Antibacterial activity of honey on some antibiotic-resistant strains, systematic review Morocco

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Abstract:

With the emergence of antibiotic-resistant strains around the world, studies are starting to look at the therapeutic benefits of certain natural products. Honey is one of these most coveted products because of its therapeutic properties. In this context, the aim of this systematic review is to explore the current scientific literature on the antibacterial activity of honey on some bacterial strains known to be resistant to antibiotics. Our results confirmed the antibacterial activity of honeys, produced in different countries, on the bacterial strains tested. The antibacterial tests showed differences in inhibition depending on the type of honey used and the bacterial strains targeted, indicating a broad spectrum of antibacterial action of honey. This natural product could be used alone or in combination with antibiotics, which have become ineffective against a set of resistant bacterial strains.

Keywords: Antibacterial activity; Antibiotic resistance; Honey.
Résumé :

Avec l’émergence des souches résistantes aux antibiotiques à travers le monde, les études commencent à s’intéresser aux vertus thérapeutiques de certains produits naturels. Le miel compte parmi ces produits les plus convoités en raison de ses propriétés thérapeutiques. Dans ce contexte, la présente revue systématique a comme objectif d’explorer la littérature scientifique actuelle sur l’activité antibactérienne du miel sur quelques souches bactériennes connues par leur résistance aux antibiotiques. Les résultats obtenus ont mis en évidence l’activité antibactérienne des miels, produits dans différents pays, sur les souches bactériennes testées. Les tests antibactériens ont montré des différences d’inhibition selon le type de miel utilisé et les souches bactériennes ciblées, indiquant un large spectre d’action antibactérien du miel. Ce produit naturel pourrait être utilisé seul ou en association avec des antibiotiques devenus inefficaces contre un ensemble de souches bactériennes résistantes.

Mots clés : Activité antibactérienne ; Miel ; Résistance aux antibiotiques.

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Introduction

Antibiotic resistance is a major public health problem and a serious threat that affects all countries, according to the World Health Organization (WHO) (Lemaoui et al. 2017; Mcloone et al. 2020). It is estimated that 60% of hospital-acquired infections worldwide are attributed to antibiotic-resistant bacteria (Carle 2010). With the emergence of these strains over the world, researchers are focusing their attention on the medicinal effects of natural products. This scientific approach is supported by the WHO, which encourages the use of alternative medicines based on natural products by member states, as an inexpensive way to achieve universal health coverage (Mama et al. 2019). Honey is one of the most appreciated and valued natural products introduced to humankind since ancient times. This natural product can be differentiated into two main types: a floral honey made from the nectar of blossoms (flower honey) and a honeydew honey prepared from the secretions of plants or the excretions of plant-sucking insects (Hegazi et al. 2017). Floral honey, the subject of this study, is presented in two categories: polyfloral honey, collected by bees using the nectar from many different flower species, and monofloral honey, produced from the nectar of one main flower. Pure monofloral honey is quite impossible to find without being contaminated with other plant flowers. However, honey is considered monofloral when it comes from at least 55% of the pollen from a single floral source (Hegazi et al. 2017).

Honey has been used as a natural medicine for 2000 years (Johnston et al. 2018). However, it was only in 1892 that its antibacterial activity was discovered (Mama et al. 2019). It has inhibitory and therapeutic properties (Merah 2010), with little or no side effects (Balas 2015) and without risk of bacterial resistance development (Majtan et al. 2020). This natural product has been reported to have an inhibitory effect to around 60 species of bacteria including gram-positives and gram-negatives, aerobes and anaerobes (Saad 2015). As well as to bacterial strains resistant to antibiotics (Mcloone et al. 2020). This antibacterial activity is indicated in terms of Minimum Inhibitory Concentrations (MIC) and Minimum Bactericidal Concentrations (MBC) using different methods: dilution tests, E-test (Amhis et al. 2001) and automated antibiogram (Quentin-Noury 2016).

Honey could inhibit bacterial growth through its high concentration of sugars, its low pH, enzymatic generation of hydrogen peroxide (H₂O₂), or the presence of certain protein or
phytochemical compounds, such as aromatic acids and phenols (Fangi 2007; Hegazi et al. 2017; Padungton and Kaneene 2003). However, to keep its inhibitory properties, honey must be stored away from heat and light (Bogdanov and Blumer 2001).

