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Health Benefits and Application of *Stevia rebaudiana Bertoni* in Dentistry

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ABSTRACT

A wide range of artificial and synthetic products have been replaced by the natural products for daily use. The natural products are believed to have more advantages and less adverse effects. The plant products such as stem, flower, fruit, seed, leaves, etc have been experimented. Stevia rebaudiana Bertoni, a perennial shrub which is a native of South America. During World War II, England used it as a sweetener as sugar was not available. By 1970, it was used as a sweetener in Japan. In 1994, US approved steviol glycosides as functional ingredient in dietary supplements. It is non-caloric sweetener which is 200-300 times sweeter than table sugar. Its use as a sweetener was approved by FDA in 2011. There is growing evidence supporting the use of stevia in diabetes, hypertension, weight loss, etc. Dental caries is an infectious microbiologic disease of the tooth that results in localized dissolution and destruction of calcified tissues. There has been an increased interest on antimicrobial and anti-plaque activity of stevia mouth rinse and chewing gums. Researches on the aqueous and alcoholic extracts of stevia have also been conducted to evaluate its potential advantages in the dental field. This review describes in detail the health benefits and application of stevia in dentistry.

Keywords: Stevia, Dental, Medical

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INTRODUCTION

Stevia rebaudiana Bertoni is a natural sweetener and an effective alternative to sugar [1]. The genus stevia belongs to *Asteraceae* family and tribe *Eupatorieae* which includes about 240 species [1,2]. Stevia was first classified in the year 1940 and it is named after Spanish botanist and physician Petrus Jacobus Stevus [3]. It is commonly known as stevia, candy leaf, sweet leaf of Paraguay, sweet-herb, honey yerba, honey leaf, yaawaan [1]. The vernacular name for Stevia are madhu patra (Sanskrit), meethi patti (Hindi), stévia or stévie (French), ka'a he'ẽ (Brazil), madhu parani (Marathi), süßkraut (German), chini biruwa (Nepal), tian ju ye (Chinese), ya-wan (Thailand) [1].

TAXANOMIC CLASSIFICATION [4]:

- Kingdom: Plantae
- Subkingdom: Tracheobionta
- Superdivision: Spermatophyta
- Division: Magnoliophyta
- Class: Magnoliopsida
- Subclass: Asteridae
- Group: Monochlamydae
- Order: Asterales
- Family: Asteraceae (Compositae formerly)
- Subfamily: Asteroideae
- Tribe: Eupatorieae
- Genus: Stevia
- Species: rebaudiana

ORIGIN AND DISTRIBUTION

Stevia is native of South America especially Paraguay, Brazil and Argentina. It is commercially cultivated in China, Japan, Brazil, Canada, USA, UK, Spain, Belgium, Australia, South Korea, Thailand, Israel and Taiwan [5]. China and Japan are the world's major producers and exporters for stevia. Japan has approved the use of stevioside in many food products including cereals, teas, and soft drinks in 2006 [6].

MORPHOLOGICAL DESCRIPTION:

Stevia is a subtropical perennial herb which has more or less pubescent stems with extensive, fibrous and filiform root system [4]. The plant grows upto 65-80 cm in height and bears sessile, oppositely arranged leaves with blunt-tipped lamina having serrate margin from the middle to the tip (Fig. 1)[5] The plant bears small (10-15 mm) white colour pentamerous flowers (Fig. 2) in capitulum surrounded by green colour bracts. Seed of stevia is a five-ribbed spindle shaped achene with feathery pappus (Fig. 3) [4].

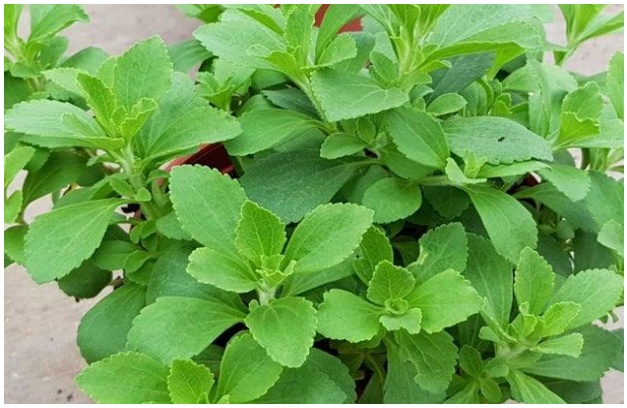

Figure 1: Stevia plant

Figure 2: Stevia flower

Figure 3: Stevia seed

COMPOSITION OF STEVIA

Gylcosides which imparts sweetness are present in stevia. There are 2 main glycosides in stevia; stevioside and Rebaudioside A. The other glycosides which yield sweetness are Steviol, Steviolbioside, Rebaudioside B, Rebaudioside C, Rebaudioside D and Dulcoside A. Stevia is a nutrient rich herb containing substantial amount of other nutrients including 80 to 85% water, protein, fibre, amino acids, lipids, ascorbic acid, chromium, cobalt, magnesium, iron, potassium, phosphorus and trace elements [7]. A bitter taste is reported after use of stevia due to the presence of tannins, flavonoids and essential oils. Table 1 illustrates the gylcosides and its sweetness relative to glucose.

