



Physicochemical parameters and chemoprofiling of honey of two species of stingless bees in the Peruvian Amazon

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ABSTRACT

The physicochemical and chemical characteristics of stingless bee honey from two commonly grown species in the Peruvian Amazon, *Melipona eburnea* and *Tetragonisca angustula*, were evaluated. Key physicochemical findings include humidity levels exceeding Codex-Alimentarius limits (28.13 g/100 g of honey for *M. eburnea* and 26.33 g/100 g for *T. angustula*), while sugar content fell below minimum requirements (54.3 g/100 g of honey and 43.5, respectively). Hydroxymethylfurfural levels were 12.5 mg/100 g of honey and 0.4, respectively. Using MALDI-TOF/TOF analysis, biologically and medicinally relevant molecules derived from plants and microbes were tentatively detected in both honey samples. These molecules encompassed properties such as anticancer, antibacterial, antifungal, anti-inflammatory, and antiviral. Notable compounds in *M. eburnea* honey included naringenin chalcone, caffeine, berberine, and glycosyl trans-zeatin-O-glucoside, previously documented in various honey types. Additionally, quinine, paclitaxel, stigmastanol, and surfactin C, with therapeutic potential, were preliminarily detected for the first time in this honey. *T. angustula* honey also contained medicinal molecules including lutein, cinnamic acid, fraxin, and hyperoside, along with newly observed compounds such as osthole, culmorin, and uncarine C (cat's claw). Both honey samples exhibited trace levels of non-natural compounds, including commercial pesticides and herbicides, suggesting environmental contaminants. Further research is needed to verify the identity of these molecules, understand their potential sources, quantify their levels in Amazonian honey, and assess consumption and health implications. This study highlights the necessity for a novel technical standard exclusive to stingless bee honey, encompassing methodologies for measuring the physicochemical parameters and for monitoring the chemical profile to assess the medicinal potential of native honey and define maximum limits for environmental pollutants. This pioneering work underscores the ecological, medicinal, and economic value of stingless bees in the Peruvian Amazon.

1. Introduction

Stingless bee honey has a long history of traditional use in medicine, food, religion, and cultural activities worldwide (Quezada-euán et al., 2018; Alves & Alves, 2011). In the Peruvian Amazon, indigenous and non-indigenous communities have utilized this honey for centuries to treat various diseases (Rasmussen & Castillo-Carrillo, 2003; Rodríguez-Malaver et al., 2009; Castillo-carrillo, Elizalde, & Rasmussen, 2016). Recent research conducted in the area has identified more than 14 diseases that are treated using stingless bee honey (Delgado et al., 2023).

Numerous studies have explored the bioactive, therapeutic, and medicinal effects of stingless bee honey derived from different species,

providing support for the traditional knowledge associated with it (Delgado et al., 2023; Oliveira et al., 2012; Rao et al., 2016; Zulkhairi Amin et al., 2018; Khongkwanmueang et al., 2020; Johnson et al., 2005; Kato et al., 2012). These studies have also investigated the physicochemical and phytochemical characteristics of stingless bee honey worldwide, highlighting variations in quality and composition parameters that exclude stingless bee honey from international quality standards (Biluca et al., 2016; Cardona et al., 2019; Costa et al., 2022; Silva et al., 2016; Delgado et al., 2020; Guerrini et al., 2009; Lemos et al., 2018; Ya' Akob et al., 2019; Khongkwanmueang et al., 2020; Agussalim et al., 2022; Vit et al., 2009; Nordin et al., 2018).

The United Nations Codex-Alimentarius, often referred to as the "Food Code", is widely recognized as the international standard for

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practices concerning food safety and quality, including honey. It defines honey as “the natural sweet substance produced by honey bees (*Apis* spp.) from the nectar of plants or from secretions of living parts of plants or excretions of plant-sucking insects on the living parts of plants, which the bees collect, transform by combining with specific substances of their own, deposit, dehydrate, store and leave in the honeycomb to ripen and mature” (Codex-alimentarius, 2001). Thus, the quality and composition criteria required for honey to be labeled as such were developed and determined based on honey obtained from honey bees of the *Apis* spp. genus, including the well-known European honey bee, *Apis mellifera*. While the Codex definition of honey does not specifically exclude honey from other bees, such as stingless bees, it must still meet the outlined criteria.

In recent years, a growing body of research has revealed significant differences in the physicochemical and chemical properties between stingless bee honey and honey bee honey (Nordin et al., 2018). These distinctions include higher water content, acidity levels, and a varied spectrum of sugars present in stingless bee honey (Ávila et al., 2018; Do Nascimento et al., 2015; Souza et al., 2006). These studies have made it evident that stingless bee honey does not conform to the existing quality standards by the International Honey Commission and the Codex-Alimentarius. Therefore, these findings have emphasized the imperative need for the development of an exclusive and independent standard specifically designed for stingless bee honey. The development of such standard is essential to facilitate the commercialization and safe consumption of stingless bee honey (Fernandes et al., 2018; Gomes et al., 2017).

In the Peruvian Amazon, there has been a limited amount of scientific research conducted on stingless bee honey (Marconi, Luna, & Giove, 2020; Rodríguez-Malaver et al., 2009). This lack of characterization hinders the establishment of specific quality and composition criteria for Amazonian Peruvian stingless bee honey, impeding its commercialization and sustainable development. Such development could potentially benefit numerous indigenous and non-indigenous communities in the Peruvian Amazon Rainforest.

The objective of this study is to conduct an initial characterization of the physicochemical and chemical parameters of honey obtained from two commonly raised stingless bee species in the Amazonia, *Melipona eburnea* and *Tetragonisca angustula*. These two bee species are widely used in indigenous and mestizo communities due to their higher honey production and their significant role in traditional medicine (Rasmussen & Castillo-Carrillo, 2003; Delgado et al., 2020).

By undertaking this research, we aim to develop a framework for proposing technical standards that support meliponiculture practices in Peru, addressing the unique qualities and characteristics of stingless bee honey in the region. Understanding the distinct properties of stingless bee honey and establishing appropriate quality criteria are necessary steps towards promoting its recognition, commercialization, and sustainable use. Such efforts will ultimately benefit the local communities and contribute to the preservation of the cultural heritage associated with stingless beekeeping in the Peruvian Amazon Rainforest.

2. Materials and methods

2.1. Study area and sample collection

Honey samples were collected from five meliponiculture communities in different regions of Peru, including:

- 1) The community of Nuevo Belén (C1: -8.759367 and -74.813817 , 317 msnm), located in the Honoría district, Puerto Inca province, Huánuco department.
- 2) The communities of San Juan de Tulumayo (C2-1: -9.267643 and -75.918480 , 819 msnm), Luyando district, and Río de Oro (C2-2: -9.1958 and -76.214 , 719 msnm), Mariano district Dámaso Beraún, both within the province of Leoncio Prado, Huánuco department.

