Chemicals structure, Properties, and Applications of High intensity sweeteners

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Agenda

- Introduction
- Known High intensity sweeteners (HIS).
- Their Chemicals structure.
- Properties, Safety, and regulatory.
- Benefits, and applications.
- Comments.

Introduction

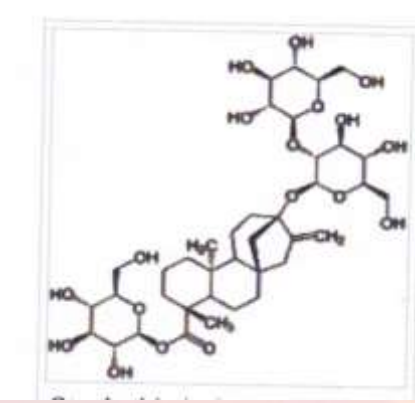
- High intensity sweeteners (HIS) are sweeter than sucrose with zero or low calories.
- Consumers are increasingly concerned with diabetes, weight gain, obesity-related disorder and dental caries.
- This is shaping the need for manufacturing something sweet that is non-nutritive and low /zero in calories .
- The global demand of HIS is over 9.00 billion dollars/year.
- Worldwide produced over 170 million metric tons of sugar per year.

Known HIS sweeteners

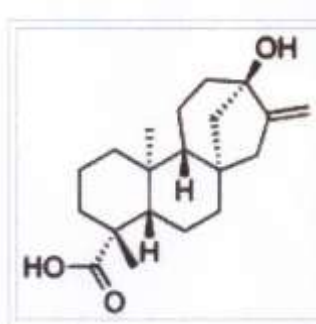
- **Natural extracts**:
  - Steviol glycosides.
  - Mogrosides.
  - Thaumatin.
  - Brazzein.
- **Semi Synthetic Sugar**:
  - Sucralose
- **Semi-Synthetic Peptides**:
  - Aspartame.
  - Neotame.
  - Advantame
  - Alitame
- **Synthetic chemicals**:
  - Saccharine.
  - Acesulfame-K.
  - Cyclamate.

High Intensity sweeteners (Natural extracts)

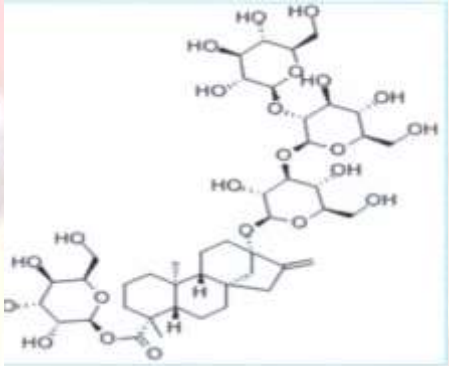
Steviol glycosides



Stevioside



Steviol glycosides



Rebaudioside-A

- It is an extract from the leaves of the stevia plant *Stevia rebaudiana*.
- This plant is originated in south America, but is also grown in several Asian countries.
- There are two chemical structure extracted from stevia leaves of stevoiside & Rebaudioside-A.

Properties

- Non-nutritive, zero calorie sweetener accompanied by aftertaste.
- It is about 200-400 sweetener than sucrose depend on the type of application and formulation.
- Its acceptable daily intake (ADI) is 4mg/kg body weight.

Status

- **Stevioside** and **rebaudioside-A** are the two sweet steviol glycosides in the stevia leaf.
- In the year 2008, the FDA approved the use of purified **rebaudioside-A** and classified it as Generally Recognized As Safe (GRAS).
- **Rebaudioside-A** is also called by the name **Reb-A** and **Rebiana-A.**
- It is blended with erythritol and marketed under the name **Truvia** and **PureVia.**

Limitation

- Stevoil glycosides sweetness accompanied by after taste (liquorices like after taste).
- Blending stevoil glycoside with the sugar alcohol erythritol helps masking this after taste property.

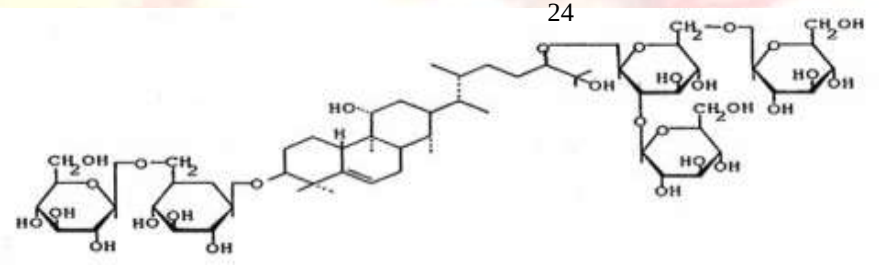
Applications

- Soft drink.
- Japanese -style vegetable products.
- Tabletop sweeteners.
- Confectionery.
- Fruit products.
- Seafood's.

Steviol glycoside Market

- Stevia manufacturer predicting continue increasing in the demand for steviol glycoside.
- The World Health Organization (WHO) estimates steviol glycoside market could eventually replace 20-30% of all non-nutritive sweeteners.