In this context, this systematic review aims to explore the current scientific literature on the antibacterial activity (bactericidal effect and bacteriostatic effect) of honey on some bacterial strains known to be resistant to antibiotics.

**Material and methods**

A systematic review examining the antibacterial effect of honey was conducted in accordance with PRISMA guidelines (Gedda 2015). The PubMed and Google Scholar electronic databases were used to perform the literature search using different combinations of the keywords from the three groups shown in table 1. Research articles with full text in English and French, published between 2000 and 2020 and dealing with the antibacterial effect of honey on bacterial strains known to be resistant to antibiotics, were included in the study. Some important articles were also taken from the reference list of included articles. The research was conducted between February and May 2021. We obtained a total of 117 scientific articles of which 9 were selected for their relevance to research on the antibacterial effect of honey (Table 2). The management of bibliographic references was done by the Zotero software.

**Results**

In this systematic review, researchers tested different types of honey (monofloral, polyfloral and artificial), from different countries, on some bacterial strains known for their resistance to antibiotics. The results showed that the majority of the honey samples tested had an antibacterial effect, regardless of the activity test used (diffusion on agar, diffusion on disk or dilution by boiling) (Table 3). Moroccan studies, testing 8 samples of natural honey (monofloal honey and polyfloral honey) for their antimicrobial effects on 3 bacterial strains of *Escherichia coli* (*E. coli*), *Staphylococcus aureus* (*S. aureus*) and *Salmonella spp.*, by using the techniques agar diffusion and serial dilution. This study showed that, the MICs of samples (orange honey, eucalyptus honey, asparagus honey and carob honey) were 75 % (p/v) against
E. coli, S. aureus and Salmonella spp. However, the MICs of samples (Tadla flower honey, oregano honey and eucalyptus honey) were 50% (p/v) against S. aureus. Moreover, the MIC of sample (spurge honey) was 25% (p/v) against Salmonella spp. (Belhaj et al. 2016) (Table 3). A second study is conducted in Chile, whose researchers used the microdilution technique, for testing 2 samples of monofloral honey for their antimicrobial effects on 5 bacterial strains of E. coli, S. aureus, Pseudomonas aeruginosa (P. aeruginosa), Salmonella typhi and Beta-hemolytic Streptococcus. This study showed that the MICs of samples range from 12.5 to 50% (p/v) against S. aureus, P. aeruginosa, Salmonella typhi and Beta-hemolytic Streptococcus, but it was no inhibition for E. coli (Montenegro et al. 2009) (Table 3).

The main results of the other studies are presented in table 3. E. coli, a Gram-negative bacterium and a major causative agent of extra-intestinal infections in humans, is known for its resistance to quinolones, fluoroquinolones, ciprofloxacin and nalidixic acid (Sabate et al. 2008) (Table 4). This bacterium was tested for antibacterial honey in 7 studies (Table 3). It showed sensitivity to the majority of honeys evaluated in this systematic review, with the exception of two monofloral Chilean honeys. While Saudi honeys showed the lowest MIC (around 20%) (Hegazi et al. 2017), those of Morocco (8 samples), Ethiopia (4 samples) and Scotland showed higher MIC values, ranging from 50 to 100% (p/v) (Belhaj et al. 2016; Mama et al. 2019; Schneider et al. 2012). The MICs ranged from 20 to 50% (p/v) for the Canadian honeys (42 samples), Argentinians (30 samples) and those from South Africa (5 samples) (Basson et al. 2008; Brudzynski 2006; Fangio 2007).

S. aureus, a Gram-positive bacterial strain, which is a pathogen involved in skin infections, is known for its resistance to methicillin, kanamycin, fusidic acid, β-lactams lactams and tetracyclines (Dumitrescu et al. 2010) (Table 4). This germ has been tested for antibacterial honey in 7 studies (Table 3). It showed sensitivity to all types of honey tested, with MICs ranging from 6 to 100% (p/v). Slovak, Ethiopian and Chilean honeys showed the strongest inhibitory effect, with MICs of 6 and 12.5% (p/v), respectively (Bucekova et al. 2019; Mama et al. 2019; Montenegro et al. 2009). While Moroccan and Scottish honeys are the least potent on the same species, with MICs of 50 to 75% (p/v) (Belhaj et al. 2016).

