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Review

Advances in the Propolis Chemical Composition between 2013 and 2018: A Review

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ABSTRACT

Propolis is a lipophilic sticky substance collected by bees that has been used by humans for centuries. Owing to its healing, antioxidant, and other medicinal properties, its chemical composition has been widely studied. Most pharmacological properties of propolis have been attributed to its phenols and terpenes, mainly flavonoids, phenolic acids, and their derivatives. More than 500 components of propolis were known from different parts of the world until 2012. In this article, 305 new constituents of propolis described between 2013 and 2018 are being reviewed, with 19 additional compounds that were discovered between 2011 and 2012, and were excluded from a similar previous review article. Altogether more than 850 compounds were isolated from propolis until 2018.

1. INTRODUCTION

Propolis or sometimes called "bee glue" is a lipophilic, adhesive, gummy, and resinous substance collected by different species of bees, including honeybees (e.g. *Apis mellifera* L.) and stingless bees (e.g. *Tetragonisca angustula* Illiger). Bees use it to seal holes in their hives, smooth out the internal walls, and protect the entrance against intruders. It also acts as a natural antibiotic to prevent bacterial, viral, or fungal infections within the hive [1–4]. Bees collect the resin from the cracks in the bark and leaf buds of different trees, including different species of poplars, conifers (e.g. pines and cypress), birches, alders, willows, palms, chestnuts, and even trees like eucalyptus, acacia, *Clusia* spp., and *Baccharis dracunculifolia* DC. Bees add salivary enzymes to the collected resin, mix it with beeswax and use this partially digested material in their hives [5–9].

The name propolis derives from the Hellenistic ancient Greek meaning "suburb/bee glue" or "defense of the city", depending on the interpretation [5,10]. The use of propolis dates back to at least 300 BC and has been used by Egyptians, Persians, Greeks, and Romans. It was used mainly as a topical cream for cuts, ulcers, wounds, and other dermatological problems, furthermore it was used for mummification by the Egyptians. However, in medieval times the use of propolis was not very popular. It remained mostly as an alternative herbal medicine, mainly in Eastern Europe, especially in Russia, where it later became known as the "Russian penicillin". The use of propolis was rediscovered again in the Renaissance with the growing popularity of ancient teachings and medicine. The first scientific researches of propolis began in the 19th century with its distillation and were closely connected with the development of chemistry. The first major chemical research was conducted at the beginning of the 20th century with its fractionation. The first isolated constituents from propolis were vanillin, cinnamic acid, and cinnamyl alcohol. Even bigger breakthrough happened at the beginning of 1970s with the advances in chromatographic analytical methods, which enabled isolation of newer and newer components from different propolis samples [10]. By the beginning of 21st century, Marcucci [6] and Bankova et al. [11] registered more than 300 constituents in propolis and just between 2000 and 2012, at least 241 new compounds have been isolated from it. Subsequently, the number of constituents grew to over 500 by 2012 and is growing every year as new components are being discovered in propolis from different regions and plant origins [8]. Despite of the progress in pharmacology, the list of preparations and uses of propolis in today's time is still enormous, mostly because of its antiseptic, bacteriostatic, antibacterial, antimycotic, antiviral, antiprotozoal, antioxidative, spasmolytic, choleric, astringent, anti-inflammatory, anesthetic, antitumor, immunostimulating, cytostatic, hepatoprotective, and other properties [7,12].

Propolis could be typified in several different ways. According to its "gatherers", two main types of propolis are known, the first being "normal" propolis that are collected by honeybees and the second being so-called geopropolis that are collected by stingless bees, which also add soil to their propolis mixtures [5,13]. According to the plant sources, propolis has been classified into seven main types [14], including poplar propolis, which is the most widespread type of propolis (Europe, North America, non-tropical regions of Asia) [11], *Baccharis* or Brazil green propolis [15], *Clusia* or Brazil red propolis [16], eucalyptus propolis [17], *Macaranga* or Taiwanese green propolis [18], birch propolis [19], and Mediterranean propolis [20]. Meanwhile Graikou et al. [9] also classified propolis into seven