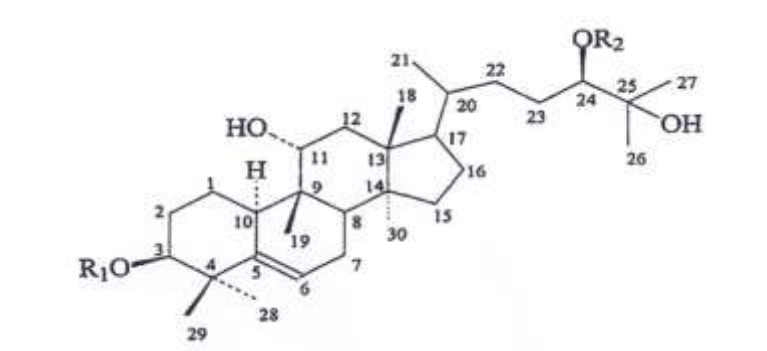
Mogrosides



Mogroside V

- Mogrosides are extracted from the plant LUO HAN GUO also known by the name monk fruit (*Siraitia grasvenorii*).
- Monk fruit has been cultivated and consumed in China for hundreds of years.
- There are five chemicals structure of mogrosides (II,III,IV,V and VI).
- These numbers are the number of glucose units that are attached to the mogroside unit

Mogrosides



Triterpene glycosides

- Mogrosides are formed of varying numbers of glucose units from 2 to 6.
  - Mogroside II : $R_1(G)$ $R_{24}(G)$
  - Mogroside III : $R_1(G)$ $R_{24}(G^{6-1}\text{---}G)$
  - Mogroside IV : $R_1(G^{6-1}\text{---}G)$ $R_{24}(G^{2-1}\text{---}G)$
  - Mogroside V : $R_1(G^{6-1}\text{---}G)$ $R_{24}(G^{6-1}<^{G}_{G}{}^{2-1})$
  - Mogroside VI : $R_1(G^{6-1}\text{---}G^{2-1}G)$ $R_{24}(G<^{6-1}_{2-1}{}^{G}_{G})$

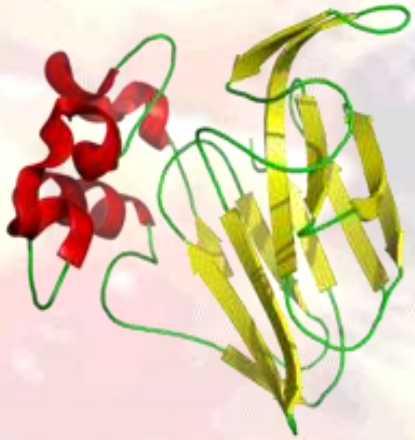
Properties

- Non-nutritive, zero calorie.
- About 100-250 times sweeter than sucrose.
- The sweeter level is vary depends on the percentage of mogroside VI and the application/ formulation.
- Pure and clean sweet taste.
- Soluble in water.
- Heat stable up to 125^0C.
- Mogrosides are Generaly Recognized as Safe (GRAS) by FDA.
- Has no limit Acceptable Daily Intake (ADI)

Applications

- Mogrosides available in the market in the form of solid or liquid under trade name ***Purefruit***.
- Its applications as sweetener and flavor for:
  - Food products.
  - Beverages and powdered drinks.
  - Chewing gums.
  - Baked goods.
  - Dietary supplements.
  - Nutritional bars and chocolates.

Thaumatin



Thaumatin I

Katenfe fruit

- ***Thaumatin II***: a 1235 amino acid. It is a precursor for Thaumatin I.

- ***Thaumatin I*** **:** a 1207 amino acid (3kDa). It is the sweetener

Thaumatin

- A low calorie protein sweetener and flavor enhancer.
- It is an extract from West African fruit (katemfe fruit) *Thaumatococcus danielli.*
- 2000-3000 times sweeter than sucrose.
- Metabolized by the body as any other protein.
- It is a Generally Recognized as Safe (GRAS) by FDA in USA.
- No limit Acceptable Daily Intake (ADI)
- Gained approval for over 30 countries around the world.

Properties

- Natural sweetener in a dried form.
- Stable in freezing temperature, heat, and pH.
- Soluble in water.
- Does not promote tooth decay.
- Synergetic when combined with other low-calorie sweetener.
- Available in the market under the trade name **Talin.**

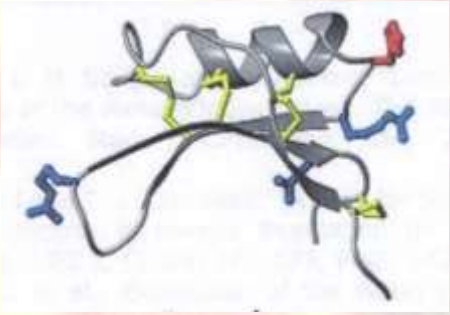
Applications

- Food and Beverages.
- Sweetener blends.
- Pharmaceutical and vitamin tablets.
- Oral care products.
- Animal feed and pet foods.

Limitation

- Delay perception of sweetness especially at high usage levels.
- Leaving aftertaste at high usage levels.