P. aeruginosa, a Gram-negative bacillus responsible for 10 to 15% of all nosocomial infections, is tested in 4 studies (Table 3). This germ is known for its resistance to at least three of the four main classes of anti-Pseudomonas antibiotics (penicillins, cephalosporins,
Antibacterial activity of honey on some strains

Salmonella (Salmonella typhi and Salmonella spp.) have been studied in 2 researches (Table 3). These germs are Gram-negative bacterial strains that have acquired some resistance to chloramphenicol, cotrimoxazole, amoxicillin, ampicillin, streptomycins, sulfonamides, chloramphenicol / florfenicol, tetracycline, erythromycin, imipenem and fusidic acid (Abba et al. 2017; Dagnra et al. 2007; Weil 2008) (Table 4). In this study, the two bacteria showed sensitivity to the different honeys tested. The MIC of Chilean honey on Salmonella typhi ranged from 12 to 50% (p/v) (Montenegro et al. 2009), against a percentage of 25% (p/v) for Moroccan honeys on Salmonella spp (Belhaj et al. 2016).

Beta-hemolytic Streptococcus is Gram-positive cocci. It is responsible for both focal infections such as tonsillitis and mild skin infections, and severe invasive infections. It is known for its resistance to macrolides (Bouvet et al. 2004) (Table 4). This bacterium exhibited sensitivity to Chilean honeys at ranging from 12.5 to 50% (p/v) (Montenegro et al. 2009) (Table 3).

Klebsiella pneumoniae, a Gram-negative bacillus and pathogen of digestive and pulmonary infections, is known for its resistance to gentamicin, ciprofloxacin and amikacin (El Bouamri et al. 2015) (Table 4). Table 3 showed that this strain is sensitive to Saudi honeys at a percentage of 20% (Hegazi et al. 2017).

Studies used high-performance liquid chromatography (HPLC) analysis to identify the phenolic compounds in the various honey extracts and showed the presence of 27 phenolic compounds which were mainly 13 flavonoids and 14 phenolic acids (Table 5) (Akalin et al. 2016 ; Biesaga and Pyrzynska 2009; Campillo et al. 2015 ; Campone et al. 2014 ; Chan et al. 2013 ; Hamdy et al. 2009 ; Kennedy et al. 2011; Ku´s et al. 2016 ; Petretto et al. 2015 ; Ranneh et al. 2018 ; Shahzad et al. 2012; Yaoa et al. 2005). These flavonoids included apigenin, catechin, chrysin, galangin, genistein,isorhamnetin, kaempferol, luteolin, myricetin, naringénine, pinocembrin, quercetin and rutin. The phenolic acids were: abscisic acid, benzoic acid, caffeic acid, chlorogenic acid, cinnamic acid, ellagic acid, ferulic acid,
gallic acid, $p$-coumaric acid, $p$-hydroxybenzoic acid, protocatechuic acid, sinapic acid, syringic acid and vanillic acid.

**Discussion**

The results of this study showed variation in the antibacterial activity. It could be attributed to the composition of the honey itself, which depends on many factors, such as: the nature of the soil, the breed of bees and the physiological state of the colony (Prost (as cited in Merah 2010)), the floral origin (Basson and Grobler 2008; Hegazi et al. 2017; Mama et al. 2019), and the storage conditions for honey (Bogdanov and Blumer 2001). This variation could also be linked to the different geographical locations where this honey is produced (Belhaj et al. 2016; Mama et al. 2019). Indeed, Manuka honey, produced from Manuka nectar flowers, has been shown to be the leader in honeys for antimicrobial activity (Jonhston et al. 2018), with a MIC of around 1% (Lin et al. 2009). However, the study carried out by Basson and Grobler (2008) concluded that honey produced locally (in South Africa) from Leptospermum scoparium (Manuka) obtained from New Zealand did not exhibit specific properties compared to other honeys used in their study and that the MIC of all the honeys tested was 50%.

The technique most commonly used in these studies is micro or macrodilution in broth. However, due to the difficulty of diffusing honey in agar, the techniques on agar are the least used. The results of the antibacterial tests showed differences in inhibition depending on the type of honey used and the bacterial strains targeted, indicating a broad spectrum of antibacterial action of honey.