- 3) The community of Puerto Pizarro (C3: -7.329728 and -76.923332 , 340 msnm), located in the Huicungo district, Mariscal Cáceres province, San Martín department.
- 4) The community of San Francisco (C4: -4.4469 and -73.5149 , 112 msnm), Nauta district, Loreto province, Loreto department.
- 5) The community of El Cóndor (C5: -5.593395 and -78.921735 , 1800 msnm), Huabal district, Jaén province, Cajamarca department (Figure 1).

Honey samples were obtained from local meliponarians who raise stingless bees in sustainable wooden technical boxes. A total of 12 honey samples were collected, with six samples obtained from *M. eburnea* and six from *T. angustula*. For the physicochemical studies, a single honey sample from a *M. eburnea* beehive was collected in each of the communities of Belén (C1), Puerto Pizarro (C3), and San Francisco (C4). Similarly, honey samples from *T. angustula* were collected from the communities of El Cóndor (C5), Puerto Pizarro (C3), and San Juan de Tulumayo (C2–1). Similarly, regarding the metabolomic studies, honey samples from *M. eburnea* were collected from the communities of Belén (C1), Puerto Pizarro (C3), and San Francisco (C4). Honey samples from *T. angustula* were collected from the communities of El Cóndor (C5), Puerto Pizarro (C3), and Río de Oro (C2–2). Honey collection was carried out using a sterile 100 mL hypodermic syringe and stored in previously sterilized glass bottles treated with a sodium hypochlorite solution.

2.2. Physicochemical profile

The physicochemical analyses were conducted in the Certificaciones del Perú (CERPER) laboratories in Lima, Peru. Each honey sample, three from *M. eburnea* (C1, C3 and C4) and three from *T. angustula* (C5, C3 and C2–1) was analyzed individually. The average value and standard deviation were calculated. The following physicochemical metrics and protocols were used:

- 1) Humidity: Determined using the NTP 209.171.1999 (2014) method (g/100 g honey).
- 2) Individual and total sugars: Analyzed using the HPLC method described in AOAC 977.20, (2019) (g/100 g honey).
- 3) Free acidity: Assessed according to the NTP 209.174.1999 (2014) method (meq of acid/kg of honey).
- 4) Ash: Measured using the NTP 209.175.1999 (2014) method (g/100 g honey).
- 5) Hydroxymethylfurfural (HMF): Quantified spectrophotometrically following the NTP 209.176.1999 (2014) method (mg of HMF/100 g of honey).
- 6) Solids insoluble in water: Determined by the NTP 209.178.1999 (2014) method (g/100 g honey).
- 7) Brookfield viscosity: Evaluated using the Rotational method described in ASTM D2196-10, (cps), which measures the rheological properties of non-newtonian materials.

2.3. Metabolomic profile

The metabolomic studies were conducted at InsectBiotec S.A.C., Tumbes, Perú. Three honey samples each from *M. eburnea* (C1, C3 and C4) and *T. angustula* (C5, C3 and C2–2) were individually extracted twice using 10 mL of methanol and subjected to 10 min of sonication. The crude extract was filtered and purified using a silica plate and a dichloromethane:methanol (12:2) solvent system. The resulting product bands were extracted and resuspended in methanol, followed by 10 min of sonication. After centrifugation, the supernatant was concentrated in vacuo.

In a new tube, 5 μ L of the concentrate was mixed with 5 μ L of the matrix to spot the OPTI-TOF plate in triplicate. The matrix solution was prepared using 699.3 μ L of 2,5-dihydroxybenzoic acid (DHB) in 1:1



Fig. 1. Google Earth map showcasing the areas of study and honey collection points.

methanol:water (15 mg of DHB diluted) and 0.7 μ l of trifluoroacetic acid (TFA). Thin-layer chromatography analysis using MALDI-TOF/TOF was performed to generate MS/MS data in both positive and negative modes for each of the six honey samples prepared.

Metabolite analysis was carried out using SimMet PREMIER Biosoft software, which compared the acquired data against HMDB, PubChem, Shimadzu, and NCBI databases. A 20.0 ppm precursor ion and MS/MS error tolerance (+/-) were applied, with a score value of 0.9 indicating 90% or higher homology, as recommended by SimMet technical experts. Statistical analyses were performed using PRISM 9 software (GraphPad Software, San Diego, CA, USA). PRISM 9 is a widely recognized statistical analysis tool used for data analysis, visualization, and hypothesis testing.

3. Results and discussion

3.1. Physicochemical components of stingless bee honey

3.1.1. Color

The color of Amazonian *M. eburnea* and *T. angustula* stingless bee honey exhibits a range of shades including light, amber, and dark hues, with *T. angustula* honey being darker in color. Rodríguez-Malaver et al. (2009) reported *T. angustula* honey as the darkest honey color among the samples collected from the Amazon Rainforest. The intensity of honey color may vary depending on factors such as the bee species, botanical origin, management, storage time, and harvesting methods.

In the Amazon Rainforest, certain species like *T. angustula* construct honey pots solely using wax, while *M. eburnea* build pots using a mixture of wax and resins extracted from neighboring trees. It is hypothesized that the physical contact between tree resin and honey during the honey maturation process facilitates the exchange of plant metabolites, including those influencing honey color (Lemos et al., 2018). When

honey is harvested using the traditional method of squeezing honey pots, the resulting honey color tends to be darker, possibly due to the resin dyes found in honey pots (Lemos et al., 2018).

3.1.2. Humidity, sugar, HMF

The average reducing sugar content (glucose + fructose) for *M. eburnea* honey was 54.32 (sd=4.32) g/100 g, and for *T. angustula* honey, it was 43.59 (sd=7.88) g/100 g. When comparing sugar levels (glucose + fructose), *M. eburnea* had a higher concentration with a minor statistically significant difference ($p = 0.0495$; Mann Whitney Test) (Tables 1 and 2). *T. angustula* honey showed high heterogeneity in sugar content with a variance of 62.11, while *M. eburnea* had a variance of 18.74. The high levels of heterogeneity were driven by samples from the El Condor community (C5). Excluding the C5 samples from the analysis resulted in homogeneous samples with a variance of 0.3. Stingless bee (*Meliponinae*) honey from Amazonian Ecuador shows relatively similar reducing sugar levels of 44.9 g/100 g (Guerrini et al., 2009), while samples from Amazonian Brazil displayed a wider range of sugar content between 53.91 and 74.63 g/100 g (Carvalho et al., 2009).