Brazzein

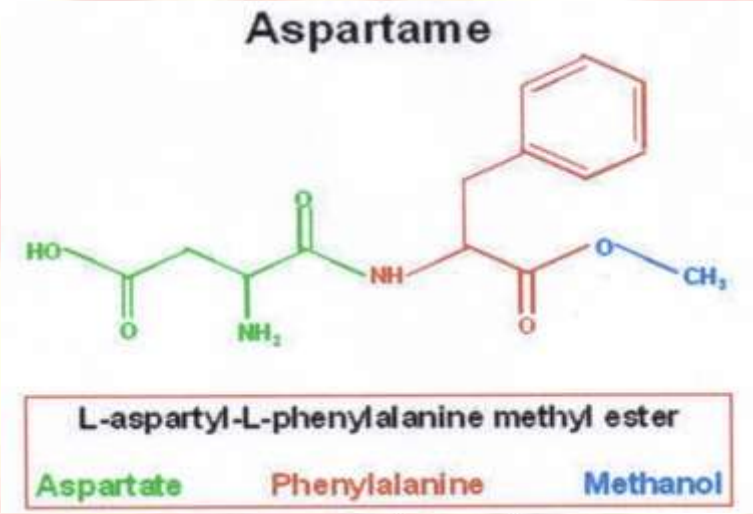


- Sweet tasting peptide extracted from west African fruit *Pentadiplandra brazzeana*.
- Consist of 54 amino acid arranged in one alpha-helix and three strands beta-sheets.
- Its large scale extraction yield from the fruit is not feasible, but it has been genetically engineered in corn.
- The gluten protein from the modified corn contains 4% brazzein.

Properties

- Non-caloric sweetener.
- 1200 times sweeter than sucrose.
- Its taste is similar to sucrose with lingering sweet after taste.
- PH stable at the range of 2.5-8.0, and heat stable at 98^0C.
- These stability properties makes it practical for many commercial applications.
- It is commercially available in small packets under the brand name **Cweet**

High Intensity sweeteners (Semi-synthetic Peptides)



[L-aspartyl-L-phenylalanine methyl ester]

- Aspartame is methyl ester of dipeptides.
- It is approved in 1981.
- It is a zero calorie sweetener.
- It is 200 times sweeter than sucrose.
- Digestible.
- Does not promote tooth decay.
- Enhance and intensified flavor (citrus and fruits)

Manufacturing process

- Aspartame is made through fermentation and synthetic chemical process.

1) **Fermentation step**:

B. flavus for L-aspartic acid production

C. glutamicum for L-phenylalanine production

Separation of L phenylalanine:

a) ***Chemical separation***: Separation of D-phenyl alanine by adding acetic anhydride and sodium hydroxide. Extraction of L-phenyl alanine from aqueous layer.

b) ***Enzymes separation***: using amino acylase enzymes from *Aspergillus oryzae*..

Manufacturing process Cont.

2) <u>Synthetic chemical step:</u>

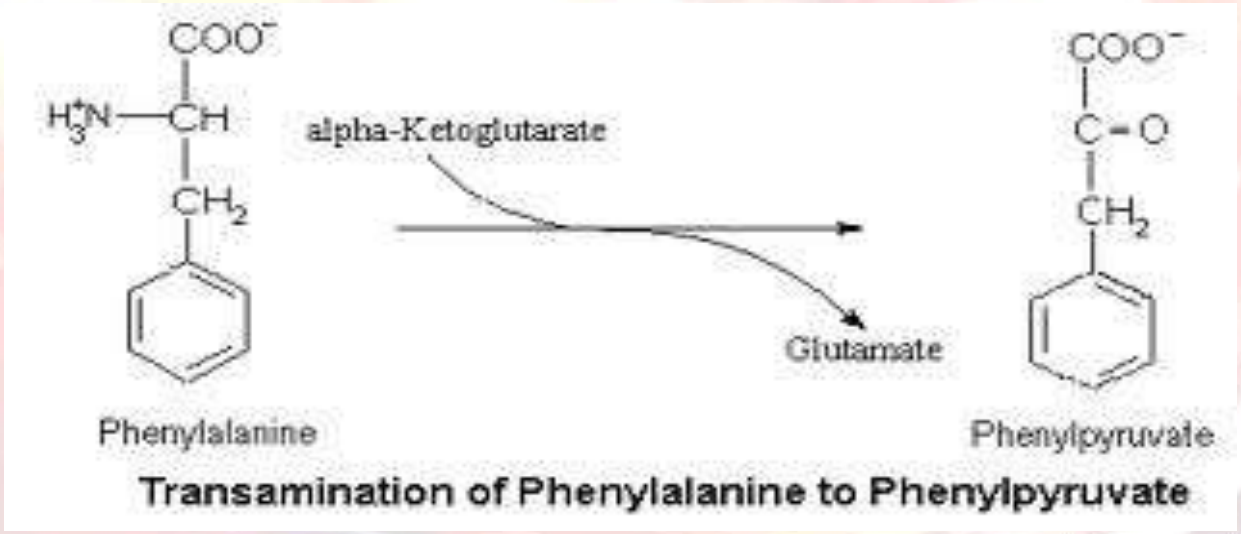
The two amino acids are modified

- L-Phenylaalanine is reacted with methanol to form methyl ester.
- L-aspartic acid is reacted with benzyl rings to shield specific sites.
- The two modified amino acids are mixed in acetic acid solution at 65^0C for 24 hrs for dipeptide formation.
- Aspartame recovery

