INNOVARE JOURNAL OF LIFE SCIENCE

INNOVARE ACADEMIC SCIENCES Knowledge to Innovation

Vol 1, Issue 1 , 2013

Research Article

APPROACHES FOR TASTE MASKING USING STEVIA LEAF IN PHARAMCEUTICALS

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Received:3 May 2013, Revised and Accepted:3 May 2013

ABSTRACT

teachniques Oral administration of pharmaceuticals is one of the most popular method of drug dilevery.Taste is an important factor in the development of dosage form. Many active Pharmaceutical ingredients are bitter and require some form of taste masking to yield palatable drug products. Proven methods for bitterness reduction and inhibition have resulted in improved palatability of oral pharmaceuticals. Several approaches like adding flavors and sweeteners, use of lipoproteins for inhibiting bitterness, coating of drug with inert agents, microencapsulation, multiple emulsion, viscosity modifiers, liposome, prodrug formation, salt formation, formation of inclusion and molecular complexes, solid dispersion system and application of ion exchange resins have been tried by the formulators to mask the unpleasant taste of the bitter drugs but these methods are highly cost effective. Stevia rebaudiana Bertoni, source of a high-potency natural sweetener and produces diterpene glycosides that are low calorie sweeteners, about 300 times sweeter than saccharose with addition inclusion of without interfere.

Keywords: Taste and types of taste, types of masking, Stevia leaf –Botanical description, Phytochemical constituents And Application of Stevia leaf.

INTRODUCTION

All over world there is increasing tendency towards consuming natural products and thus living a natural life and. At the same time our life styles have changed so much over the last 4-5 decades that sweeteners (either high calorie natural or proceeded sugars or high potency and low calorie sweeteners such as Aspartame) have become integral part of our natural daily diet.

Due to sedentary life styles that we all tend to lead these days the incidence of obesity and diabetic conditions are increasing dramatically. In India number of diabetic people in the age group of 25-45 is about 15% and is increasing at an alarming pace. In addition, we are largest consumers of sugar in the world. This single factor, we have come to understand, would greatly contribute to increasing the number of diabetic people and related problems.

Stevia, botanically known as Stevia rebaudiana Bertoni (Family-Asteraceae) is a sweet herb. A perennial herb, Stevia is a member of the daisy family. The leaves are mid green and intensely sweet. The compounds in the leaves are called stevioside and rebaudioside and they can be more than 200 times sweeter than sugar. The plant bears greenish cream flowers in autumn.

Although Stevia has been in use in Asia and Europe for years, it was only in the past couple of years that is really started to capture attention in the India market as a healthy alternative sweetener to sugar. Stevia has no calcium cyclamate, no saccharin, no aspartame and no calories. It is safe for diabetics, as it does not affect blood sugar levels; it does not have the neurological or renal side effects associated with some of the artificial sweeteners.

Stevia is a new crop in that is gaining very high popularity amongst all type of sweetener users as most ideal substitute for sugar. Sugar is basically a chemical that has grown in market over last many years. But in this age of changing life styles and people becoming more conscious of their health, the worldwide sugar consumption is going down and is getting replaced by low calorie sweeteners. Many of these Sweeteners are complex chemicals or many times naturals as well.

Stevia is gaining more acceptances amongst countries of eastern block such as Japan and Korea. There are many advantages of using Stevia over conventional sweeteners the main one being:Stevia leaves are 20-30 times sweeter than sugar. Stevia leaves can be dried and stored. Stevia can be used in raw from. Stevia is short duration crop. It is harvested 3/4 times a year. The yearly yields can be in the range of 3-4 tons. Stevia can be sold @ 40-70 Rs per kilo so dried leaves and is thus economically extremely beneficial to growers.

TASTE AND TYPES OF TASTE SENSATION

Taste is ability to respond to dissolved molecules and ions called tastants. It is defined as the sense that distinguishes sweet, sour, salty and bitter qualities of dissolved substances in contact with the taste buds on the tongue and this sense in combination with the sense of smell and touch together receive a sensation of a substance in the mouth.

Physiology of taste

Chemicals from a food or oral ingested mendicants are dissolved by saliva and enter via the taste pore. There they either interacts with surface protein known as taste receptor or with pore like proteins called ion channels. These interactions cause electrical change with the taste cell that triggers them to send chemicals signals that translates in to neurotransmission to the brain. Salt and sour responses, while sweet and bitter are surface protein responder. The electrical responses that send the signal to the brain area result of varying concentration of charged atoms or ions within the taste cell. This information gets to the brain via three different nerves facial nerve (VII), pharyngeal and vegus nerve(X).Since there are three different information pathways to the brain through these three nerves the sense of stimuli .If damage occurs to one of these nerves, the other two nerves are strengthened through inhibitor reduction.

Humans commonly recognize five types of taste

Sweet Taste -Usually indicates energy rich nutrients.
Umami Taste -The taste of amino acids(e.g. meat broth or aged cheese)
Salty Taste-Allows modulating diet for electrolyte balance.
Sour Taste -Typically the taste of acids.
Bitter Taste-Allows sensing of diverse natural toxins.