In the case of *M. eburnea* honey, the average hydroxymethylfurfural (HMF) content was measured to be 12.5 (sd=21.2) mg/100 g. On the other hand, *T. angustula* honey exhibited an average HMF content of 0.4 (sd=0.4) mg/100 g. Notably, a high level of heterogeneity in HMF content was observed in *M. eburnea* honey samples from the San Francisco community, specifically measuring 36.99 mg/100 g. However, the remaining five *M. eburnea* samples consistently exhibited HMF levels below 0.4 mg/100 g. Other studies conducted on honey from different bee species in the Peruvian Amazon reported HMF values ranging from 1.7 to 12 mg/100 g. Regarding stingless bee honey obtained from other regions within the Amazon Rainforest, Guerrini et al. (2009) reported HMF levels of 15.0 mg/100 g, while Carvalho et al. (2009) observed a

Table 1
Physicochemical parameters for *M. eburnea* and *T. angustula* honey extracted from 5 regions in the Peruvian Amazon Rainforest.

| Parameters | Unit | <i>Melipona eburnea</i> | | | <i>Tetragonisca angustula</i> | | |
|---------------------------|--------------------------|-------------------------|----------------|---------------|-------------------------------|----------------|----------------------|
| | | Nuevo Belén | Puerto Pizarro | San Francisco | El Cónдор | Puerto Pizarro | San Juan de Tulumayo |
| Humidity | | 26 | 29 | 29.4 | 27.8 | 25.8 | 25.4 |
| Sugars (glucose+fructose) | g/100 g | 59.03 | 53.43 | 50.51 | 34.5 | 47.75 | 48.52 |
| Glucose | g/100 g | 28.18 | 24.46 | 22.78 | 15.69 | 22.06 | 22.1 |
| Fructose | g/100 g | 30.85 | 28.97 | 27.23 | 18.81 | 25.15 | 26.42 |
| Saccharose | g/100 g | 2.88 | 3.22 | 4.52 | 18.99 | 11.47 | 10.14 |
| Solids insoluble in water | g/100 g | 0.01 | 0.01 | 0.02 | 0.04 | 0.02 | 0.04 |
| Free acids | meq of acid/kg of honey | 61.11 | 97.18 | 124.09 | 183.5 | 112.23 | 119.34 |
| Hydroxymethylfurfural | mg of HMF/100 g of honey | 0.1 | 0.35 | 36.99 | 0.83 | 0.08 | 0.15 |
| Ash | g/100 g | 0.01 | 0.01 | 0.01 | 0.37 | 0.45 | 0.57 |

Table 2
Average physicochemical parameters for *M. eburnea* and *T. angustula* honey compared to the parameters established in the Codex-Alimentarius.

| Parameters | Unit | <i>M. eburnea</i> | <i>T. angustula</i> , | <i>M. eburnea</i> (Delgado et al., 2020) | Codex –Alimentarius |
|-----------------------------|----------------------|-------------------|-----------------------|--|---------------------|
| Humidity | g/100 g | 28.13 | 26.33 | 31.76 | < 20 |
| Sugars (glucose + fructose) | g/100 g | 54.32 | 43.59 | 55.59 | > 60 |
| Glucose | g/100 g | 25.14 | 19.95 | 26.61 | |
| Fructose | g/100 g | 29.01 | 23.46 | 28.98 | |
| Saccharose | g/100 g | 3.5 | 13.53 | < 7 | < 5 |
| Solids insoluble in water | g/100 g | 0.01 | 0.03 | - | < 0.1 |
| Free acids | meq of acid/1000 g | 94.13 | 138.35 | | < 50 |
| pH | | | | 3.22 | |
| Diastase activity | 1% starch solution/g | | | 9.8 | > 8 |
| Hydroxymethylfurfural | mg/1000 g | 12.48 | 0.353 | 12.04 | < 40 * * |
| Electrical conductivity | mS/cm | | | | < 0.8 |
| Ash * | g/100 g | 0.01 | 0.46 | 0.06 | |

* * < 80 for honey samples of tropical origin

Table 3
Notable molecules of natural origin in *M. eburnea* honey.

| Molecule | Relative abundance % (S. D.) | Known origin | Known function | Previously detected in honey |
|----------------------------|------------------------------|--------------|---|----------------------------------|
| Naringenin chalcone | 0.45 (0.03) | Plant | Potential therapeutic against COVID-19 (Alberca et al., 2020) | Yes (Guerrini et al., 2009) |
| L-glutamine | 0.46 (0.04) | Plant | Vital nitrogen source (Kowalski et al., 2017) | Yes (Kowalski et al., 2017) |
| Caffeine | 0.32 (0.02) | Plant | Flavor molecule and stimulant (Júnior et al., 2020) | Yes (Swaileh & Abdulkhalq, 2013) |
| Berberine | 1.4 (0.15) | Plant | Natural dye and antitumor abilities (Rauf et al., 2021) | Yes (Guo et al., 2022) |
| Trans-zeatin-O-glucoside | 3.6 (0.2) | Plant | Regulates chlorophyll biosynthesis (Hošek et al., 2020) | No |
| L-saccharopine | 3.6 (0.2) | Plant | Precursor in the lysine degradation pathway (Antony et al., 2000) | No |
| Surfactin C | 3.4 (0.1) | Microbial | Antibiotic, antifungal, antiviral (Seydlová & Svobodová, 2008) | No |
| Paclitaxel | 0.60 (0.02) | Plant | Antineoplastic agent (Howat et al., 2014) | No |
| Stigmastanol | 0.64 (0.04) | Plant | Inhibits cholesterol biosynthesis (Habiger et al., 1992) | No |
| Riboprine | 0.59 (0.03) | Plant | Antiviral properties (Rabie & Abdalla, 2022) | No |
| Glandicoline B | 0.64 (0.03) | Microbial | Antibacterial properties (Subko et al., 2021) | No |
| Oleandomycin | 0.51 (0.03) | Microbial | Antibacterial properties (Lowbury & Hurst, 1959) | No |
| Tetrahydropalmatine | 0.37 (0.04) | Plant | Analgesic properties (Liu et al., 2021) | No |
| Camptothecin | 0.43 (0.04) | Plant | Inhibits replication of cancer cells (Hsiang et al., 1985) | No |
| Quinine | 0.37 (0.05) | Plant | Antimalarial medicine (Gachelin et al., 2017) | No |
| Diammonium glycyrrhizinate | 0.37 (0.04) | Plant | Active ingredient in Traditional Chinese Medicine (Feng et al., 2007) | No |
| Zeaxanthin | 0.32 (0.03) | Plant | Color molecule | No |
| Capsanthin | 0.27 (0.04) | Plant | Color molecule | No |

range of values between 12.7 and 66.5 mg/100 g. It is important to note that HMF serves as an indicator of freshness and spoilage in honey, with its levels increasing over prolonged storage time. However, the HMF levels reported in this study are below the limits established by the Codex-Alimentarius (<40 mg/100 g) (Delgado et al., 2020), indicating the freshness and quality of the honey samples analyzed.