The comparison of the antibacterial effect of honeys tested on different strains also showed differences (Table 3). Indeed, honey from the same floral source and the same geographical area can have different antibacterial effect on bacterial strains with different membrane structures (Gram). This is the case of samples of monofloral honey from the Chilean species which showed a remarkable inhibitory effect on $S. \text{aureus}$ (Gram positive), while they did not inhibit $E. \text{coli}$ (Gram negative) (Montenegro et al. 2009). This is in agreement with the results of the study conducted by Belhaj and al. (2016) who demonstrated that Gram-positive bacteria are more sensitive than Gram-negative bacteria. This is due to the 3-layered cell envelope that Gram negative bacteria have and which gives them additional protection.
compared to Gram positive bacteria (Johnston et al. 2018). In contrast, Merah (2010) confirmed that Gram-positive bacteria with thick, dense walls are more resistant to high osmotic pressures exerted by sugar than Gram-negative bacteria with thin, loose walls.

However, it is recognized that the antibacterial properties of honey come from several physicochemical factors contributing to the reduction or elimination of bacterial activity, notably the high sugar content of up to 82%, which attributes to honey a hyper-osmolarity helping to extract the water contained in bacteria, which results in their dehydration and lysis (Belhaj et al. 2016). The low pH of honey between 3.0 and 4.5 gives it a fairly high acidity capable of causing the inhibition of several types of bacteria (Brudzynski 2006). Another factor responsible for the antibacterial activity of honey is the generation of hydrogen peroxide (H$_2$O$_2$). The production of H$_2$O$_2$ is attributed to the action of glucose oxidase, an enzyme that bees add to the nectar of foraged flowers (Fangio 2007). Also, the antibacterial activity of honey is mainly due to other components such as phenolic compounds (Bogdanov and Blumer 2001; Brudzynski 2006). As early as the 1990s, phenolic acids and flavonoids were recognized as important components of the antibacterial substances in honey (Lugrin 2014). In this context, researches showed a good correlation between honey total phenolic compounds and the antibacterial activity of honey (Brudzynski et al. 2011; Cianciosi et al. 2018).

In terms of composition, Biesaga and Pyrzynska (2009) have reported that all the honey samples that they assessed contained traces of similar phenolic compounds but in different quantities. The phenolic acid level in honey can be affected by its botanical and geographical origin as it depends upon the source of the nectar (Saad 2015). Moreover, it is evident that the season also has a noticeable effect on the total phenolic acid content of honey. To illustrate this, Lachman et al. (2010) found the highest total phenolic acid content occurred in the honey collected at the beginning of June and July. Whereas, it was much lower in samples collected during the other months. This could be explained by the fact that plants in spring and early summer produce polyphenols as part of the interactions of plants with their biological and physical environment to provide protection against ultraviolet rays and to attract insects which will allow effective pollination (Muanda 2010). The color of honey can reflect also the phenolic acid level in honey (Brudzynski and Miozzo 2011; Gomes et al. 2010). Actually, studies showed a good correlation between honey color and total phenolic
content. Hence, dark honey has a high level of phenolic compounds (Estevinho 2008; Taormina 2001).

Several studies have evaluated the antibacterial effect of individual phenolic compounds or phenolic compounds combined with antibiotic on the growth of several pathogenic bacteria, including antibiotic resistant isolates. In vitro investigation of flavonoids against several oral microbes showed that quercetin had potent activity against *Prophyromonas gingivalis* with MIC value of 0.0125 µg/ml (Geoghegan et al. 2010). Pinocembrin is a compound that present proven antibacterial activity on *Neisseria gonorrhoeae* with MIC of 64µg/ml (Fikri et al. 2020). In addition, Vaquero et al. (2007) reported that *Klebsiella pneumoniae* was inhibited by gallic and vanillic acids as well as quercetin with a MIC ranged from 100 to 500 mg/l. Caffeic acid produced a good antibacterial activity on *E. coli* with a low concentration (1 mg/l). Furthermore, Pacheco-Ordaz et al. (2018) revealed that the MIC of gallic and vanillic acids ranged from 15-20 mmol/l and 20-30 mmol/l against *E. coli* and *Salmonella Typhimurium*, respectively. In another study, the antibacterial activities of quercetin against amoxicillin-resistant *S. epidemidis* were assessed. The results indicated that quercetin presented synergistic effect with amoxicillin and bacterial resistance to this traditional antibiotic was remarkably reversed (Siriwong et al. 2016). Caffeic acid presented a synergistic effect with two antibiotics against *Pseudomonas aeruginosa*. With gentamicin, it reduced the MIC from 625 µg/ml to 24.61 µg/ml. With imipenem, it reduced the MIC from 1250 µg/ml to 78.13 µg/ml (Lima et al. 2016).