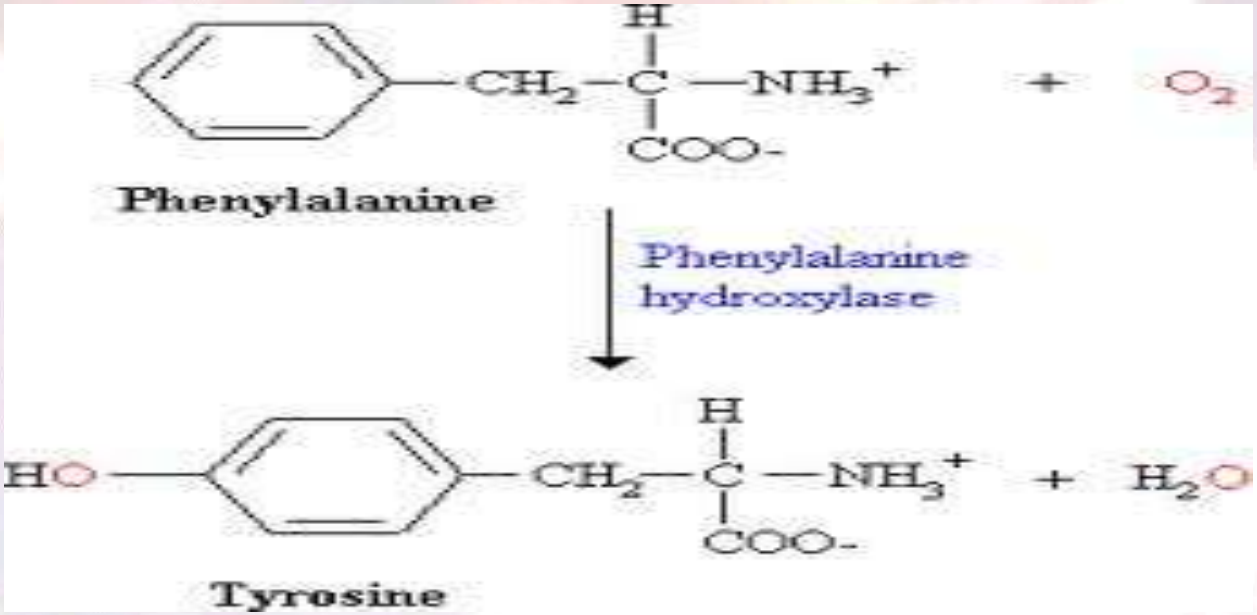
Safety

- It is safe and approved for people with diabetes, pregnant and nursing women.
- Acceptable daily intake (ADI) is 33mg/kg body weight.
- Aspartame is metabolized in the digestive system into the two amino acids (phenyl-alanine and aspartic acid.
- **Restriction:**
  - People with phenyl-ketonuria (PKU) disease.
  - PKU is a rare inherited disease that prevent the metabolism of essential amino acids.
  - Accumulation of phenyl-alanine in the body could cause health problems including mental retardation.

Phenyl alanine metabolism



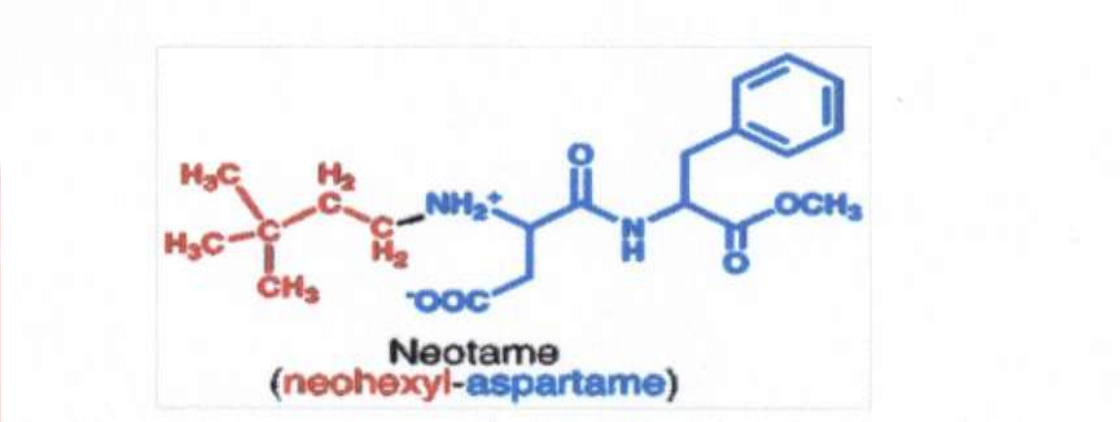
Transamination of Phenylalanine to Phenylpyruvate



Applications

- Tabletop sweetener.
- A wide variety of foods, including chewing gums, candies, cold breakfast, cereals, beverages, drinks and desserts.
- It is not suitable for baked goods or any other products required heat during production or service.
- The heat instability due to its dipeptide structure.
- The heat break down the dipeptide bond into the two free amino acids causes the loss of the sweetness property.