The average humidity for *M. eburnea* honey was measured to be 28.13 (sd=1.8) g/100 g, while *T. angustula* honey exhibited an average humidity of 26.33 (sd=1.2) g/100 g. A comparison of humidity levels between the two species indicated a slight concentration difference that was not statistically significant ($p = 0.1266$; Mann Whitney Test).

Previous studies have reported humidity values ranging from 28.9 to 31.7 g/100 g for honey from various bee species in Peru (Delgado et al., 2020; Ormeño Luna et al., 2021; Guerrini et al., 2009; Vit, 2008; Cardona et al., 2019; Biluca et al., 2016); between 23.1 and 43.5 g/100 g in Brazil (Lemos et al., 2018; Costa et al., 2022); between 22.21 and 31.49 g/100 g in Colombia (Cardona et al., 2019) and between 21.1 and 26.8 g/100 g in Malaysia (Shamsudin, A et al., 2019; Agussalim et al., 2019; Agussalim, 2022). In a comprehensive assessment by Nordin et al. (2018) on physicochemical parameters of stingless bee honey from 67 species and 12 countries worldwide, humidity values varied from 13.26 to 45.8 g/100 g, with an average of 28.6 g/100 g and a standard

Table 4
Notable molecules of non-natural origin in *M. eburnea* honey.

| Molecule | Relative abundance % (S. D.) | Known function | Previously detected in honey |
|-------------------------------|------------------------------|--|--------------------------------------|
| Sudan IV | 1.0 (0.3) | Synthetic dye providing red tones (Kutt et al., 1959) | Yes (Zhao et al., 2015) |
| Propiconazole | 0.46 (0.04) | A triazole fungicide (Battaglin et al., 2011) | Yes (Rondeau and Raine, 2022) |
| Mono-demethylated isoproturon | 0.28 (0.06) | Active component of herbicide isoproturon (Kędzierska-Matysek et al., 2022) | Yes (Calatayud-Vernich et al., 2016) |
| Methoxyfenozide | 0.28 (0.03) | Commercial insecticide (Carlson et al., 2001) | Yes (Song et al., 2018) |
| N4-acetylsulfamethazine | 3.4 (0.4) | Active ingredient in sulfamethazine, used to prevent bee disease (Wang et al., 2019) | Yes (Wang et al., 2019) |
| Dodemorpha | 1.2 (0.2) | Commercial fungicide (Vorkamp et al., 2003) | Yes (Prasanth et al., 2017) |
| Myclobutanil | 1.2 (0.5) | Commercial fungicide (Bonde et al., 1995) | No |
| Paramethasone | 1.6 (0.3) | Commercial corticosteroid (Bel et al., 2006) | No |
| DAMGO | 1.5 (0.3) | Synthetic peptide (Baldo & Rose, 2022) | No |
| Eprosartan | 1.1 (0.1) | Commercial drug to treat hypertension (Plosker, 2009) | No |

Table 5
Relevant molecules of natural origin in *T. angustula* honey.

| Molecule | Relative abundance % (S. D.) | Known origin | Known function | Previously detected in honey |
|------------------------------|------------------------------|------------------|---|------------------------------|
| Fraxin | 0.72 (0.06) | Plant | Anti-inflammatory and hepatoprotective molecule (Sarfraz et al., 2017) | Yes (Guerrini et al., 2009) |
| Cinnamic acid | 0.58 (0.05) | Plant | Produces a honey-like scent and used as condiment (Gießel et al., 2019) | Yes (Da Silva et al., 2013) |
| Lutein | 0.58 (0.08) | Plant | Provides essential nutrients and antioxidants (Niu et al., 2020) | Yes (Kolayli et al., 2017) |
| Hyperoside | 0.46 (0.02) | Plant | Antibacterial properties (Van der Watt & Pretorius, 2001) | Yes (Wang et al., 2023) |
| Naringenin | 0.31 (0.05) | Plant | Potential treatment for COVID-19 (Alberca et al., 2020) | Yes (Guerrini et al., 2009) |
| Citrinin | 0.52 (0.07) | Microbial | Antimicrobial and may act as a toxin for mammals (Doughari, 2015) | Yes (Wyllie, 1945) |
| Petunidin-3-O-beta-glucoside | 0.60 (0.02) | Plant | Antineoplastic agent (Howat et al., 2014) | No |
| Isorhamnetin-3,7-diglucoside | 0.61 (0.05) | Plant | Antioxidant properties with potential to treat diabetes (Yokozawa et al., 2002) | No |
| Culmorin | 0.78 (0.08) | Plant | Antifungal agent (Takasu et al., 2000) | No |
| Eschscholtzanthin | 0.51 (0.04) | Plant | Natural pigment (Strain et al., 1961) | No |
| Remerine | 2.8 (0.3) | Plant | Plant metabolite (Alias et al., 2010) | No |
| Cyclopyroxanthin | 1.3 (0.4) | Plant and animal | Natural carotenoid (Marak et al., 2023) | No |
| Angustifoline | 1.2 (0.3) | Plant | Antiproliferative properties (Vishnyakova et al., 2020) | No |
| Laudanosine | 0.43 (0.04) | Plant | Derived to produce atracurium, a muscle relaxant (Fodale & Santamaria, 2002) | No |
| Uncarine C | 0.38 (0.03) | Plant | Used to treat asthma, fever, urinary and viral infections (Batiha et al., 2020) | No |
| Osthole | 0.32 (0.03) | Plant | Anticancer and hepatoprotective properties (Zhang et al., 2015) | No |
| Unshuaside A | 0.26 (0.02) | Plant | Light sedative to treat insomnia (Adhikari-Devkota et al., 2019) | No |

Table 6
Relevant molecules of non-natural origin in *T. angustula* honey.

| Molecule | Relative abundance % (S. D.) | Known function | Previously detected in honey |
|----------------------------------|------------------------------|--|------------------------------|
| Ametryn | 0.32 (0.03) | Breakdown product of the herbicide propazine (Yang et al., 2018) | Yes (Yang et al., 2018) |
| Velpar | 0.29 (0.05) | Known herbicide (Albero et al., 2004) | Yes (Albero et al., 2004) |
| Eprosartan | 0.67 (0.04) | Commercial drug to treat hypertension (Plosker, 2009) | No |
| Molinate | 0.52 (0.07) | Commercial pesticide | No |
| Propazine-2-hydroxy | 0.52 (0.03) | Commercial herbicide | No |
| Ethyl 4-(dimethylamino) benzoate | 3.0 (0.5) | Synthetic molecule used as a UV filter in sunscreen (Li et al., 2017) | No |
| N4-acetylsulfamethazine | 2.1 (0.4) | Active ingredient in sulfamethazine, used to prevent bee disease (Wang et al., 2019) | Yes (Wang et al., 2019) |
| Paramethasone | 1.0 (0.2) | Commercial corticosteroid (Bel et al., 2006) | No |

deviation of 5.7 g/100 g. Notably, 97% of the samples exceeded the humidity limit established by the Codex-Alimentarius (20 g/100 g).