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types, but a bit differently: poplar type (Europe, non-tropical parts of Asia, New Zealand, and North America), birch type (Russia), green type (Brazil), red type (Brazil, Cuba, and Mexico), *Clusia* type (Cuba and Venezuela), Pacific or *Macaranga* type (Okinawa prefecture in Japan, Taiwan, and Indonesia), and Mediterranean type (Greece, Sicily, and Malta). Nonetheless, classification of propolis differs among authors as more and more types of propolis of different plant origins are being discovered. For example, Park et al. [21] already described about 12 types of Brazilian propolis; however, a few years later, a new, red Brazilian propolis type was added. From all propolis types, poplar and Brazil green propolis are the most commercially available and widely studied because of their strong pharmacological activities [14].

The composition of propolis is highly dependent on its main plant source and season, as well as of the bee species; however, in general it is composed of 50% plant balsam and resin, 30% bees wax, 10% essential and aromatic oils, 5% pollen, and 5% other organic and inorganic molecules. This is especially true for poplar type propolis [7,10,22,23]. The color of propolis depends on its age and primary plant source and varies from yellow, green to red, and dark brown; there have even been reports about transparent propolis [3]. Its chemical composition is extremely diverse. Until 2012, more than 500 constituents have been recorded in propolis from different plant sources and countries [8] and until 2018 this number grew by at least 305. However, each propolis sample contains approximately 80–100 different constituents [10]. Among those are phenolic acids and esters, many types of flavonoids and other phenolic molecules, terpenes, ketones, aromatic aldehydes and alcohols, proteins, fatty acids, waxy acids, amino acids, steroids, stilbenes, sugars, vitamins (B_1, B_2, B_3, B_5, B_6, C, and E), minerals (at least 35, some only found in traces), and even enzymes (e.g. β-glycosidase) [5,6,8,24–27]. Some groups of compounds, e.g. glycosides, were discovered quite late [28] and some, e.g. alkaloids and tannins, were found only recently [29–31].

Each year, more and more constituents are reported from propolis for the first time, some of them being completely new to science. In this paper, 305 constituents found in propolis for the first time between 2013 and 2018 are being reviewed, with the addition of 19 compounds found between 2011 and 2012 that were not included in Huang et al. [8], a similar review article. The constituents originating from propolis are from different regions and countries around the world, some countries being represented more than once. New constituents were isolated from propolis originating from North America (Mexico and United States), Oceania (Australia 3× and Pitcairn Island), Middle East (Saudi Arabia 2× and Oman), Asia (Thailand 2×, Malaysia 2×, China, Fiji, and Korea), Europe (Portugal, Bulgaria, France, Italy, United Kingdom, and Serbia), South and Middle America (Brazil 6×, Ecuador, Honduras, Bolivia, Chile, and Argentina), and Africa (Cameroon 5×, Algeria 3×, Nigeria 3×, Ghana, Congo, and Egypt). Components isolated from propolis for the first time between 2013 and 2018 (also those missing in Huang et al. [8]) were scouted and summarized from databases including BioMed Central, PubMed, and others, or were found via Google Scholar search engine.

2. PHENOLS AND FLAVONOIDS

Phenols, or sometimes referred to as polyphenols, are one of the most numerous and widely distributed groups of substances in the plant Kingdom. They are products of the secondary metabolism of plants. They can range from simple molecules, such as phenolic acids, to highly polymerized compounds, such as tannins. Their most characteristic feature is their aromatic ring and the alcohol (–OH) group associated with it. Phenols are further divided into at least 18 classes: simple phenols, benzoquinones, phenolic acids, acetophenones, phenylacetic acids, hydroxycinnamic acids, phenylpropenes, coumarins and isocoumarins, chromones, naftoquinones, xanthones, stilbenes, anthraquinones, flavonoids, lignans, neolignans, lignins, and condensed tannins. More than 8000 phenolic structures are known, most of them belong to the subclass of flavonoids (5000) [32,33].