Neotame



(N-[N-(3,3-dimethylbutyl)-L- α-aspartyl]-L-phenylalanine 1-methyl ester)

- Peptide derivative of aspartic acid & Phenyl-alanine.
- Approved as a sweetener and flavor enhancer.
- 7,000-13,000 times sweeter than sucrose.
- 30-60 times sweeter than aspartame
- Rapidly metabolized by human.

Manufacturing process

- Neotame is also made through fermentation step and synthetic chemical step.

1) <u>Fermentation step</u>:

Similar to Aspartame

2) <u>Synthtic chemicals step</u>:

Similar to aspartame (peptide formation)

Plus

The addition of 3,3 dimethyl-butyl to the *N*-terminal of L-Aspartic acid.

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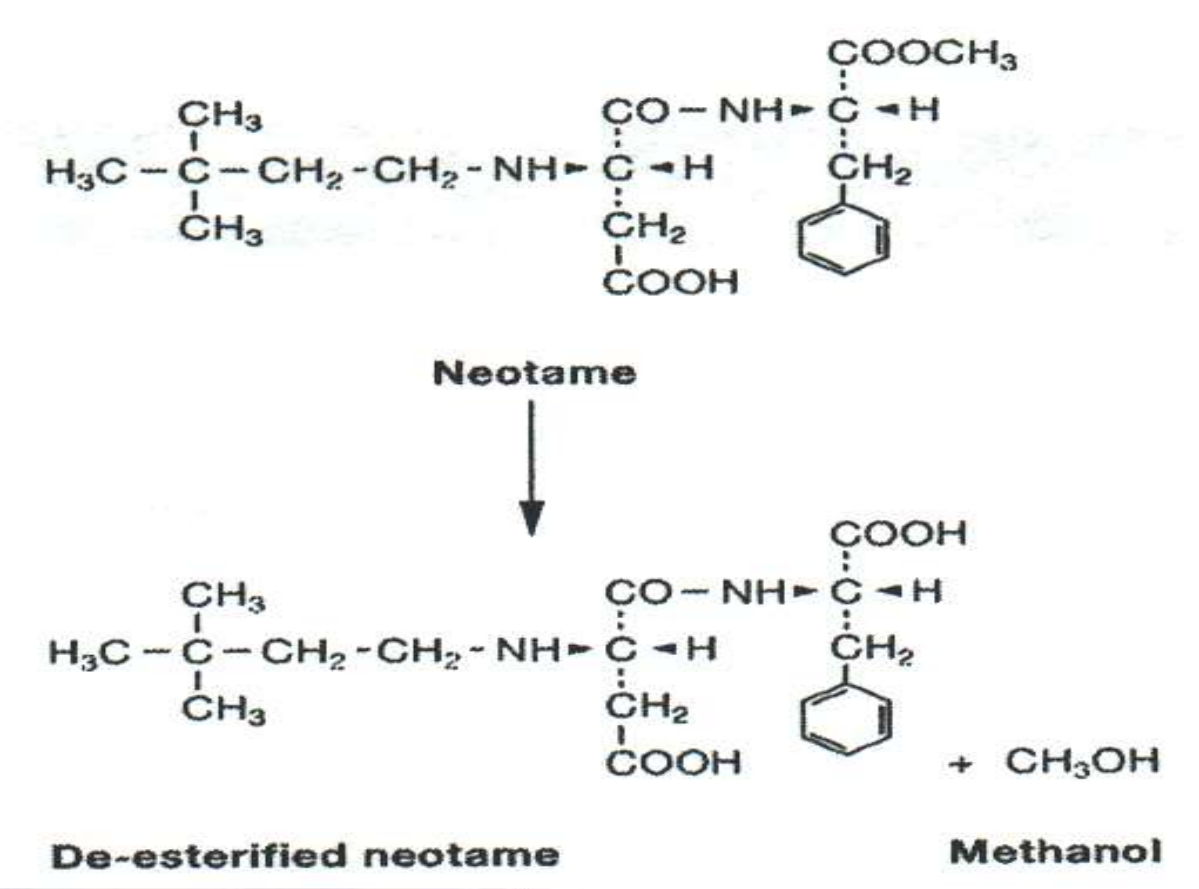
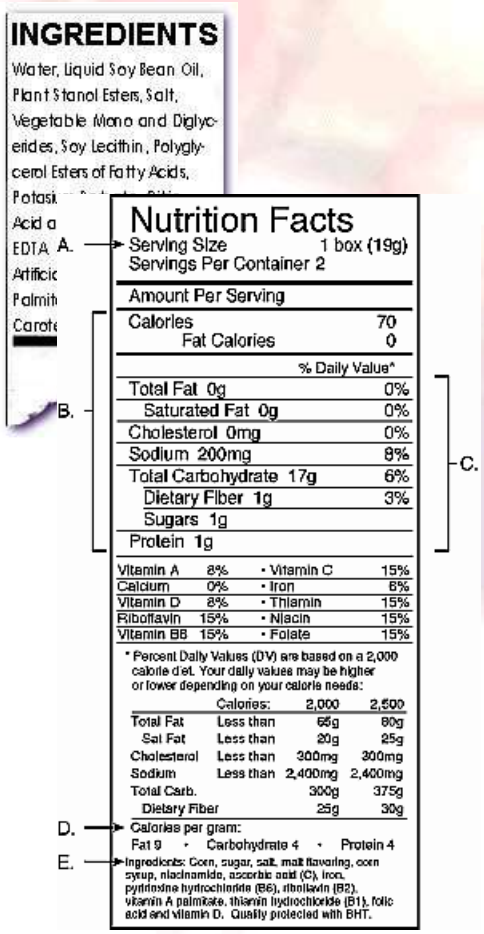
Advantages