Sweet Taste

Amino Acids such as Glycine are sweet. Glycine in combination of saccharine is used as sugar substitute. The sodium salt and calcium salt of cyclohexyl sulfuric acid (cyclamates) and dipeptide.
Esters aspartame is thirty times more sweetener than sugar substitute saccharine contains benzene nucleus and is intensely sweet in taste, otherwise naturally occurring glycosides frequently contains benzene nucleus but are bitter. Any single class of common sweet substances .i.e. sugars (sucrose, fructose and glucose) and glycerine which contribute to sweetness.

E.g. sugars, saccharin.

Salty taste

The salty taste is elicited by ionized salt. Sodium chloride has a salty taste. Chlorides of potassium, ammonium and calcium have similar salty taste, but they have different solution taste. Taste sensitivity of salt changes to bitterness as the molecular weight increases .e.g. Potassium bromide and Ammonium iodide have salty, bitter taste but potassium iodide is intensely bitter.

Umami Taste

Umami is the taste of certain amino acids (e.g glutamate,aspartate and related compounds)Recently it has been shown that the metabotropic glutamate receptor mediated Umamai Tastes. Binding to the receptor activates a G protein and this may elevate intracellular Ca^{2+} and transmitter release and increased firing in primary afferent nerve.

Sour taste

Acid causes sour taste and the intensity of Taste sensation is proportional to the logarithm hydrogen ion concentration. In case of dilute solution it is tasteless at the same concentration. It indicates that sour taste is due to hydrogen ions not due to chloride ions. It implies that sour sensation in solution ca be eliminated by appropriate counter ions. It has been demonstrated that addition of sodium acetate to acetic acid reduces the hydrogen ion concentration, there by eliminating the sour sensation in acetate solution. Sour taste is not entirely dependent on hydrogen ions however the concentration of anions and undissociated species in solution is also important.

Bitter Taste

A bitter taste like sweet taste is found in wide variety of compounds most of which are salts of organic acids. There are two classes of substances which causes bitterness.

- Long chain organic substances that contain Nitrogen.
- Alkaloids and Aspirin [1].

TASTE MASKING OF PHARMACEUTICALS

Various methods are available to physically mask the undesirable taste of drugs, some of which are described below

- Taste masking with flavors, sweeteners, and amino acids
- Polymer coating of drug:
- Formation of inclusion complexes:
- Ion exchange resin complexes:
- Solid dispersion
- Microencapsulation
- Mass extrusion
- Multiple Emulsions
- Development of Liposome
- Prodrug concept
- Taste masking by spray drying technique
- Taste masking by adsorption
- Taste Masking with Lipophilic Vehicles like lipids and lecithins

Taste masking with flavors, sweeteners, and amino acids

This technique is fore the most and the simplest approach for taste masking, especially in the case of pediatric formulations, chewable tablets, and liquid formulations. But this approach is not very successful for highly bitter and highly water soluble drugs. The materials for taste masking purpose have often been classified depending upon the basic taste that is masked. Natural products include fruit juices, aromatic oils such as peppermint and lemon oils, herbs, spices and distilled fractions of these. The list of flavoring agents is shown in (table no.1.1). They are available as concentrated extracts, alcoholic or aqueous solutions, syrups or spirit.
Clove oil and calcium carbonate, which has been found to be particularly useful to mask the unpalatable active in formulations which are intended to be chewed or dissolve in mouth prior to ingestion in solution. Aspartame and sodium saccharine are the sweeteners used to mask the bitter taste of drugs. List of sweeteners are shown in (table no.1.2) Monosodium glycyrrhizin together with flavors has been used to mask the bitter taste of guaifenesin, Rannitidine, Loratadine [5, 6, 7].

Table no 1.1: List of Flavouring Agents

Flavour Natural	Synthetic Flavours	Basis of Choosing a Flavor
Juices – Raspberry	Alcoholic solutions	Complementary to existing flavor of the drug
Extracts – Liquorice	Aqueous solutions	Known popularity of particular flavors
Spirits - Lemon & Orange	Powders	Age of patients
Aromatic Oils Peppermint & Lemon.	-	Allergy

Table 1.2: List of Sweetener

Natural Sweetener	Artificial sweetener
Sucrose, Glucose, Fructose	Saccharin, Saccharin sodium
Sorbitol, Mannitol, Glycerol	Aspartame
Honey, Liquorice	Artificial Sweetener

***Stevia rebaudiana* Bertoni, source of a high-potency natural sweetener**

Stevia rebaudiana Bertoni, an ancient perennial shrub of South America, 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. Stevioside and rebaudioside A are the main sweetening compounds of interest. They are thermostable even at temperatures of up to 200°C.