Phenols are also the most abundant constituents in propolis, especially in those of poplar origin. On average, they represent around 28 ± 9% of whole mass of poplar type propolis, of which 8 ± 4% are flavones/flavonols and 6 ± 2% are flavanones/dihydroflavonols. The isolated phenols belong to many different classes of compounds, such as flavonoids, lignans, stilbenes, phenylpropanoids (including different acids), and others, among which flavonoids are the most important molecules in propolis [8,11,34]. Ghisalberti [5] mentioned more than 20 isolated phenols in propolis until the year 1979 and until 1987, at least 59 different phenol constituents have been found in propolis samples [24]). The number rapidly grew and Marcucci [6] reported 100 phenol constituents isolated from propolis until the year 1995. From 1995 to 2000, Bankova et al. [11] reported 40 new phenols and from 2000 to 2012, astounding 184 new phenols have been isolated [8]. Additional six were found in 2011 [35] and thirteen in 2012 [36,37], which were previously not included in Huang et al. [8]. Altogether, at least 330 phenols have been isolated in propolis until the year 2012 and despite those numbers, just between 2013 and 2018, 92 flavonoids (including their glycosides) and altogether 218 new phenols were isolated from propolis, which brings the final number of isolated phenols from propolis to at least 548 until 2018.

From all the constituents, phenols (such as flavonoids, lignans, caffeoylquinic acid derivatives, and hydroxycinnamic acid derivatives) and terpenes are also thought to be the main active molecules of propolis from temperate climates, whereas for the tropical regions and also some Mediterranean regions, the predominant active constituents of propolis are phenols, different from those found in poplar propolis (prenylated ρ-coumaric and cinnamic acids, lignans, stilbenes), and diterpenic acids [1,3,8,9,11,34]. Owing to their abundance and activity, phenols are regarded as the most important constituents of propolis [38,39].

As mentioned, among phenols, flavonoids are the most important propolis constituents, acting as the main biologically active ingredients. They are also used in determining the quality of propolis samples [39]. Walker and Crane [24] reported at least 40 known flavonoids from propolis, whereas Marcucci [6] reported at least 44 in 1995. Bankova et al. [11] mentioned seven newly isolated flavonoids in propolis between 1995 and 2000, but just between 2000 and 2012, an astounding 113 new flavonoids were isolated [8]. Despite high numbers of already isolated flavonoids, 92 (including their glycosides) were discovered in propolis for the first time between 2013 and 2018. According to their chemical structure, isolated flavonoids are classified into 11 subclasses: flavans, isoflavans, flavanones, flavanonols, flavones, isoflavones, isodihydroflavones, flavonols, chalcones, dihydrochalcones, and

neoflavonoids (Figure 1). Besides flavonoids, their glycosides are also being discovered in propolis, although until 2012 they were considered very rare. Only two flavonoid glycosides were isolated from propolis until 2009 and until 2012 their number grew only by one [8,40]. Yet in the past 6 years, 57 flavonoid glycosides were isolated from propolis for the first time, making flavonoid glycosides an important group of compounds in propolis samples. In 2004, some speculations were made that propolis samples could also contain anthocyanidins, although they have yet to be reported in propolis [41].

Among the 92 newly isolated flavonoids, their glycosides (57) are one of the biggest discoveries in the recent years because of their earlier rarity. They were isolated from European (Serbia, United Kingdom, and Portugal) and South American (Brazil) samples. Some other new flavonoid compounds were also isolated from Middle East (Oman and Saudi Arabia), Europe (France and Serbia), Asia (Thailand, Korea, and Fiji), Middle and South America (Ecuador, Argentina, and Brazil), and Africa (Algeria, Congo, Cameroon, and Nigeria). The newly isolated flavonoids are listed in Table 1.