- The major metabolic pathway is hydrolysis of the methyl ester by esterase enzymes.

Advantages (cont.)

- The presence of 3,3-dimethybutyl in the structure blocks peptidases enzymes in releasing the amino acid L-phenylalanine.
- No need to add special labeling for phenyketonuric (PKU) individual.



INGREDIENTS

Water, Liquid Soy Bean Oil, Plant Stanol Esters, Salt, Vegetable Mono and Diglycerides, Soy Lecithin, Polyglycerol Esters of Fatty Acids, Potasi... Acid a... EDTA A. Artificic... Palmit... Carote...

B.

Nutrition Facts

Serving Size 1 box (19g)
Servings Per Container 2

Amount Per Serving	
Calories	70
Fat Calories	0
	% Daily Value*
Total Fat 0g	0%
Saturated Fat 0g	0%
Cholesterol 0mg	0%
Sodium 200mg	8%
Total Carbohydrate 17g	6%
Dietary Fiber 1g	3%
Sugars 1g	
Protein 1g	

C.

Vitamin A	8%	• Vitamin C	15%
Calcium	0%	• Iron	8%
Vitamin D	8%	• Thiamin	15%
Riboflavin	15%	• Niacin	15%
Vitamin B6	15%	• Folate	15%

* Percent Daily Values (DV) are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs:

	Calories:	2,000	2,500
Total Fat	Less than	65g	80g
Sat Fat	Less than	20g	25g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carb.		300g	375g
Dietary Fiber		25g	30g

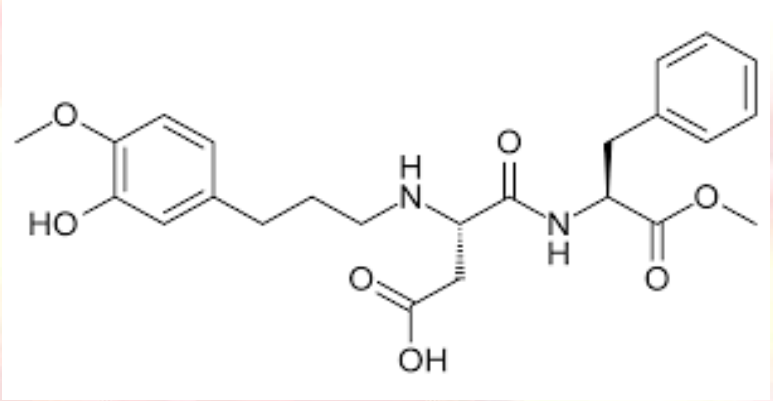
D. Calories per gram:
Fat 9 • Carbohydrate 4 • Protein 4

E. Ingredients: Corn, sugar, salt, malt flavoring, corn syrup, niacinamide, ascorbic acid (C), iron, pyridoxine hydrochloride (B6), riboflavin (B2), vitamin A palmitate, thiamin hydrochloride (B1), folic acid and vitamin D. Quality protected with BHT.

Applications

- Neotame is approved for use as sweetener and flavor enhancers in foods and beverages.
- It can be blended with nutritive sweeteners (HFCS, sucrose) to match the taste while providing significant cost savings.
- It has a wide application for:
  - Beverages and cereals.
  - Tabletop sweeteners
  - Chewing gums and confectionary.
  - Frozen desserts, ice cream, yogurt.
  - Not suitable for baked goods.

Advantame



(N-[N-(3-(3-hydroxy-4-methyloxyphenyl) propyl] α-aspartyl]-L-phenylalanine 1 methyl ester

- Advantame is a new intensive sweeteners derived from aspartame and vanillin.
- It is similar in structure to neotame except in side chain to the *N*- terminal of L-aspartic acid.
- No need to add special labeling for phenyketonuric (PKU) individual.

Manufacturing process

- Advantame is also made through fermentation step and synthetic chemical step.

1) <u>Fermentation step</u>:

Similar to Aspatame

2) <u>Synthetic chemical step</u>:

Similar to aspartame (dipeptide formation)

plus

The addition to the *N*-terminal of L- aspartic acid the side chain (HMPA)

3-(3-hydroxy-4-methyloxyphenyl) propyonaldehyde.