When assessing honey quality, humidity content is considered a crucial factor as it reflects stability and resistance against spoilage. Higher humidity content is often associated with a greater likelihood of fermentation and spoilage. However, Vit et al. (1994) previously reported that stingless bee honey demonstrates high resistance to undesired fermentation due to the presence of elevated concentrations of polyphenolic compounds and enzymatic processes facilitated by bee

cerumen within the hive.

When comparing the essential composition and quality parameters of stingless bee honey with the standards set by the Codex-Alimentarius (2001), it was observed that both *M. eburnea* and *T. angustula* honey exceeded the permissible limit for humidity content, which is set below 20%. Additionally, their sugar contents were found to be below the minimum allowed level of more than 60 g/100 g of honey according to the Codex-Alimentarius guidelines.

3.2. Metabolomic profile

3.2.1. *M. eburnea* honey

The three samples of *M. eburnea* honey demonstrated highly similar MSMS profiles, showing only minor variations in the abundance of molecules rather than in the identification of molecules. The flora surrounding the beehives at the sample collection points exhibited a high degree of similarity, although not complete identity. Based on these findings, we hypothesize that the presence of a similar flora contributes to maintaining consistency in the chemical profiles observed. However, additional research is necessary to comprehensively understand the factors that may contribute to the observed similarity in molecular features, including the analysis of the bees' microbiome.

In total, approximately 555 molecular features were tentatively detected in *M. eburnea* honey, each with a similarity score of 0.90 or higher, indicating a substantial 90% match to the identified molecules cataloged in library databases. Among these features, 11 molecules were consistently found at relative abundances of 1% or higher on average, which we define as high abundance for this study. Additionally, a total of 33 molecular features were detected with medium average relative abundances ranging between 0.50% and 0.90%. Furthermore, the analysis revealed the presence of 49 molecules with lower abundance, falling between 0.25% and 0.50% relative abundance.

3.2.1.1. Molecules of natural origin. Naringenin chalcone, with an average relative abundance of 0.45% (sd=0.03), was identified within the molecular composition of *M. eburnea* honey. This intriguing compound can undergo a spontaneous cyclic reaction, leading to the formation of naringenin. Naringenin, a flavonoid commonly found in citrus trees such as oranges, has recently gained attention for its potential therapeutic properties against COVID-19 (Alberca et al., 2020). It has also been previously reported in Ecuadorian stingless bee honey (Guerrini et al., 2009), highlighting its presence in diverse honey sources.

The free amino acid L-glutamine was detected at an average relative abundance of 0.46% (sd=0.04). L-glutamine, a primary metabolite of plants, serves as a vital nitrogen source. Although present in trace amounts, its detection in honey aligns with previous findings (Kowalski et al., 2017).

Furthermore, caffeine was observed with an average relative abundance of 0.32% (sd=0.02). This well-known flavor molecule has been identified in various native Amazonian plants, including cacao (Júnior et al., 2020), and has been previously detected in honey samples (Swailah & Abdulkhalig, 2013).

Berberine, with an average abundance of 1.4% (sd=0.15), was also identified. This natural compound is commonly derived from plants belonging to the turmeric family and is renowned for its vibrant yellow color, often used as a natural dye for leather and wood. However, berberine's significance extends beyond its colorant properties, as it is currently under investigation for its potential as a cancer treatment due to its notable antitumor abilities (Rauf et al., 2021). Interestingly, berberine has been previously detected in a honey sample from China, as part of a study focused on identifying plant toxins in honey and tea beverages (Guo et al., 2022). While its presence in honey has been documented, the exact role of berberine in honey composition and quality remains to be fully elucidated. It is worth noting that some studies have suggested a potential toxicity of berberine to honey bees (Boncristiani et al., 2021). However, further research is necessary to comprehensively understand the impact and implications of berberine on honey and its potential interactions with bee health.

Moreover, our analysis revealed the presence of previously unreported plant-derived and microbial-derived molecules in the honey samples, highlighting the intricate and diverse nature of honey's chemical composition. Multiple factors, including the nectar source, bee species characteristics, geographic origin, climate (temperature and

humidity), beekeeping practices, and potential contaminants, contribute to the rich chemical diversity observed in honey (Silva et al., 2016; Estevinho et al., 2016; De Sousa et al., 2016; Shamsudin et al., 2019; Ya'akob et al., 2019). The presence of previously unidentified molecules underscores the complex interactions between bees, plants, and their environment. Further research is needed to understand the origin and significance of these newly detected molecules in *M. eburnea* honey composition and their potential implications for honey quality and safety.

Amongst these identified molecules, glycosyl trans-zeatin-O-glucoside was detected (3.6%, sd=0.2). This glucoside has been found to regulate chlorophyll biosynthesis in plants and is an important cytokinin present in plant sap and tissues (Hošek et al., 2020). While trans-zeatin-O-glucoside is not commonly reported in honey, it is known that certain plant-derived molecules can be transferred to honey, leading to variations in honey composition depending on floral sources and bee foraging habits.

Additionally, L-saccharopine and surfactin C were detected in relative abundances of 3.6% and 3.4% (sd=0.2 and 0.1), respectively. L-saccharopine is a common plant metabolite and a precursor in the lysine degradation pathway. It forms during the Maillard reaction, which occurs between reducing sugar and amino acids under specific storage conditions or thermal processes in honey and other foods (Antony et al., 2000). The Maillard reaction is responsible for the development of brown-like tones and flavor in honey.

Surfactin C, on the other hand, is a naturally occurring surfactant derived from microorganisms. It possesses diverse biological properties, including antibiotic, antifungal, antiviral, and inhibition of platelet aggregation (Seydlová & Svobodová, 2008). The presence of microbial colonization in plant nectar, bees, and honey has been associated with the generation of antibacterial compounds, suggesting a defense mechanism in these natural sources and organisms. Similar structurally related surfactants have been previously detected in honey and have been linked to the broad-spectrum activity of honey (Brudzynski et al., 2021).

Our analysis revealed the presence of additional several interesting molecules in the honey samples, including paclitaxel, stigmastanol, riboprine, and glandicoline B, with relative abundances ranging from 0.59% to 0.65% (sd=0.02, 0.04, 0.03, 0.03, respectively). Of particular significance is the detection of paclitaxel, an important antineoplastic agent widely used in cancer treatments (Howat et al., 2014). Originally isolated from the bark of *Taxus* trees, paclitaxel has been found in various plant species. Stingless bees in the Amazon Rainforest have been reported to collect resin and potentially other substances from the bark of medicinal trees in their vicinity. One such tree is the Dragon Blood Tree (*Croton lecheri*), known for its pharmacologically active compounds. Considering this, it is plausible that the observed presence of paclitaxel in the *M. eburnea* honey could be attributed to interactions between the bees and tree barks containing paclitaxel. However, further investigation is required to confirm this relationship and determine the specific floral origin of these compounds.