The mechanism by which phenolic compounds exerted their antibacterial activity against bacteria is still not fully understood but may be related to their chemical structure. They can cause morphological changes in microorganisms, damage bacterial cell walls and influence biofilm formation. Polyphenols also influence protein biosynthesis, change metabolic processes in bacteria cells and inhibit ATP and DNA synthesis (suppressing DNA gyrase) (Efenberger-Szmeczyk et al. 2021).

Moreover, the antibacterial effect of honey can be catalyzed by vitamin C. This compound has been found in almost all type of honey (Ciuluet al. 2011) but it represents a minor part of honey compounds (Combarros-Fuertes et al. 2018). In this context, a recent study proved that vitamin C supplementation of honey significantly increased the antibacterial activity of honeys tested against *Pseudomonas aeruginosa* in planktonic cultures (Majtan et al. 2020).
Conclusion

From the results of this study, it concluded that honey, collected from different countries, inhibit the growth of the majority of the bacterial strains tested. It could be used as an antibacterial agent against antibiotic-resistant strains. It is noticed that although the botanical origins for some honeys were different, they all exhibit antibacterial activities against the strains tested. It seems important to explore other factors responsible for the antibacterial activity of honey, such as the race of the bee, harvesting technique as well as the mode of packaging and storage of the honey.

Conflict of interest: Authors declare no conflict of interest.

Table 1. Keywords used in the study

<table>
<thead>
<tr>
<th>Keyword (group 1)</th>
<th>Keyword (group 2)</th>
<th>Keyword (group 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Honey</td>
<td>Bacterial strains</td>
<td>Antibacterial effect</td>
</tr>
<tr>
<td></td>
<td>Resistant bacteria</td>
<td>Antimicrobial effect</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bactericidal effect</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bacteriostatic effect</td>
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<tr>
<td></td>
<td></td>
<td>Inhibitory effect</td>
</tr>
</tbody>
</table>

Table 2. Table created in accordance with PRISMA guidelines indicating the number of articles identified and included in this systematic review (Gedda 2015)

<table>
<thead>
<tr>
<th>Research strategy</th>
<th>Number of articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification</td>
<td>117</td>
</tr>
<tr>
<td>Screening</td>
<td>74</td>
</tr>
<tr>
<td>Eligibility</td>
<td>35</td>
</tr>
<tr>
<td>Included</td>
<td>9</td>
</tr>
</tbody>
</table>
### Table 3. The main works relating to the antibacterial activity of honey.

<table>
<thead>
<tr>
<th>Area of study</th>
<th>Numbers of samples of types of honey</th>
<th>Tested Microorganisms</th>
<th>Used methods</th>
<th>Main results</th>
<th>References</th>
</tr>
</thead>
</table>
| Canada        | 6 samples of polyfloral honey, 36 samples of monofloral honey | *E. coli*  
*B. subtilis* | Serial dilution | MICs of all samples range from 25 to 50% against *E. coli* and *B. subtilis* | (Brudzynski 2006) |
| Argentina     | 30 samples of polyfloral honey | *E. coli* | Serial dilution  
Nutrient agar  
Diffusion on agar plate | MICs of all samples range from 25 to 50% against *E. coli* | (Fangio 2007) |
| South-Africa  | 4 samples of monofloral honey, 1 artificial honey | *E. coli*  
*S. aureus*  
*P. aeruginosa*  
*Salmonella typhi*  
Beta-hemolytic S. | Microdilution by boiling | MICs of samples (1-3-4) are 25% against *E. coli*.  
MICs of samples (2-5) are 50% against *E. coli*.  
MICs of samples (1-2-3-4-5) are 25% against *S. aureus* | (Basson and Grobler 2008) |
| Chile         | 2 samples of monofloral honey | *E. coli*  
*S. aureus*  
*P. aeruginosa*  
*Salmonella typhi*  
Beta-hemolytic S. | Microdilution | For *E. coli*: no inhibition  
For other bacteria:  
MICs of all samples range from 12.5 to 50% | (Montenegro et al. 2009) |
| Scotland      | 1 sample of polyfloral honey | *E. coli*  
*S. aureus*  
*P. aeruginosa* | Serial dilution  
Disc broadcast | MICs range from 50 to 70% against *E. coli*, *S. aureus* and *P. aeruginosa* | (Schneider et al. 2012) |
| Morocco       | 2 samples of polyfloral honey, 6 samples of monofloral honey | *E. coli*  
*S. aureus*  
*Salmonella spp* | Serial dilution  
Agar diffusion | MICs of samples (1-4-5-6) are 75% against *E. coli*, *S. aureus* and *Salmonella spp*.  
MICs of samples (2-3-4) are 50% against *S. aureus*  
MIC of sample (8) is 25% against *Salmonella spp*. | (Belhaj et al. 2016) |
| Saudi Arabia  | 10 samples of monofloral honey | *E. coli*  
*S. aureus*  
*S. mutans*  
*K. pneumoniae*  
*P. aeruginosa* | Serial dilution | MICs of all samples are 20% against *E. coli*, *S. aureus*, *S. mutans*, *K. pneumoniae* and *P. aeruginosa* | (Hegazi et al. 2017) |
| Slovakia      | 57 samples of monofloral honey | *S. aureus*  
*P. aeruginosa* | Serial dilution  
Agar diffusion | MICs of all samples range from 25 to 50% against *S. aureus* and *P. aeruginosa* | (Bucekova et al. 2019) |
| Ethiopia      | 4 samples (Type of honey not specified) | *S. aureus* | Kirby-Bauer  
Disc broadcast  
Serial dilution | MICs of samples (1-3-4) range from 50 to 100% against *S. aureus*  
MIC of sample 2 against *S. aureus* isolates range from | (Mama et al. 2019) |
Table 4. Resistance of bacterial strains to antibiotics

