

the taste of sweet

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Humans have always sought to make life sweeter. In prehistoric times, sugar cane was already being grown for its sweetening powers, and the sugar added to beverages and food. But why do humans like what is sweet so much? This may well have evolved from our distant ancestors, as far back as those who bore little resemblance to us. In the wild, animals have to depend on colour but also taste – and its very close sister, smell – to distinguish what is edible from what is likely to be toxic. On the whole, bitter is better left alone. As things evolved, a sweet taste became a feeling that was comforting one way or another. So, slowly but surely, sweetness was added to all sorts of foods and liquids. And, today, sugar is usually part of a Westerner's diet – whether we are aware of it or not. As a result, towards the end of the 20th century, it had become clear that sugar – or an excess of it – was proving to be harmful to the human population, and it was necessary to find ways of making life sweeter without the nasty side effects. In the early 1980s, one such sweetener was rediscovered in a South American plant, *Lippia dulcis*. Known as Hernandulcin, researchers have recently managed to isolate a key enzyme in its synthesis, known as (+)-epi-alpha-bisabolol synthase.



Lippia dulcis

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Over time, animals developed their tasting abilities to detect the difference between bitter and sweet, in order to shun poison. Coupled with the ability to discern colour and texture such behaviour helps to keep a species alive. Including *Homo sapiens*. The human taste for sugar – and its addition to foods and beverages – seems to stretch as far back as prehistoric times where sugar cane plantations are known to have been grown in Asia. The expensive

refined sugar made its way to Europe in the Middle Ages only and, much like the advent of cocoa centuries later, was introduced into the upper class circles as a delicacy. By the 18th century, however, sugar was being refined from the less expensive sugar beet and a taste for things sweet slowly spread to all social classes.

Sucrose was soon within everyone's economic reach, gradually paving the way to health problems that are currently ravaging many developed societies. Sucrose substitutes - in particular Saccharine – had already appeared on the market as early as 1879. However, this was less for health reasons than to make sweetness accessible to those who had little means; Saccharine was also known as the poor man's sugar. Ever since, the quest for artificial sweeteners has never ceased and everyone is acquainted with names such as Assugrin and Aspartame. So why is yet another sweetener, i.e. hernandulcin, of so much interest? Many artificial sweeteners are ten times or hundreds of times sweeter than refined sugar. Hernandulcin, however, is one thousand times sweeter – a godsend for the industry.

Hernandulcin – named after the man who brought it back to Europe – is an essential oil found in a plant known as *Lippia dulcis*, or Aztec sweet herb. *Lippia dulcis* grows extensively in tropical America and can be found on the markets where it is sold not only for its sweetness but also for its

abortifacient and infertility qualities – which may be the result of some of its toxic substances, such as camphor. Though the plant was first described by the Spanish physician Francisco Hernández de Toledo in the 16th century – following the first scientific trip ever made to South America by the Spaniards – its properties were only rediscovered in the 1980s following research carried out on ancient botanical literature. There are many types of *Lippia* that are used to treat all sorts of afflictions ranging from indigestion, hepatic diseases and cutaneous disease, to burns, wounds and menstrual disorders. Certain sorts are also used as sedatives, stimulants and insect repellants while others are used for food seasoning and beverage flavouring. In Cuba, the juice of *Lippia* is used to dye cigarette paper.

Hernandulcin is extracted from the leaves of *Lippia dulcis*, in the form of an essential volatile oil. Besides its natural sweetening properties, it is also sold in South America as a herbal remedy for coughs, bronchitis, urinary retention and inflammation! From a chemical point of view, hernandulcin is part of the very large family of terpenoids – which are known to have many different properties and are widely used for flavouring, in cosmetics, as fuel substitutes and in all sorts of medicines. Among the terpenoids, hernandulcin is a sesquiterpene ketone, whose backbone is (+)-epi-alpha-bisbolol. Though scientists still do not know which terpene synthase actually synthesizes hernandulcin, they have managed to isolate the enzyme responsible for the synthesis of (+)-epi-alpha-bisbolol, which they have prosaically baptised: (+)-epi-alpha-bisbolol synthase. In fact, four forms of epi-alpha-bisbolol

were characterised; three of which, however, had either a bitter or pungent taste.

In the realm of sweetness, terpenoids have been used for many years now to replace the old-fashioned refined sugar from cane or beet, whose sucrose side effects – when absorbed exaggeratedly – can be very harmful. Obesity is the major one; a condition which haunts our societies and lays the foundations for serious afflictions such as heart disease and diabetes. Sugared foods and beverages have become the basis of most of the world's diets nowadays, to the extent that millions of people cannot imagine doing without and are usually unaware of the amounts they swallow on a daily basis. This is why it is so important to find sugars that are less harmful to human health – such as those based on terpenoids. Hernandulcin is ideal in that it is not only a powerful harmless sweetener but, so far, has also proved to be non-carcinogenic.

Scientists have rediscovered a seemingly harmless hernandulcin and found the synthase that is the designer of its backbone. So now what? Bacteria can be engineered for the large scale production of (+)-epi-alpha-bisbolol and, ultimately, the low calorie sweetener hernandulcin. But this last step still requires the intervention of yet another synthase – which remains to be brought to light... For the sake of global human health and all instances related to it, being able to provide a powerful sweetener that has none of the drawbacks that sucrose involves is great. However, would it not be a good thing to start promoting tastes that are not so sweet, by adding less sugar – whatever its nature – to food and drink, instead of continuing to encourage a sweet tooth?

Cross-references to UniProt

(+)-epi-alpha-bisabolol synthase, *Lippia dulcis* (Aztec sweet herb) : J7LH11

References

1. Attia M., Kim Soo-Un, Ro D.-K.
Molecular cloning and characterization of (+)-epi-alpha-bisbolol synthase
Archives of Biochemistry and Biophysics 527:37-44(2012)
PMID: 22867794
2. Compadre C.M., Pezzuto J.M., Kinghorn A.D., Kamath S.K.
Hernandulcin: an intensely sweet compound discovered by review of ancient literature
Science 227:417-419(1985)
PMID: 3880922