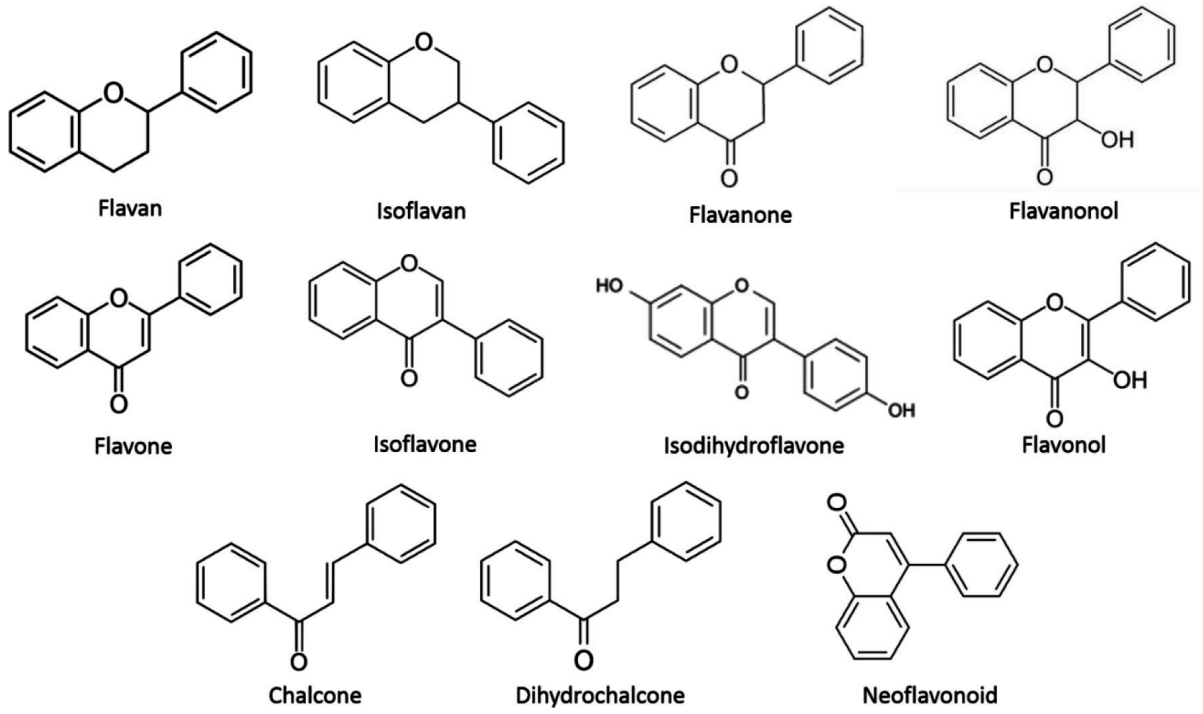

Figure 1 | Flavonoid groups/classes isolated from different propolis samples around the world.

Table 1 | Flavonoids identified in propolis for the first time since 2011

No.	Chemical name	Geographic location	References
Flavans			
1	Fisetinidol[a]	Oman	Popova et al. [42]
2	2,3-*trans*-3,4-*trans* Mollisacacidin[a]	Oman	Popova et al. [42]
3	2,3-*trans*-3,4-*cis* Mollisacacidin[a]	Oman	Popova et al. [42]
4	3,4-Dihydro-2-(3,4-dihydroxyphenyl)-2*H*-chromene-3,7-diol[a,1]	Saudi Arabia	Almutairi et al. [43]
5	8-[*E*-phenylprop-2-en-1-on]-5-methoxy-(±)-catechin[a,1]	France	Boisard et al. [44]
Flavanones			
6	8-[1-(4′-Hydroxy-3′-methoxyphenyl)prop-2-en-1-yl]-(2*S*)-pinocembrin[a,1]	Thailand	Athikomkulchai et al. [45]
7	5,4′-Dihydroxy-7,3′-dimethoxyflavanone[a]	Ecuador	Cuesta-Rubio et al. [46]
8	Mepuberin[b]	Brazil	Cisilotto et al. [47]
Flavanonols			
9	Pinobanksin 3-(*E*)-caffeate[a]	Algeria	Piccinelli et al. [48]
10	3,5,4′-Trihydroxy-7,3′-dimethoxy flavanonol[a]	Ecuador	Cuesta-Rubio et al. [46]
Flavones			
11	Psiadiarabin[a]	Saudi Arabia	Almutairi et al. [43]
12	Tangeritin[a]	Serbia	Ristivojević et al. [49]
13	5,7-Dihydroxy-6,4′-dimethoxyflavone (pectolinarigenin)[a]	Algeria	Segueni et al. [50]
14	6,7-Dihydroxy-7,4′-dimethoxyflavone (ladanein)[a]	Algeria	Segueni et al. [50]
15	5,7-Dihydroxy-2-(3,4-dihydroxyphenoxy)-4*H*-chromen-4-one (2-phenoxychromone)[a,1]	Brazil	Mitsui et al. [51]