SAFETY ASPECTS AND ADVERSE EFFECTS

In 2004, under safety standard limit, steviol glycoside was given temporary authorization by Joint Expert Committee of the Food and Agriculture Organization/World Health Organization (FAO/WHO) on food additives (JECFA) [5]. In 2008, 4 mg/kg/day was approved as the Acceptable Daily Intake (ADI) for purified steviol glycosides and its use was validated as a sweetener in food and beverages [5]. Its use has been added to the European Union (EU) list of permitted sweeteners. Following its approval by the United States Food and Drug Administration (USFDA) in 2016 and the European Union (EU) in 2011, Food Safety and Standards Authority of India (FSSAI) in 2017 accepted steviol glycoside as a sweetener in selected food products within ADI limits [12]. Geuns (2003) in a review concluded that stevioside has very low acute toxicity, and no allergic reactions when used within ADI limits [8].

Table 1: Major steviol gylcosides and its sweetness relative to glucose

Stevia components	Amount of sweetness relative to glucose
Stevioside	150-300
Rebaudioside A	200-400
Rebaudioside B	330-350
Rebaudioside C	50-120
Rebaudioside D	200-300
Rebaudioside E	250-300
Rebaudioside F	Not available
Rubusoside	110
Steviolmonoside	Not available
Steviolbioside	100-125
Dulcoside A	50-120

ADDITION OF STEVIA IN FOOD PRODUCTS

FSSAI has approved the use of stevia in following 11 food products; dairy based flavoured drinks and desserts, yoghurt, fruit nectars, non-carbonated water based beverages, ice lollies/edible ice, jams, jellies, marmalades, ready to eat cereals, carbonated water, soft drink concentrate and chewing gum [5].

PHARMACOLOGICAL APPLICATIONS

Antibacterial and anti-fungal activity:

Vitery et al (2010) studied the inhibitory action of stevia against bacterial and fungal species. They reported that inhibitory action were present when extracts from stevia leaves were dissolved in solvents like water, methanol, ethyl acetate and hexane against four gram-positive cells (*B. subtilis*, *S. aureus*, *M. letus*, *B. megaterium*), four gram-negative cells (*S. marcensens*, *P. aeruginosa*, *E. coli*, *P. valgaris*) and fungus such as *R. oligosporus* and *A. niger* [9].

Anti-viral activity:

Takahashi et al (2001) analysed the anti-rotavirus activity of stevia. The study reported inhibitory action of steviol on anti-human rotavirus effect (HRV) because it inhibited the binding of VP7 to the cellular receptors further leading to blockade of HRV attachment to the cells [10].

Anti-inflammatory activity:

The anti-inflammatory property of stevioside was evaluated by Fengyang et al (2012). They concluded that stevioside exerts anti-inflammatory effect by inhibiting the activation of NF-κB and mitogen-activated protein kinase signalling and the release of pro-inflammatory cytokines [11] Borojeni et al (2017) in a review concluded that stevioside can reduce inflammation and mediate immunomodulation through inhibition of pro-inflammatory cytokines at the level of gene expression [12].

Anti-diabetic properties:

Xiao and Hermansen (2005) and Chen et al. (2006) found that stevioside enhances glucose-stimulated insulin secretion, but does not affect fasting insulinemia [13,14].

Anti-hypersensitive properties:

Chan et al (1998) showed that intravenous administration of stevioside in spontaneously hypertensive rats (SHR) lowered blood pressure but had no effect on heart rate [15]. The study also reported that there was no change in levels of catecholamines present in blood, although there was a decrease in plasma levels of norepinephrine. Kaushik et al (2010) found that stevia helped in reduction in weight in humans as it cannot be metabolized in body to produce energy [16].

Action on renal function:

Melis (1992) evaluated effect of stevioside on renal function in normal and hypertensive patients. The author reported that stevioside provoked hypotension and it also led diuresis and natriuresis by increase in renal plasma flow and glomerular filtrate rate [17].

EFFECT OF STEVIA ON DENTAL HEALTH

In vitro studies in dentistry:

Gambao et al (2012) conducted an in vitro study to determine the antibacterial activity of stevia on 16 bacterial strains of Streptococcus and Lactobacillus. The study concluded that antibacterial activity was highest when the extract was diffused in ethanol and methanol compared to hexane, ethyl acetate and chloroform in both the species [18]. Similarly, Ajagannanavar et al (2014) reported that, the inhibitory effect of alcoholic stevia extract against S. mutans and L. acidophilus was superior when compared to aqueous form and was inferior when compared with Chlorhexidine [19].