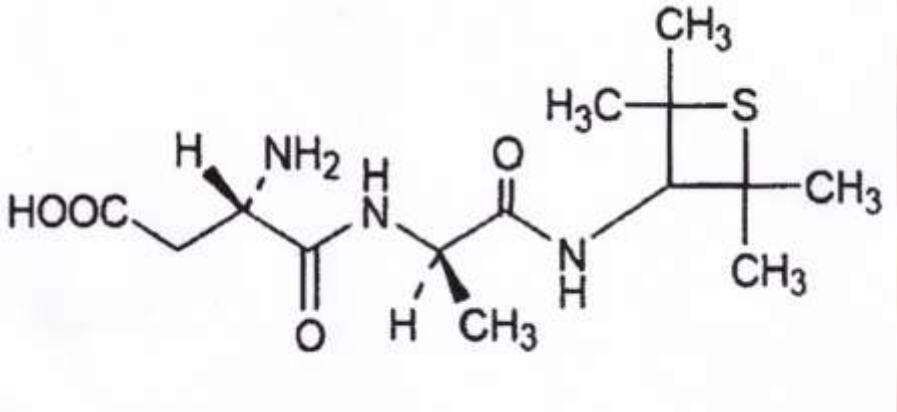
Properties

- Advantame is about 20,000 times sweeter than sucrose and 100 times sweeter than aspartame.
- It is suitable for use in foods as non-nutritive sweeteners.
- It has a clean sweet taste very similar to aspartame with only a slightly longer sweetness.
- It is heat stable making it suitable as a sugar substitute in baked goods.
- It is less stable in the acidic conditions such as beverages products.

Applications

- FDA has approved Advantame, as new sweetener, for general use in foods and beverages.
- Advantame can be used to partially replace sugar, high fructose corn syrup or other high potency sweeteners to reduce cost, calories, while maintaining the same taste profile of the products.
- Or improving the taste and flavor profile of the products.
- Acceptable daily intake (ADI) is 5 mg/kg. body weight.
- It is available in 200g and 1Kg bags under trade name Ajisweet®

Alitame



[L-alpha –Aspertyl-N-D-alaninamide]

- It is a dipeptides of L-aspartic acid and D-alanine, with a terminal *N*-substituted by tetramethyl-thietanly-amine.
- It is 200-300 times sweeter than sucrose and 10 times sweeter than aspartame.
- Soft drink with aspartame develop off taste after long storage.

Manufacturing process

1) **Fermentation step:**

- Production of L-aspartic acid.
- Production D-alanine.

1) **Chemical step:**

- Multistep synthesis involving the reaction between two intermediates.

  - (S)-[2,5-dioxo-(4-thiozolidine)]acetic acid.

  - (R)-2-amino-N-(2,2,4,4-tetramethyl-3- thietanyl) propanamide.

- The final product is isolated and purified by crystallization.

Properties

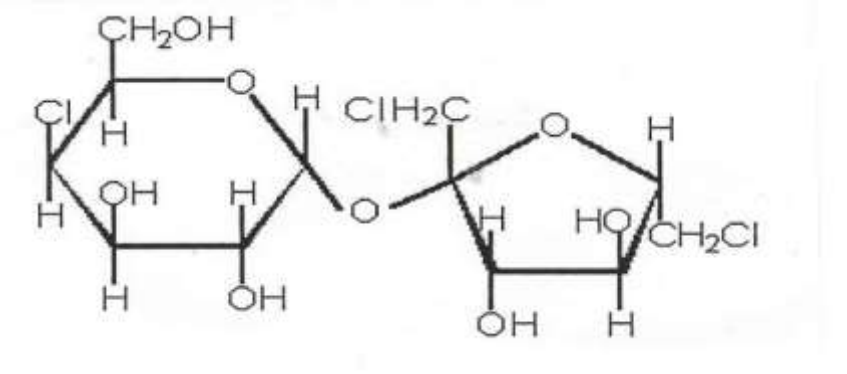
- Clean sweet taste.
- Excellent stability at high temperature.
- Suitable for diabetics.
- Safe for teeth.
- Synergetic when combined with other low calorie sweeteners.
- Its caloric contribution to the diet is negligible.

Safety

- Safe for human consumption.
- Acceptable daily intake (ADI) is 1mg/ kg. body weight.
- The aspartic acid is metabolized normally, but alanine amid does not further hydrolyze.
- Alitame has been approved under the brand name **Aclame®** for use in a variety of food and beverage products in Australia, New Zealand, Mexico and China.
- In USA its petition as a sweetening agent or flavoring in foods has been withdrawn due to manufacturing cost.

High Intensity sweeteners (Semi-synthetic sugar)

Sucralose



[Trichloro-galactosucrose]

- It is a high intensity sweetener derived from sucrose.
- It is about 600 times sweeter than sucrose.
- Produced by the selective chlorination of sucrose.
- Its Acceptable Daily Intake (ADI) 15mg/kg. body weight.

Benefits

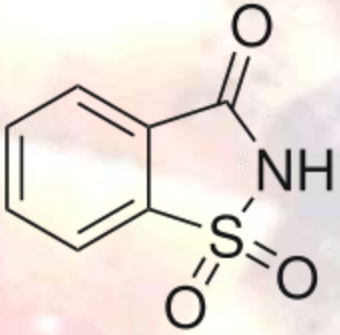
- Non-cloric and does not breakdown in the body.
- Does not promote tooth decay.
- Excellent stability in wide range of processed foods and beverages.
- Soluble in water.
- Heat stable.