<table>
<thead>
<tr>
<th>Bacterial strain</th>
<th>Gram staining</th>
<th>Antibiotic resistance</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>Gram negative</td>
<td>Quinolones Fluoroquinolones Ciprofloxacin Nalidixic acid</td>
<td>(Sabate et al. 2008)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Gram positive</td>
<td>Methicillin Kanamycin Fusidic acid ß-lactams lactamins Tetracyclines</td>
<td>(Dumitrescu et al. 2010)</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Gram negative</td>
<td>Penicillins Cephalosporins Aminoglycosides Fluoroquinolones</td>
<td>(Barbier and Wolff 2010)</td>
</tr>
<tr>
<td><em>Salmonella typhi</em> and <em>Salmonella spp</em></td>
<td>Gram negative</td>
<td>Cotrimoxazole Amoxicillin Ampicillin Streptomycins Sulfonamides Chloramphenicol / Florfenicol Tetracycline Erythromycin Imipenem Fusidic acid</td>
<td>(Abba et al. 2017; Dagnra et al. 2007; Weiil 2008)</td>
</tr>
<tr>
<td><em>Beta-hemolytic Streptococcus</em></td>
<td>Gram positive</td>
<td>Macrolides</td>
<td>(Bouvet et al. 2004)</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>Gram negative</td>
<td>Gentamicin, Ciprofloxacin Amikacin</td>
<td>(El Bouamri et al. 2015)</td>
</tr>
</tbody>
</table>