Classification of plant
Kingdom- Plantae
Subkingdom- Tracheobionta
Super division- Spermatophyta
Division -Magnoliophyta
Class -Magnoliopsida

Subclass -Asteridae
Group -Monochlamydae
Order -Asterales
Family -Asteraceae (Compositae formerly)
Subfamily -Asteroideae
Tribe-Eupatorieae
Genus- *Stevia*
Species- *rebaudiana*

Figure 1: *Stevia rebaudiana* Bertoni leaves

Botanical description

Stevia is a genus of about 200 species of herbs and shrubs in the sunflower family (Asteraceae). It grows up to 1 m tall.The plant is a perennial herb with an extensive root system and brittle stems producing small, elliptic leaves.The leaves are sessile, 3–4 cm long, elongatelanceolate or spatulate shaped with blunt-tipped lamina, serrate margin from the middle to the tip and entire below. The upper surface of the leaf is slightly granular pubescent. The stem is woody and weak-pubescent at the bottom. The rhizome has slightly branching roots. The flowers are pentamerous, small and white with a pale purple throat. They are composite surrounded by an involucre of epicalyx. The capitula are in loose, irregular, sympodial cymes. The tiny white florets are borne in small corymbs of 2–6 florets.

Stevia will grow well on a wide range of soils given a consistent supply of moisture and adequate drainage; plants under cultivation can reach up to 1 m or more in height. It is being cultivated in continental China, Taiwan, Thailand, Korea, Brazil, and Malaysia. Besides the

Above-mentioned countries, Stevia is also grown in Israel, the Ukraine, the UK, the Philippines, Canada, Hawaii, California and all over South America.

Phytochemical constitutes

Diterpene glycosides

Glycosides are compounds containing a carbohydrate molecule (sugar) bound to a non-carbohydrate moiety. These compounds are mainly found in plants, and they can be converted, by hydrolytic cleavage, into a sugar and a non-sugar component (aglycone). They are named specifically by the type of sugar that they contain, as glucosides (glucose), pentosides (pentose), fructosides (fructose), etc.

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. Stevioside and rebaudioside A are the main sweetening compounds of interest. *S. rebaudiana has* a great potential as a new agricultural crop since consumer demand for herbal foods is increasing and proximate analysis has shown that Stevia also contains folic acid, vitamin C and all of the indispensable amino acids with the exception of tryptophan. *Stevia* cultivation and production would further help those who have to restrict carbohydrate intake in their diet to enjoy the sweet taste with minimal calories.

Eight diterpene glycosides with sweetening properties have been identified in leaf tissues of stevia. The four major sweeteners are stevioside, rebaudioside-A, rebaudioside-C and dulcoside-A. The two main glycosides are stevioside, traditionally 5-10% of the dry weight of

the leaves, and rebaudioside-A (Reb-A), 2-4%; these are the sweetest compounds. There are also other related compounds including minor glycosides, such as rebaudioside-B, rebaudioside-C (1_2%), rebaudioside- D, rebaudioside-E, rebaudioside-F, dulcoside-A, dulcoside-C and steviolbioside, as well as flavonoid glycosides, coumarins, cinnamic acids, phenylpropanoids and some essential oils.

Stevioside was reported to be the most abundant stevia glycoside (4–13% w/w) found in the plant leaves. It is followed by rebaudioside A (2–4% w/w), rebaudioside C (1–2% w/w) and dulcoside A (0.4–0.7% w/w). Steviolbioside, rebaudioside B, D, E and F were also identified in the leaf extracts, but as minor constituents .In addition to these compounds, Stevia extracts were also reported to contain flavonoids, sterebins A to H, triterpenes, volatile oil components, pigments, gums and inorganic constituents [2-3].

Among the components of stevia, one, called rebaudioside-A, is of particular interest because it has the most desirable flavour profile.Stevioside traditionally makes up the majority of the sweetener (60-70% of the total glycosides content) and is assessed as being 110-270 times sweeter than sugar. It is also responsible for the bitter after taste, sometimes reported as a "licorice" taste. As well as sweetness, stevioside may have a lingering effect or certain degree of pungency, which is not appreciated by the majority of people, and which reduces its acceptability. Rebaudioside- A is usually present as 30_40% of total sweetenerand has the sweetest taste, assessed as 180_400 times sweeter than sugar with no bitter aftertaste (licorice taste or lingering effect).

The sweetness of any of the stevia compounds is greater than that of saccharose: rebaudioside A (250–450 times); rebaudioside B (300–350 times); rebaudioside C (50–120 times); rebaudioside -D (250–450 times); rebaudioside E (150–300 times); dulcoside A (50–120 times); and steviolbioside (100–125 times). On average, the sweetness of the steviol glycosides is 250–300 times greater than that of saccharose, with low water solubility and high melting points Stevioside, the most abundant steviol glycoside in the leaf of the plant, has become well known for its intense sweetness (250–300 times sweeter than solutions containing 0.4% saccharose), and is used as a non-caloric sweetener in several countries.

Other Applications of *Stevia* Leaf

Anti oxidant activity
Anti Hypertensive Activity

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