(*Continued*)

Table 1 | Flavonoids identified in propolis for the first time since 2011—*Continued*

No.	Chemical name	Geographic location	References
Flavonoles			
16	Pinobanksin-*O*-hexenoate[a]	Portugal	Falcão et al. [52]
17	3,5,3′,4′-Tetrahydroxy-6,7-dimethoxy flavone (eupatolitin)[a]	Ecuador	Cuesta-Rubio et al. [46]
Chalcones			
18	(*E*)-4′-metoxy-4,2′-dihidroxy-3′-(2″,3″-dihydroxy-3″-methylbutyl)-chalcone (Jejuchalcone A)[a,1]	Korea	Shimomura et al. [53]
19	(*E,E,E*)-4,2′,4′-trihydroxy-3′-(7″-hydroxy-3″,7″-dimethyloct-2″,5″-dienyl)-chalcone (Jejuchalcone B)[a,1]	Korea	Shimomura et al. [53]
20	(*E,E*)-4,2′,4′-trihydroxy-3′-(5″-hydroxy-3″,7″-dimethyloct-2″,6″-dienyl)-chalcone (Jejuchalcone C)[a,1]	Korea	Shimomura et al. [53]
21	(*E*)-4′-metoxy-4,3″,4″-trihydroxy-2″,2″-dimethyldihydropyrano-(2′,3′)-chalcone (Jejuchalcone D)[a,1]	Korea	Shimomura et al. [53]
22	(*E*)-4′-metoxy-4,3″-dihidroxy-2″-(1‴-hydroxyisopropyl)-dihydrofurano-(2′,3′)-chalcone (Jejuchalcone E)[a,1]	Korea	Shimomura et al. [53]
23	(*E*)-4,4′-dihydroxy-2″-(1‴-hidroxy-1‴,5‴-dimethylhex-4‴–enyl)-dihydrofurano-(2′,3′)-chalcone ((−)-Jejuchalcone F)[a,1]	Korea	Shimomura et al. [53]
24	(*E*)-4,2′-dihydroxy-2″-methyl-2″-(3‴,4‴-dihydroxy-4‴-methylpentanyl)-2*H*-pyrano-(3′,4′)-chalcone ((+)-Jejuchalcone G)[a,1]	Korea	Shimomura et al. [53]
25	(−)-(*E*)-4,2′-dihydroxy-2″-methyl-2″-(3‴,4‴-dihydroxy-4‴-methylpentanyl)-2*H*-pyrano-(3′,4′)-chalcone ((−)-Jejuchalcone H)[a,1]	Korea	Shimomura et al. [53]
Flavonoid glycosides			
26	Quercetin-3-*O*-glucuronide[a]	Portugal	Falcão et al. [52]
27	Quercetin-3-*O*-glucoside[a]	Portugal	Falcão et al. [52]
28	Kaempferol-3-*O*-rutinoside[a]	Portugal	Falcão et al. [52]
29	Isorhamnetin-*O*-pentoside[a]	Portugal	Falcão et al. [52]
30	Quercetin-3-*O*-rhamnoside[a]	Portugal	Falcão et al. [52]
31	Isorhamnetin-*O*-glucuronide[a]	Portugal	Falcão et al. [52]
32	Kaempferol-methyl ether-*O*-glucoside[a]	Portugal	Falcão et al. [52]
33	Isorhamnetin-*O*-acetylrutinoside[a]	Portugal	Falcão et al. [52]
34	Rhamnetin-*O*-glucuronide[a]	Portugal	Falcão et al. [52]
35	Quercetin-dimethyl ether-*O*-rutinoside[a]	Portugal	Falcão et al. [52]