Stigmastanol is a naturally occurring sterol with medicinal properties that inhibit cholesterol biosynthesis (Habiger et al., 1992). Riboprine is a metabolite that regulates plant growth in *Arabidopsis thaliana* and has potent antiviral properties (Rabie & Abdalla, 2022). Glandicoline B is an indole alkaloid with antibacterial properties that was first isolated from the fungus *Penicillium* (Subko et al., 2021).

Additional molecules identified in the honey samples including oleandomycin, tetrahydropalmatine, camptothecin and quinine. Oleandomycin (0.51%, sd=0.03) is a microbial-derived antibiotic macrolide that inhibits the 50S subunit in bacterial ribosomes (Lowbury & Hurst, 1959). Tetrahydropalmatine (0.37%, sd=0.04) is an isoquinoline alkaloid with analgesic properties used in found in Traditional Chinese Medicine (TCM) (Liu et al., 2021). Camptothecin (0.43%, sd=0.04) is a cytotoxic alkaloid derived of *Campototheca acuminata* trees known for its ability to inhibit replication of cancerous cells (Hsiang

et al., 1985).

Quinine (0.37%, $sd=0.05$), an important antimalarial drug derived from the bark of *Cinchona* tree was also detected (Gachelin et al., 2017). This medicinal tree is highly abundant in the Amazon Rainforest. Diammonium glycyrrhizinate was also observed (0.37%, $sd=0.04$). This compound is extracted from *Glycyrrhiza* plants and an active ingredient in TCM that prevents T-cell-mediated hepatitis (Feng et al., 2007).

Furthermore, natural colorants such as zeaxanthin and capsanthin were identified in the honey samples. Zeaxanthin (0.32%, $sd=0.03$) is a carotenoid responsible for the distinct colors of certain foods, and capsanthin (0.27%, 0.04), found in red peppers (Murillo et al., 2019; Kennedy et al., 2021).

The tentative presence of these molecules in *M. eburnea* honey highlights its potential as a source of bioactive compounds with pharmaceutical properties. Understanding the floral sources and mechanisms of their incorporation into honey could provide valuable insights for honey production and the discovery of new natural compounds with therapeutic potential.

3.2.1.2. Molecules of non-natural origin. Several man-made molecules were tentatively detected in *M. eburnea* honey, potentially indicating traces of environmental contamination. Sudan IV was found to have an average relative abundance of 1% ($sd=0.3$). This molecule is a synthetic dye known for providing red tones when coloring lipids, lipoproteins, and triglycerides (Kutt et al., 1959). Although Sudan IV is not typically present in honey, it has been previously detected as a contaminant (Zhao et al., 2015).

We also detected the presence of propiconazole, a triazole fungicide (Battaglin et al., 2011), mono-demethylated isoproturon, an active component of the herbicide Isoproturon (Kędzierska-Matysek et al., 2022), and methoxyfenozide, a commercial insecticide (Carlson et al., 2001) in the honey samples. It is worth noting that these pollutants have been previously observed in honey (Rondeau & Raine, 2022; Calatayud-Vernich et al., 2016, and Song et al., 2018). The average relative abundances of propiconazole, mono-demethylated isoproturon, and methoxyfenozide were 0.46% ($sd=0.04$), 0.28% ($sd=0.06$), and 0.28% ($sd=0.03$), respectively.

N4-acetylsulfamethazine was found with a relative abundance of 3.4% ($sd=0.4$). This molecule is the active ingredient in sulfamethazine, a sulfonamide veterinary medicine used to treat bacterial infections in animals including disease prevention in bees. When used in excess, residual amounts of sulfamethazine have been previously detected in honey (Wang et al., 2019). Its presence in *M. eburnea* honey may indicate environmental contamination, calling for monitoring and control measures to ensure quality and safety.

Additionally, commercial fungicides dodemorph and myclobutanil were observed in the honey, each with a relative abundance of 1.2% ($sd=0.2$ and 0.5, respectively). Dodemorph is used to treat powdery mildew, a fungal disease that affects a wide range of plants including roses (Vorkamp et al., 2003), while myclobutanil is a broad-spectrum triazole chemical with fungicide properties (Bonde et al., 1995). Dodemorph has been previously detected in honey samples collected from various parts in India using a targeted MS and MS/MS approach (Prasanth et al., 2017). The presence of these fungicides in stingless bee honey in the Amazon Rainforest suggests environmental pollution in the area or misuse of these products. However, further validation through secondary assays is necessary to confirm the identity of the molecules and assess the pathway of contamination.

Moreover, non-natural molecules that have not been previously reported in honey, such as paramethasone, DAMGO, eprosartan, were detected. Paramethasone (1.6%, $sd=0.3$) is a commercial corticosteroid medicine with anti-inflammatory and immunosuppressant properties, typically administered orally or through injections (Bel et al., 2006). While rare, honey may be contaminated with residues from environmental sources or during sample collection or handling. Additional

targeted analytical studies are required to assess potential contamination sources to account for the tentative detection of paramethasone.

DAMGO (1.5%, $sd=0.3$) is a synthetic peptide currently evaluated in research and experimental studies to reduce opium tolerance (Baldo & Rose, 2022). Eprosartan (1.1%, $sd=0.1$) is a commercial drug used to treat hypertension (Plosker, 2009). It is highly unlikely that these molecules are naturally present in honey. Thus, their presence could indicate molecular misidentification or environmental contamination, such as residues found in wastewater (Bayer et al., 2014), which need to be traced and quantified to ensure quality and composition of the honey.

3.2.2. *T. angustula* honey

For *T. angustula*, a total of 541 molecular features were tentatively identified, on average, each with a similarity score of 0.9 or higher. Most of the identified molecules were consistent amongst the three honey samples from *T. angustula*. Within this set of features, 8 molecules consistently exhibited average relative abundances of 1% or higher, while 24 molecules were detected at medium relative abundances ranging from 0.50% to 0.90%. Additionally, 90 molecules displayed lower relative abundances between 0.25% and 0.50%.

3.2.2.1. Molecules of natural origin. Fraxin, a hepatoprotective and anti-inflammatory molecule derived from *Fraxinus excelsior* plant leaves (Sarrazin et al., 2017), was detected in *T. angustula* honey with an average relative abundance of 0.72% ($sd=0.06$). This molecule has been previously detected in stingless bee honey from the Amazonian Ecuador (Guerrini et al., 2009).

Isorhamnetin-3,7-O-diglucoside was observed with an average relative abundance of 0.61% ($sd=0.05$). This glycoside is often found in *Sedum acre* and *Lotus* plants and has antioxidant properties with the potential of treating diabetes (Yokozawa et al., 2002). Structurally related isoharmnetin molecules have been previously detected in stingless bee honey (Guerrini et al., 2009) as well as in tree nectar sources (Gasić et al., 2014).

