration and leads to lithium toxicity [18].
2. Given along with antidiabetic agents like glimepride, pioglitazone etc may cause decrease in blood sugar levels hence needs close monitoring of blood sugar levels.
3. Stevia may also interact with monoketocholate (a substance that may affect glucose and lipid levels), diuretics, anti inflammatory, anticancer agents or hypocalcaemia agents [25].
4. Verapamil tends to increase the renal and systemic effects of stevia [29].

**Adverse Effects and Contraindications:**

- Generally it is considered to be safe, with minimal side effects that include; nausea, abdominal fullness, myalgia, muscle weakness, dizziness, asthenia and allergy [5, 6].
- It is used with caution in diabetes as it is known to reduce the blood sugar levels.
- In hypertensive patients it is used with caution as it is likely to reduce the blood pressure.
- It may affect the renal activity and perfusion, sodium excretion and

urinary flow hence, cautious use is indicated in patients with renal disease or with impaired renal function [18].

- With lack of evidence for its effect on pregnancy and lactation Stevia is not recommended during pregnancy and lactation.

**Safety and Health issues of Stevia:**

In 1985, Steviol a break down product of Stevia was reported as a mutagen based on animal studies. Later with serial of bioassays, cell cultures animal studies that were conducted revealed no evidence of stevia constituents causing genotoxicity, cancer or birth defects [30, 31].

In 2009, US FDA recognized rebaudioside A as safe. In 2012 the European food safety, established an accepted daily intake for steviol glycoside expressed as 4mg/kg body weight/day. In 2011, the European Commission allowed usage of steviol glycoside as food additive, establishing maximum content levels for different types of foods and beverages.

**Conclusion:**

Stressful and sedentary life styles of present days alarmingly increase the incidence of diabetes, hypertension and obesity affecting mainly the young adults. If adequate care and regularity in treatment is neglected these problems lead to complications, which further increase morbidity and mortality rate.

A little health conscience knowledge and modification of life style will help us fight these conditions. Stevia being herbal natural product, with virtually calorie free status causing less harm, benefits several health conditions and has a bright future with other medicinal values apart from its use as a sweetener.

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