36	Quercetin-dimethyl ether-*O*-glucuronide[a]	Portugal	Falcão et al. [52]
37	Kaempferol-*O*-*ρ*-coumaroylrhamnoside[a]	Portugal	Falcão et al. [52]
38	Caffeic acid 4-*O*-glucoside[a]	Brazil	Righi et al. [54]
39	Caffeic acid 4-*O*-arabinoside[a]	Brazil	Righi et al. [54]
40	Caffeic acid 4-*O*-xyloside[a]	Brazil	Righi et al. [54]
41	Dimethoxy-luteolin-glucoside[a]	Brazil	Righi et al. [54]
42	Methylkaempferol-*O*-rutinoside[a]	Brazil	Righi et al. [54]
43	Naringenin-*C*-glucoside[a]	Brazil	Righi et al. [54]
44	Apigenin-*O*-rutinoside[a]	Brazil	Righi et al. [54]
45	Delphinidin arabinoside[a]	Brazil	Righi et al. [54]
46	Catechin arabinoside[a]	Brazil	Righi et al. [54]
47	Apigenin-di-*C*-glucosyl rhamnoside[a]	Brazil	Righi et al. [54]
48	Apigenin-*C*-rhamnoside (isomer 1)[*,a]	Brazil	Righi et al. [54]
49	Apigenin-6,8-di-*C*-glucoside (vicenin-2)[a]	Brazil	Righi et al. [54]
50	Apigenin-*C*-rhamnosyl arabinoside[a]	Brazil	Righi et al. [54]
51	Apigenin-6-*C*-glucosyl-8-*C*-arabinose (isoschaftoside)[a]	Brazil	Righi et al. [54]
52	Luteolin-*O*-glucuronide[a]	Brazil	Righi et al. [54]
53	Apigenin-8-*C*-glucosyl-6-*C*-arabinose (schaftoside)[a]	Brazil	Righi et al. [54]
54	Luteolin-6,8-di-*C*-glucoside (lucenin-2)[a]	Brazil	Righi et al. [54]
55	Apigenin-*C*-rhamnoside (isomer 2)[a,*]	Brazil	Righi et al. [54]
56	Luteolin acetylglucoside[a]	Brazil	Righi et al. [54]
57	Chrysoeriol-*C*-glucoside[a]	Brazil	Righi et al. [54]
58	Dimethoxy naringenin-diglucoside[a]	Brazil	Righi et al. [54]
59	Apigenin-di-*O*-glucoside[a]	Brazil	Righi et al. [54]
60	Quercetin-*O*-arabinoside[a]	Brazil	Righi et al. [54]
61	Isorhamnetin-glucoside[a]	Brazil	Righi et al. [54]
62	Apigenin-*O*-glucuronide[a]	Brazil	Righi et al. [54]
63	Naringenin-4′-*O*-*β*-glucopyranoside[b]	Brazil	Da Silva et al. [55]
64	Myricetin-3-*O*-*β*-glucopyranoside[b]	Brazil	Da Silva et al. [55]
65	Chrysin glycoside formate adduct[a,*]	United Kingdom	Saleh et al. [56]
66	Galangin glycoside[a,*]	United Kingdom	Saleh et al. [56]

(*Continued*)

Table 1 | Flavonoids identified in propolis for the first time since 2011—*Continued*