Cinnamic acid and lutein were detected with an abundance of 0.58% each ($sd=0.05$ and 0.08, respectively). Cinnamic acid is a plant metabolite known to produce a honey-like scent and often used as a condiment (Gießel et al., 2019). It has been previously observed in *Melipona* stingless bee honey from the Amazon in Northern Brazil (Da Silva et al., 2013). Lutein, a carotenoid found in vegetables that provides essential nutrients and antioxidants (Niu et al., 2020), has also previously been observed in honey samples (Kolaylı et al., 2017).

Additionally, the presence of hyperoside and the flavonoid naringenin in the honey samples was observed, with relative abundances of 0.46% ($sd=0.02$) and 0.31% ($sd=0.05$), respectively. Hyperoside, a plant-derived phenol, exhibits antibacterial properties (Van der Watt & Pretorius, 2001) and has recently been identified in honey (Wang et al., 2023). Naringenin, which is currently being investigated as a potential treatment for COVID-19 (Alberca et al., 2020), has been previously detected in Ecuadorian stingless bee honey (Guerrini et al., 2009).

The fungal-derived mycotoxin, citrinin, was also found (0.52%, $sd=0.07$). This natural product confers antimicrobial properties and may act as a toxin for mammals (Doughari, 2015). The microscopic producing fungus has been previously recovered from honey (Kačaniová et al., 2012). The presence of citrinin in honey is relatively rare, but studies have shown that its production can increase when the producing fungus is experimentally grown in honey (Wyllie, 1945).

The anthocyanin compound petunidin-3-O-beta-glucoside, which is typically found in fruits such as red grapes (*Vitis vinifera*), was also detected in *T. angustula* honey with an abundance of 0.38% ($sd=0.05$). It is worth noting that related anthocyanin glycosides have been previously identified in honey (Tena et al., 2020). This finding suggests that the presence of petunidin-3-O-beta-glucoside in the honey may be attributed to the incorporation of these compounds from natural sources, contributing to its overall chemical composition and potential

health benefits.

The chemical profiling of *T. angustula* honey revealed the presence of several natural compounds that have not been previously reported in honey samples. These compounds may have been infused into the honey through the complex interactions between the bees and the surrounding flora. However, further research is necessary to validate these results and gain a better understanding of the specific sources and origins of these compounds.

One of the identified compounds was culmorin, with a relative average abundance of 0.78% (sd=0.08). Culmorin is known to inhibit detoxification reactions in plants and act as an antifungal agent, primarily associated with agricultural crops of grains and cereal products (Takasu et al., 2000). Another compound detected in the honey was eschscholtzanthin (0.52%, sd=0.04), a carotenoid derived from *Eschscholzia californica* used as a natural pigment (Strain et al., 1961), which had not been previously reported in honey.

Remerine (2.8%, sd=0.3) is a plant metabolite that is primarily found in the bark of *Fissistigma latifolium* (Annonaceae) (Alias et al., 2010). Given that some species of the Annonaceae family are found throughout the Amazon Rainforest (Taha et al., 2013), it is possible that interactions with these plants contribute to the presence of remerine in *T. angustula* honey.

We also detected cyclopyroxanthin with a relative abundance of 1.3% each (sd=0.4). Cyclopyroxanthin is a natural carotenoid known for protecting photosynthetic organisms against high levels of UV (Borodina, 2022). While primarily associated with sea mollusks, it has been detected in algae and plants (Marak et al., 2023), suggesting its collection from nectar sources containing this carotenoid.

Angustifoline (1.2%, sd=0.3), often found in the flower, leaves or stem of the plant *Lupinus angustifolius*, is an alkaloid with potential antiproliferative properties against colon cancer cells (Vishnyakova et al., 2020). While alkaloids have shown food deterrence effects on honey bees (Reinhard et al., 2009), no similar study has been performed on stingless bees, warranting further investigation into their attraction or avoidance of nectar containing these molecules.

Additionally, laudanosine, uncarine C, osthole, and unshuoside A were detected with relative abundances of 0.43%, 0.38%, 0.32%, and 0.26% (sd=0.04, 0.03, 0.03, 0.02), respectively. Laudanosine, a naturally occurring in opium in minimal concentrations and synthetically derived to produce atracurium, is a muscle relaxant drug used during surgical procedures (Fodale & Santamaria, 2002). Uncarine C, also known as *uña de gato* or cat's claw, is an indol derived from *Uncaria* plants that is vastly used in traditional medicines to treat asthma, fever and urinary and viral infections (Batiha et al., 2020).

Osthole, often found in the Chinese herbal medicine *Cnidium monnieri*, has shown anticancer and hepatoprotective properties (Zhang et al., 2015). Lastly, unshuoside A (0.26%) is an active metabolite found in *Citrus* plant flowers and used as a light sedative to treat insomnia in traditional medicines (Adhikari-Devkota et al., 2019).

3.2.2.2. Molecules of non-natural origin. Our chemoprofiling study revealed the presence of various synthetic compounds in *T. angustula* honey, indicating the potential influence of environmental pollutants. Amongst these molecules, we identified ametryin (0.32%, sd=0.03) and velpar (0.29%, sd=0.05). Ametryin is a breakdown product of the herbicide propazine, while velpar is a known herbicide and environmental pollutant. Trace amounts of both these compounds have been previously detected in honey (Yang et al., 2018; Albero et al., 2004).

Furthermore, we detected eprosartan, molinate and propazine-2-hydroxy with abundances of 0.67%, 0.52% and 0.52% (sd=0.04, 0.07, 0.03) respectively. Eprosartan, which was also observed in *M. eburnea* honey, is a commercial pharmaceutical drug, while molinate and propazine-2-hydroxy are pesticides and herbicides.

Additionally, we identified non-natural molecules including ethyl 4-(dimethylamino) benzoate, N-4 acetylsulfamethazine, and

paramethasone in abundances ranging from 1.0% to 3.0%. The benzoate (3.0%, sd=0.5) is a synthetic molecule commonly used as an ultraviolet (UV) filter in sunscreen (Li et al., 2017). Sulfamethazine (2.1%, sd=0.4) and paramethasone (1.0%, sd=0.2) have been discussed in more detail in previous paragraphs. The presence of these compounds suggests the possibility of pharmaceutical and environmental pollution resulting from the use of non-organic pesticides and improper disposal of commercial drugs or products in the area (Mitchell et al., 2017).