Applications

- Sucralose has a wide range of applications.
- It is marketed under trade name Splenda®

High Intensity sweeteners (Synthetic chemicals)

Saccharin



Benzoic sulfimine

- Saccharine was discovere in 1879.
- It is zero calorie non-nutritive sweetener
- It is 200-700 times sweeter than sucrose.
- Its Acceptable Daily Intake (ADI) 15mg/kg bodyweight.
- Applied in both food, beverages and non-food products.
- It is marketed under names Twin® and Sweet in low®

Acesulfame-K (Ace K)

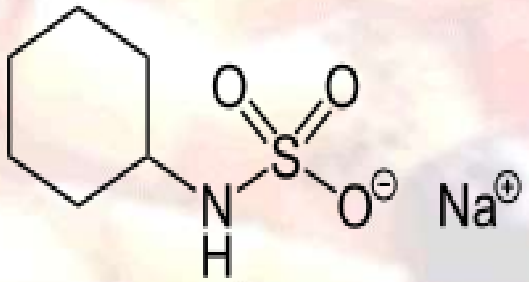
potassium 6-methyl-2,2-dioxo-2*H*-1,2λ6,3-oxathiazin-4-olate

- 180-200 times sweeter than sucrose with slight better taste.
- It is sweet as aspartame, about 1/2 as sweet as saccharine and about 1/4 as sweet as sucralose.
- It is usually used in combination with another sweetener, such as aspartame or sucralose.

Applications

- It is stable under heat and under moderately acidic or basic conditions.
- It is being used in baking, carbonated beverages, protein shakes, pharmaceutical products and in products that require a long shelf life.
- Its ADI is 15 mg./kg, body weight.
- Available under trade names **Sunett** and **Sweet One**.
- In Europe it is known by the name **E950**

Cyclamate



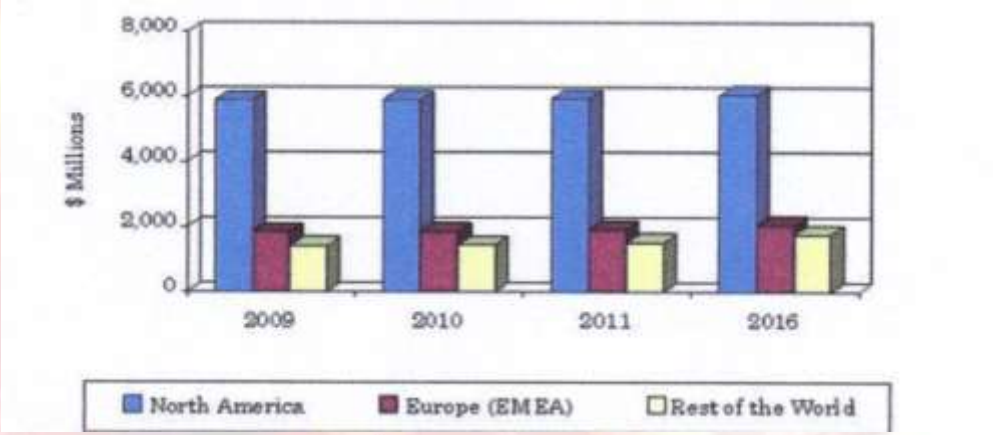
Sodium N cyclohexilesulfamate

- It is 30-60 times sweeter than sucrose.
- Used in Canada and over 50 other countries.
- Its ADI is 11 mg/kg body weight.
- Approved by FDA after the Cancer Assessment Committee decided that cyclamate is not carcinogenic.
- It is marketed as table top sweetener under trade name Twin®.

Applications

- Cyclamate has a wide range of applications.
- Ice cream, soft drinks, cola, milk, canned food, biscuits, sweets, preserved fruits, pickles, wine.
- Family seasoning, cooking.
- Pharmaceutical & cosmetic such as toothpastes, mouth freshness & lipstick.
- It is suitable use for diabetes, and high blood pressure people.

Global food and beverages market of Intense sweeteners



- Global market for the year 2010 was $ 9.2 billion.
- Global market for the year 2011 is $ 9.3 billion.
- Global market for the year 2016 is expected to reach $ 9.9 billion.
- U.S. market in the year 2011 was $ 5.9 billion and is expected to reach 6 billion in the year 2016.
- European market in the year 2011 was $ 1.9 billion and is expected to reach $ 2 billion in the year 2016.

Comment

- High Intensity sweeteners from natural sources (plant extracts) are refer to natural sweeteners.
- Natural sweeteners are recognized as safe with GRAS status (Generally Recognized as Safe).
- Semi-Synthetic and synthetic sweeteners refer to artificial sweeteners.
- Artificial sweeteners required FDA approval because they are not natural.

Comment

- Aspartame is facing a strong competition from newly developed high intensity sweeteners HIS (Sucralose: Splenda & Stevia: Truvia & PureVia).
- World Health Organization (WHO) estimates stevia market (Truvia & Pure Via) could eventually replace 20-30% of all dietary sweeteners.
- The long used sweetener *saccharine* is continuing to decline.

Thank you for your attention