Giacaman et al (2013) determined the effect of commercially available sweeteners such as stevia, sucralose, saccharin, aspartame and fructose in tablet or powder form on enamel demineralisation. They also evaluated its effect on *Streptococcus* mutans biofilms in an artificial caries model. The study was done for 5 days and the slabs/ biofilms of bovine enamel were exposed to the sweeteners for three times per day for 5 minutes. Enamel demineralization before and after 5 days was assessed by measuring surface microhardness. They reported less demineralization with all the sweeteners except fructose. They also reported that stevia reduced the number of bacterial counts as compared to sucrose [20]. Likewise, Derani et al (2016) reported no difference in hardness score of extracted bovine teeth when 5% xylitol and 5% stevia was compared with phosphate buffer and 0.5% stevia [21].

Korte et al (2019) evaluated the effect of commercially available low-calorie soda beverages on enamel of primary teeth. The study consisted of 56 enamel slabs which were divided into 5 groups; 0.9% NaCl, Coca-Cola Classic (sucrose), Diet Coke (aspartame), Zevia Cola (erythritol), Coca-Cola Life (stevia). The slabs were exposed for 60 minutes and the surface roughness was measured before and after exposure. The surface roughness was less in stevia as compared to aspartame and sucrose but this difference was not statistically significant [22].

In vivo studies in dentistry:

Das et al (1992) conducted an in vivo study in rats to determine the cariogenic potential of stevioside and Rebaudioside A and found that neither stevioside nor Rebaudioside A had potential to develop caries [23]. de Slavutzky (2010) evaluated the effect on plaque formation after rinsing with stevia solution. The study consisted of 8 dental students who were given sucrose solution to rinse for 1 minute four times a day for 5 days. After a washout period of 2 days, the same volunteers were given stevia solution to rinse in similar way. The stevia solution was prepared by boiling 100 grams of stevia leaves for two hours in 3 litres of distilled water. They reported reduction in dental plaque in stevia group as compared to sucrose [24]. Correspondingly, Vandana et al (2017) determined the effect of daily prepared 10% stevioside mouth rinse on gingival and plaque status. The study consisted of four groups, 0.2% chlorhexidine gluconate; 0.05% sodium fluoride, 10.6% stevioside and placebo. Each group consisted of 27 females between the age group of 12-15 years. They concluded that stevia had an anti-plaque and anti-gingivitis properties as compared to other mouth rinses at end of 6 months trial [25].

Giongo et al (2014) evaluated the effect of commercially available lactose-containing stevioside sweetener on biofilm acidogenicity. They reported that sweetener containing 6.8% saccharin with 13.6% cyclamate and 0.82% stevioside was least cariogenic followed by 93% lactose combined with 7% stevioside and 93% lactose [26]. Brambilla et al (2014) evaluated the effect of different stevia extracts on salivary pH. The study consisted of 20 volunteers between 19-26 years. Three 10% solutions of stevioside, rebaudioside A and sucrose were prepared and each participant was asked to rinse with the solution for 1 minute. The salivary pH was noted at baseline and 5, 10, 15, 30, 45, 60 minutes after rinsing with mouth rinse. After a washout period of 48 hours the participants were asked to rinse with the next solution. They reported decrease in salivary pH after rinsing with sucrose solution as compared to stevia from baseline to 30 minutes [27].

Siraj et al (2019) evaluated the efficacy of stevioside on plaque pH in 22 under graduate dental student volunteers between 18-25 years of age. The participants were given to rinse 10 ml of freshly prepared solution comprising either 0.2% aqueous stevia, 10% sucrose and 1% stevia product for 1 minute. The plaque pH was measured on the interproximal area of molar and premolar in first and second quadrant using a digital pH meter. The pH was recorded at baseline and 5, 10, 15, 30 minutes after rinsing. They reported that there was statistically significant difference in mean plaque pH values between aqueous stevia extract and stevia product when compared with sucrose solution [28].

Shinde and Winnier (2020) evaluated the effect of commercially available chewing gums containing stevia and xylitol respectively on salivary *S. mutans*, pH, flow rate and taste acceptance in 8-13-year-old children. They reported that stevia is equally effective to Xylitol chewing gum in reducing salivary *S. mutans* and increasing salivary flow rate and salivary pH. Stevia due to its bitter aftertaste is less accepted in children as compared to Xylitol [29,30].

CONCLUSION

Stevia is non-caloric natural sweetener which has numerous medicinal and dental benefits. It is used as an alternative sweetening agent for dental products such as chewing gums and mouth rinses. It also has lower demineralizing and cariogenic potential. Further long-term studies are required to determine the efficacy of commercially available products and extracts of stevia on dental health.

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