Further comprehensive studies encompassing ethnobotanical, biochemical, and medicinal investigations are necessary to validate the presence of the molecular features identified in this study. Numerous intriguing questions remain unanswered, such as: 1) Do these molecules exhibit consistent presence in each honey batch throughout the year, or are they significantly influenced by variations in climate, temperature, soil composition, water sources, and surrounding vegetation? 2) Which specific metabolites are directly derived from the nectar and resin obtained from neighbouring flowers, plants, and trees? To what extent do the bees' gut microbiome and associated mandibular and gut enzymes impact the production and composition of these compounds? 3) What are the concentrations per 100 g of honey of the detected molecules, rather than the percent relative abundance, and how are these values relevant for human consumption, quality, and safety? 4) How do non-natural molecules find their way into honey? Could it be attributed to human error during hive management, honey extraction, or sample transportation? Are the pesticides identified in this study commonly used in the area for agricultural purposes to combat pests and plant diseases? Is it plausible that rainwater, already contaminated with residual chemicals, infiltrates the beehives? 5) What is the chemical profile of honey produced by other bee species raised in the same geographical regions, and how does it compare to the molecules reported in this study? By addressing these inquiries, we can deepen our understanding of the complex dynamics between bees, their environment, and the composition of honey, leading to valuable insights for both the scientific community and honey industry.

4. Conclusion and future outlook

Stingless bee honey from the Peruvian Amazon has been utilized for centuries in traditional medicine and cultural practices. However, its physicochemical and chemical properties differ significantly from honey produced by honey bees, necessitating the development of specific quality criteria. In this study, we conducted an initial in-depth characterization of the physicochemical parameters and chemical composition of stingless bee honey from two commonly raised native bees, *M. eburnea* and *T. angustula*, uncovering their unique composition and potential medicinal and nutritional properties.

The physicochemical components of stingless bee honey were analyzed. The color of Amazonian *M. eburnea* and *T. angustula* honey ranged from light to dark hues, with *T. angustula* honey being darker. Variations in honey color can be attributed to factors such as bee species, botanical origin, management, storage time, and harvesting methods. Despite the higher sugar content in *M. eburnea* honey compared to *T. angustula* honey, both types had reducing sugar content levels below the minimum requirement specified by the Codex-Alimentarius for commercial honey. This indicates the potential use of these honeys for sugar-sensitive communities. The hydroxymethylfurfural (HMF) content, which serves as an indicator of freshness and spoilage, was found to be low in both types of honey, well below the quality parameters set for honey bee honey. Both *M. eburnea* and *T. angustula* honeys exhibited similar levels of humidity, although these levels were higher than the maximum allowed by international quality standards. These results emphasize the need to develop criteria for physicochemical characteristics exclusive to stingless bee honey.

The chemical profile analysis revealed the presence of various molecules in *M. eburnea* honey. Notable natural compounds included naringenin chalcone, L-glutamine, caffeine, berberine, and glycosyl trans-

zeatin-O-glucoside. These molecules have been previously identified in honey and are known for their therapeutic or biological properties. Of particular interest, berberine is currently undergoing investigation as a potential cancer treatment while naringenin, a derivative spontaneously formed from naringenin chalcone, is being studied for its potential as a therapeutic agent against COVID-19. Additionally, the detection of previously unreported plant-derived and microbial-derived molecules highlighted the complexity of the honey's chemical composition. Some of these compounds, such as paclitaxel, surfactin C, stigmastanol, quinine, riboprime, and tetrahydropalmatine, are of particular interest due to their potential anti-cancer, anti-microbial, anti-cholesterol, antiviral and analgesic properties. The presence of these molecules suggests interactions between bees, plants, and the environment, contributing to the diverse composition of stingless bee honey. Further research is necessary to unravel the origin, significance, and potential implications of these compounds on the medicinal value, quality, and safety of honey.

The chemical profile analysis of *T. angustula* honey also unveiled the presence of various natural molecules that have been previously observed in honey samples. These include fraxin, isorhamnetin-3,7-O-diglucoside, cinnamic acid, hyperoside, lutein and naringenin. These compounds have significant medicinal and nutritional properties, such as anti-inflammatory, anti-diabetic, antioxidant, and antibacterial effects. Additionally, previously unreported plant-derived compounds with biological relevance were identified in this honey. These compounds include culmorin, known for its antifungal properties, as well as angustifoline and osthole, which have demonstrated antiproliferative abilities against cancer. Another noteworthy compound is uncarine C, also known as cat's claw, which holds traditional importance as an anti-inflammatory and anti-viral medicine.

Furthermore, non-natural molecules were detected in both *M. eburnea* and *T. angustula* honey, suggesting potential environmental contamination. Among these molecules are commercial herbicides, fungicides, and insecticides, including ametryn, velpar, propiconazole, and methoxyfenozide. The presence of these pollutants in other honey samples worldwide emphasizes the urgent requirement for stringent regulations regarding the use of toxic chemicals in agricultural practices. Such regulations are necessary to safeguard the health of bees and ensure the high quality of their derived products, such as honey.

Our findings contribute to the scientific understanding of meliponiculture practices and provide a basis for the development of technical standards, including a quality criteria exclusive to stingless bee honey that facilitates its commercialization and sustainable development. Stingless bee honey from the Peruvian Amazon exhibits unique physicochemical and metabolomic properties, highlighting its potential for consumption, nutritional, and medicinal applications. However, it is evident that the existing quality standards outlined by the Codex Alimentarius are not applicable to this specific type of honey. Therefore, the establishment of an independent standard tailored to the characteristics of stingless bee honey is imperative.

The metabolomic analysis of the honey samples revealed the presence of diverse molecular features, potentially possessing medicinal properties. This initial study enhances the empirical traditional knowledge of meliponiculture communities in the Amazon, elevating the relevance of stingless bee honey in the local market. Furthermore, the detection of environmental pollutants, including pesticides, emphasizes the need to establish maximum residue limits in the new technical standard, ensuring the safety and quality of the honey.

To validate the presence of the molecular features described in this study, further investigations are needed. An expanded sample size encompassing a larger geographical area will provide a more comprehensive understanding of the chemoprofile of stingless bee honey. Additionally, it is important to use pure internal standards for the molecules tentatively identified in this work to ensure accurate identification and quantification. Furthermore, conducting studies to monitor the floral sources and investigating the impact of the bees' gut microbiome on the honey's chemical composition are crucial for gaining a

deeper understanding of its unique properties.

The significance of this investigation extends beyond scientific exploration. It contributes to the revalorization of native stingless bees and their honey, highlighting the importance of their protection against increasing environmental and human threats. This study also opens avenues for potential industrial applications, as the diverse metabolomic profile of stingless bee honey offers opportunities for the development of novel therapeutic and nutraceutical products.

In conclusion, our study provides valuable insights into the physicochemical and chemical characteristics of stingless bee honey from the Peruvian Amazon. It underscores the necessity for the development of technical standards and quality criteria specific to stingless bee honey, supporting its commercialization and sustainable use. Moving forward, future research should focus on addressing the identified gaps and recommendations, advancing our knowledge of stingless bee honey and its potential benefits for human health and well-being.

Declaration of Competing Interest

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.foohum.2023.08.017](https://doi.org/10.1016/j.foohum.2023.08.017).

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