9.38 to 37.5%
Table 5. Common phenolic compounds identified in honey

<table>
<thead>
<tr>
<th>Compound names</th>
<th>Brute formula</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flavonoids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apigenin</td>
<td>C_{15}H_{10}O_{5}</td>
<td>(Biesaga and Pyrzynska 2009; Estevinho et al. 2008; Ku´s et al. 2016)</td>
</tr>
<tr>
<td>Catechin</td>
<td>C_{15}H_{14}O_{6}</td>
<td>(Hamdy et al. 2009; Ku´s et al. 2016; Shahzad et al. 2012)</td>
</tr>
<tr>
<td>Chrysine</td>
<td>C_{15}H_{10}O_{4}</td>
<td>(Hamdy et al. 2009; Estevinho et al. 2008; Ku´s et al. 2016)</td>
</tr>
<tr>
<td>Galangin</td>
<td>C_{15}H_{10}O_{5}</td>
<td>(Hamdy et al. 2009; Ranneh et al. 2018)</td>
</tr>
<tr>
<td>Genistein</td>
<td>C_{15}H_{10}O_{5}</td>
<td>(Hamdy et al. 2009; Ranneh et al. 2018)</td>
</tr>
<tr>
<td>Isorhamnetin</td>
<td>C_{16}H_{12}O_{7}</td>
<td>(Kennedy et al. 2011; Shahzad et al. 2012)</td>
</tr>
<tr>
<td>Kaempferol</td>
<td>C_{15}H_{10}O_{6}</td>
<td>(Hamdy et al. 2009; Estevinho et al. 2008; Ku´s et al. 2016)</td>
</tr>
<tr>
<td>Luteolin</td>
<td>C_{15}H_{10}O_{6}</td>
<td>(Akalin et al. 2017; Hamdy et al. 2009)</td>
</tr>
<tr>
<td>Myricetin</td>
<td>C_{15}H_{10}O_{8}</td>
<td>(Biesaga and Pyrzynska 2009; Hamdy et al. 2009)</td>
</tr>
<tr>
<td>Naringenin</td>
<td>C_{15}H_{12}O_{5}</td>
<td>(Akalin et al. 2017; Ku´s et al. 2016)</td>
</tr>
<tr>
<td>Pinocembrin</td>
<td>C_{15}H_{12}O_{4}</td>
<td>(Hamdy et al. 2009; Estevinho et al. 2008; Ku´s et al. 2016)</td>
</tr>
<tr>
<td>Quercetin</td>
<td>C_{15}H_{10}O_{7}</td>
<td>(Hamdy et al. 2009; Petretto et al. 2015)</td>
</tr>
<tr>
<td>Rutin</td>
<td>C_{27}H_{30}O_{16}</td>
<td>(Campillo et al. 2015; Estevinho et al. 2008; Ku´s et al. 2016)</td>
</tr>
<tr>
<td><strong>Phenolic Acids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abscisic acid</td>
<td>C_{15}H_{20}O_{4}</td>
<td>(Biesaga and Pyrzynska 2009; Yaoa et al. 2005)</td>
</tr>
<tr>
<td>Benzoic acid</td>
<td>C_{7}H_{6}O_{2}</td>
<td>(Estepinho et al. 2008; Ku´s et al. 2016; Shahzad et al. 2012)</td>
</tr>
<tr>
<td>Caffeic acid</td>
<td>C_{9}H_{8}O_{1}</td>
<td>(Biesaga and Pyrzynska 2009; Hamdy et al. 2009; Ku´s et al. 2016)</td>
</tr>
<tr>
<td>Chlorogenic acid</td>
<td>C_{16}H_{16}O_{9}</td>
<td>(Biesaga and Pyrzynska 2009; Estevinho et al. 2008; Yaoa et al. 2005)</td>
</tr>
<tr>
<td>Cinnamic acid</td>
<td>C_{9}H_{8}O_{2}</td>
<td>(Campillo et al. 2015; Ku´s et al. 2016; Shahzad et al. 2012)</td>
</tr>
<tr>
<td>Ellagic acid</td>
<td>C_{14}H_{14}O_{8}</td>
<td>(Chan et al. 2013; Hamdy et al. 2009; Yaoa et al. 2005)</td>
</tr>
<tr>
<td>Ferulic acid</td>
<td>C_{10}H_{12}O_{4}</td>
<td>(Campillo et al. 2015; Shahzad et al. 2012)</td>
</tr>
<tr>
<td>Gallic acid</td>
<td>C_{7}H_{6}O_{5}</td>
<td>(Yaoa et al. 2005)</td>
</tr>
<tr>
<td>p-Coumaric acid</td>
<td>C_{7}H_{6}O_{1}</td>
<td>(Estepinho et al. 2008; Ku´s et al. 2016; Shahzad et al. 2012; Yaoa et al. 2005)</td>
</tr>
<tr>
<td>p-Hydroxybenzoic acid</td>
<td>C_{7}H_{6}O_{3}</td>
<td>(Estepinho et al. 2008; Ku´s et al. 2016; Shahzad et al. 2012)</td>
</tr>
<tr>
<td>Protocatechuic acid</td>
<td>C_{7}H_{6}O_{4}</td>
<td>(Chan et al. 2013; Estevinho et al. 2008; Ku´s et al. 2016)</td>
</tr>
<tr>
<td>Sinapic acid</td>
<td>C_{11}H_{12}O_{5}</td>
<td>(Campone et al. 2014; Shahzad et al. 2012)</td>
</tr>
<tr>
<td>Syringic acid</td>
<td>C_{9}H_{10}O_{5}</td>
<td>(Biesaga and Pyrzynska 2009; Hamdy et al. 2009)</td>
</tr>
<tr>
<td>Vanillic acid</td>
<td>C_{8}H_{8}O_{4}</td>
<td>(Biesaga and Pyrzynska 2009; Estevinho et al. 2008; Ku´s et al. 2016)</td>
</tr>
</tbody>
</table>
References:


