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Occurrence of 3-methoxytyramine in Cuban honeys

William E. Cáceres-Hernández [a], Adolfo Pérez-Piñeiro [a], Dámarys Suárez-Gómez [a], Alen N. Baeza-Fonte [b,c,*]

[a] Beekeeping Research Center, Carretera de El Cano a El Chico, Km 0, El Cano, Arroyo Arenas, La Lisa, La Habana, 17100, Cuba
[b] Universitat Autònoma de Barcelona, Cerdanyola del Vallès, Cataluña, 08193, Spain
[c] Institute of Science and Technology of Materials, University of Havana, Zapata y G, S/N, Plaza, La Habana, 10400, Cuba

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ABSTRACT

Honey adulteration is a subject of great concern worldwide. The compound 3-methoxytyramine (3-MT) is one of the biomarkers used to determine adulteration or contamination with sugar, syrups, and other products of beetroot (*Beta vulgaris*) from *Amaranthaceae* family. However, there is scientific evidence of the presence of 3-methoxytyramine in other species of this family, some of which, reported in Cuba. As honey plants, bees use them to carry nectar and pollen to hives to make honey, therefore, there is a possibility to detect 3-methoxytyramine in these samples, not only in Cuban's honeys samples, but also worldwide.

1. Introduction

Honey, one of the most natural sweetener mixture, contains not only sugars but also other elements and organic compounds (Tafere, 2021) with special nutraceutical properties for human consumption and with many other pharmaceutical uses (Pashte et al., 2020; Ranneh et al., 2021; Elbargisy, 2020; Pleeging et al., 2020). Nature, *per se,* shows very complex interactions between living beings and bees use plants of *Amaranthaceae* family as source for honey production transferring some compounds from these plants to the honey and probably, their pharmaceutical or nutraceutical properties.

In the Cuban archipelago, plant species from *Amaranthaceae* family can be found, most of them, often, from the nearby geographical environment. Due to the humid and warm climate of Cuba island, many of these plants find a space with suitable conditions for their growth, reproduction, and expansion (Greuter and Rankin Rodríguez, 2017; González-Oliva et al., 2014).

The *Amaranthaceae* family is widely represented in Cuba and *Celosia argentea*, belonging to this family, is known worldwide, and used for medicinal purposes (Thorat, 2018). This plant can be found growing wild in subtropical zones and warm temperate zones. It is a slow-growing plant, but blooms can appear within 6–7 weeks of germination. It grows best in areas where the temperature is in the range of 25–30 °C, can tolerate temperatures between 20 and 40 °C but fails to survive below 5 °C. This species finds very favorable conditions in the Cuban climate with a wide range of dispersion and variability, and its presence on the island has been reported by researchers from the National Botanical Garden of Cuba (Oviedo & González-Oliva, 2015), a leading institution in flora taxonomy located in Cuban territory. The wide distribution of this family of honey plants in Cuba and Central America can introduce their natural chemical compounds in honey by bees.

2. Discussion

The compound 3-methoxytyramine (3-MT), also known as 3-methoxy-4-hydroxyphenethylamine (Fig. 1), is a metabolite present in different species of plants in the *Amaranthaceae* family (Deladino et al., 2017; Ahmed et al., 2022; Grabowska et al., 2023; Luzardo-Ocampo et al., 2021) of which, more than seventy different species have been identified, including beets (*Beta vulgaris*) (Pashte et al., 2020) This compound is a natural betalamic acid conjugate (a betaxanthin, Fig. 2) (Gandía-Herrero & García-Carmona, 2013) and can be found in different species of the genera *Celosia* (Divya et al., 2019; Cai et al., 2001; Schliemann et al., 2001). Its chemical identification was carried out for the first time in flowers of *Celosia argentea* var. *cristata* L. in 2001 (Pleeging et al., 2020; Greuter & Rankin Rodríguez, 2017) using high performance liquid chromatography (HPLC-PDA and HPLC-ESI-TOF-MS) (Gandía-Herrero & García-Carmona, 2013). Some authors relate the presence of this compound in these species with potential pharmacological properties (Kanu et al., 2017).

The different products obtained from beets, such as sugar, syrups,

* Corresponding author. Institute of Science and Technology of Materials, University of Havana, Zapata y G, S/N, Plaza, La Habana, 10400, Cuba.
E-mail address: AlenNils.baeza@uab.cat (A.N. Baeza-Fonte).

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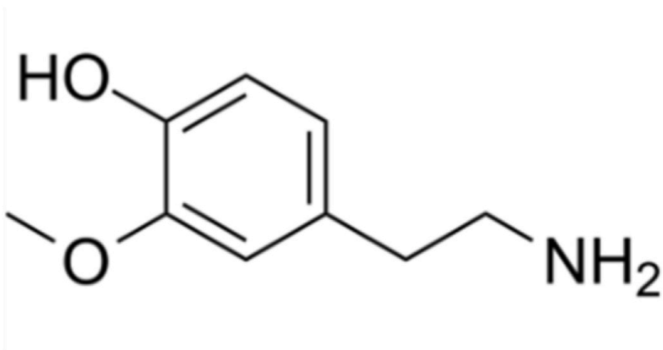

Fig. 1. 3-Methoxytyramine chemical structure.

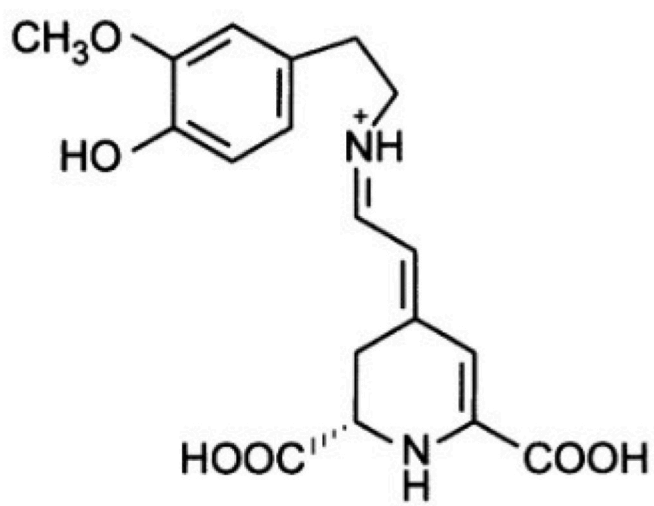

Fig. 2. 3-Methoxytyramine betalamic acid conjugate.

and other industrial extracts, are sometimes, used in the adulteration of honey (Cárdenas-Escudero et al., 2023; Jaafar et al., 2020; Brar et al., 2023) or to feed bees, and this is why determination of 3-MT has been considered clear evidence of such manipulation. In this sense, in 2015, a method for the detection of this type of adulteration was patented measuring with Liquid Chromatograph coupled to High Resolution Mass Spectrometry (HPLC-HRMS), pointing 3-MT as a chemical marker, detected at a mass-to-charge ratio of 168.1016 (positive mode) (Xiang et al., 2016). The use of LTQ-Orbitrap detector in this methodology offers the combination of linear ion trap with an Orbitrap analyzer, provided high resolution, mass accuracy and specificity, being adequate during adulteration studies. However, the patent does not report the limit of detection for the technique, therefore, its direct application is limited. Otherwise, no studies with natural honeys containing pollen grains of *Amaranthaceae* family, with possible presence of 3-MT, were reported.

However, it is usual to find *Amaranthaceae* family pollen in honey samples from *Apis mellifera* worldwide (Abdulrahaman et al., 2017; Moraes et al., 2019) as predominant (Vazquez-Fuentes et al., 2019), secondary or minor pollen groups (Singh & Kaur, 2020; Özler, 2018). This shows that bees visit these plants and consequently the 3-MT detected might sometimes come from natural sources such as these honey plants, and not always due to adulteration.

The presence of 3-MT is also described in other genera of the *Amaranthaceae family* such as *Alternanthera, Amaranthus* and *Gomphrena* (Miguel, 2018). In Cuba, Diamante (*Alternanthera halimifolia* Lam.) and San Diego (*Gomphrena globosa* L.) plants are described while, Bledo (*Amaranthus dubius* Mart.), Bledo manso (*Amaranthus viridis* L.) and Bledo espinoso (*Amaranthus spinosus* L.) plants are reported as weeds or associated with ornamental plants. Studies by the Cuban Academy of Sciences (Acuña Galé, 1970) and other institutions (Batis et al., 2023) mention that these species are visited by bees presumably for their nectar and not only for their pollen.

Other plants species of this family have been identified in Cuba, including endemic species (Table 1) (Sauget & Liogier, 1951; Greuter & Rankin, 2022). However, no scientific reports have been found on the detection of 3-MT directly in all these plants (Tafere, 2021; Yap et al., 2023) because it is usually determined and reported in total betaxanthins analysis (Sarker & Oba, 2021). The identification of 3-MT in other genera/species of the *Amaranthaceae*, also honey plants, has been well documented (Y. Cai, Sun, & Corke, 2005b; Y.Z. Cai, Sun, & Corke, 2005a; Mastuti et al., 2021; Singh & Singh, 2018; Tripathi & Khan, 2021) in fact, many of the Cuban plants of the *Amaranthaceae* family could potentially contain this chemical compound and could be detected in honey samples. This assumption is based on the fact that Cuba is a traditional producer of sugar cane due to its favorable climatic conditions and does not produce or import sugar or sweeteners made from sugar beet. The above criteria affect honeys obtained from *Apis mellifera* as they are classified as low-quality honeys.

On the other hand, the production of stingless bee honey is inferior to that of *Apis mellifera* but its specific composition in flavonoids and polyphenols with higher acidity and moisture and lower sugar content, makes it a fantastic nutritional food in addition to its pharmaceutical properties. The latter related to its extraordinary antibacterial, anti-inflammatory, antidiabetic, and anticancer properties, among others (Zulkhairi A. et al., 2018). In that way, the presence of 3-MT may also affect the trade of stingless bee honey and its use as a medicine.

In this regard, some reports have identified minor pollen of the

Table 1
Species (37) and genera (13) of the Amaranthaceae family identified in the Cuban flora as origin of 3-methoxytyramine in Cuban honeys.

Family	Genera	Species
Amaranthaceae	*1. Celosia*	*argentea* L.
		nitida Vahl
		virgata Jacq.
	2. Chamissoa	*altissima* (Jacq.) Kunth
	3. Amaranthus	*caudatus* L.
		crassipes Schltdl.
		dubius Mart. ex Thell.
		hybridus L.
		palmieri S. Watson
		polygonoides L.
		spinosus L.
		viridis L.
		minimus Standl.
		australis (A. Gray) J. D. Sauer
	4. Cyathula	*achyranthoides* (Kunth) Moq.
	5. Achyranthes	*aspera* L., nom. cons.
	6. Alternanthera	*axillaris* (Willd.) D. Dietr.
		caracasana Kunth
		crassifolia (Standl.) Alain
		halimifolia (Lam.) Standl. ex Pittier
		maritima (Mart.) A. St.-Hil.
		pungens Kunth
		paronychioides A. St.-Hil.
		sessilis (L.) R. Br. ex DC.
		cubensis Borsch & al.
	7. Iresine	*brittonii* (Standl.) T. Ortuño & Borsch
	8. Gomphrena	*globosa* L.
	9. Gomphrena	*serrata* L.
		angustifolia Euphrasén
	10. Iresine	*cubensis* Borsch & al.
		diffusa Humb. & Bonpl. ex Willd.
		flavescens Humb. & Bonpl. ex Willd.
		herbstii Hook.
	11. Gomphrena	*muscoides* (Sw.) T. Ortuño & Borsch
	12. Blutaparon	*vermiculare* (L.) Mears
	13. Froelichia	*interrupta* (L.) Moq.

Amaranthaceae family in these honeys, i.e., *Amaranthus viridis* (Maitip, J. et al., 2024), besides *Achyranthes velutina* and *Amaranthus lividus* (Selvaraju K. et al., 2019), all rich in betaxanthins, and probably containing 3-MT, which could also be potentially present in stingless bee honey naturally without any adulteration.

In both types of honeys, the variability and even the presence of 3-MT is subject to the access of plants of the *Amaranthaceae* family to bees. The random distribution of these plants near the hives and the season of the year can affect the concentration of their pollen in honey, its study and classification. The situation is more complex because 3-MT sometimes is detected in plants as betaxanthins without discrimination techniques or are not fully studied.

3. Conclusion

3-Methoxytyramine is a compound present in the nectar and pollen of different plant species of the *Amaranthaceae* family, especially in *Celosia argentea* Linn*,* a species widespread in Cuba and valued as a honey plant. The nectar of *Amaranthaceae* is mainly used by honeybees to produce honey. The presence of their pollen in honey is additional evidence that distinguishes this family as honey plants. Considering the current state of the art on the presence of 3-MT in different types of honeys from other countries with a similar location to Cuba in the world, it is possible to find 3-MT of natural origin, not only in Cuban honeys from *Apis mellifera* and stingless bee, but in other honeys from all over the world, if bees find species of this family as a nectar source. For the reasons stated above, this chemical compound does not necessarily represent evidence of adulteration of honey with beet (*Beta vulgaris*) derivatives, so that, in terms of availability and trading, fewer honeys will be rejected or considered low-quality honeys.

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CRediT authorship contribution statement

William E. Cáceres-Hernández: Writing – original draft, Investigation, Conceptualization. **Adolfo Pérez-Piñeiro:** Writing – original draft, Investigation, Conceptualization. **Dámarys Suárez-Gómez:** Writing – review & editing, Supervision, Methodology. **Alen N. Baeza-Fonte:** Writing – review & editing, Writing – original draft, Supervision, Investigation.

Declaration of competing interest

All authors declare no conflict of interest between them or with any institution.

Data availability

Data is inside of the manuscript

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