No.	Chemical name	Geographic location	References
67	7-Methoxy-5-hydroxy-8-*C*-flavone rhamnoside[b]	Brazil	Coelho et al. [57]
68	Acacetin-di-*C*-acetyl dirhamnoside[b]	Brazil	Coelho et al. [57]
69	Apigenin-6,8-di-*C*-malonyl glucoside dihexoside (isomer 1)[b,*]	Brazil	Coelho et al. [57]
70	Apigenin-6,8-di-*C*-malonyl glucoside dihexoside (isomer 2)[b,*]	Brazil	Coelho et al. [57]
71	Apigenin-di-*C*-malonyl trihexoside (isomer 1)[b,*]	Brazil	Coelho et al. [57]
72	Acacetin-di-*C*-malonyl trihexoside[b,*]	Brazil	Coelho et al. [57]
73	Apigenin-di-*C*-malonyl trihexoside (isomer 2)[b,*]	Brazil	Coelho et al. [57]
74	Acacetin-8-*C*-arabinoside-7-*O*-rhamnoside[b]	Brazil	Coelho et al. [57]
75	Apigenin-di-*C*-malonyl trihexoside (isomer 3)[b,*]	Brazil	Coelho et al. [57]
76	Catechin rhamnoside[b]	Brazil	Coelho et al. [57]
77	Chrysin-8-*C*-rhamnoside-7-*O*-rhamnoside[b]	Brazil	Coelho et al. [57]
78	Luteolin-8-*C*-caffeoyl rhamnoside[b]	Brazil	Coelho et al. [57]
79	Caffeoylquinic acid-*O*-arabinoside[b]	Brazil	Coelho et al. [57]
80	Apigenin-7-*O*-glucoside (apigetrin)[a]	Serbia	Ristivojević et al. [49]
81	Apigenin 8-*C*-xyloside-6-*C*-glucoside (vicenin 3)[b]	Brazil	Cisilotto et al. [47]
82	Apigenin 6-*C*-xyloside-8-*C*-glucoside (vicenin 1)[b]	Brazil	Cisilotto et al. [47]
Prenylated flavonoids			
83	7-*O*-methyl-8-prenylnaringenin[a]	Oman	Popova et al. [42]
84	3′,8-Diprenylnaringenin[a]	Oman	Popova et al. [42]
85	8-Prenyl-5,7-dihydroxy-3′-(3-hydroxy-3-methylbuthyl)-4′-methoxyflavanone[a]	Oman	Popova et al. [42]
86	Lonchocarpol A[a]	Congo and Cameroon	Papachroni et al. [58]
87	6,8-Diprenyl-eriodictyol[a]	Congo	Papachroni et al. [58]
88	6,8-Diprenyl-aromadendrin[a]	Cameroon	Papachroni et al. [58]
89	Lespedezaflavanone[a]	Cameroon	Papachroni et al. [58]
90	Glyasperin A[a]	Fiji	Trusheva et al. [59]
91	8-Prenylnaringenin[a]	Nigeria	Omar et al. [60]
92	6-Prenylnaringenin[a]	Nigeria	Omar et al. [60]

[*]The molecular structure of the compound is not completely defined. [a]Constituent isolated from the honeybee propolis (from the genus *Apis* sp.). [b]Constituent isolated from the stingless bee propolis (from genera *Scaptotrigona* sp. or *Melipona* sp.). [1]Newly discovered compound. Compounds already mentioned in Huang et al. [8] are excluded.

Among other 126 isolated "non-flavonoid" phenols, compounds from stilbenes and phenolic acids groups were the most abundant. Five of the isolated phenols were found in 2011 [35], whereas one phenolic acid ester [36] and twelve phenylpropanoids [37] were isolated in 2012. All of them are included in this review as they were excluded from the previous review article [8]. Otherwise, phenols were isolated from propolis from Europe (Italy, Portugal, Serbia, and United Kingdom), South and Middle America (Chile, Honduras, Brazil, and Argentina), Africa (Egypt, Nigeria, Ghana, Algeria, and Cameroon), Asia (Thailand, Fiji, China, and Malaysia), Middle East (Saudi Arabia), Oceania (Australia), and North America (United States and Mexico). The phenols are listed in Table 2.

Table 2 | Phenolic compounds identified in propolis for the first time since 2011

No.	Chemical name	Geographic location	References
Phenolic glycerides			
93	Caffeoyl glycerol[a]	Serbia	Ristivojević et al. [49]
94	Tricoumaroyl glycerol[a]	Serbia	Ristivojević et al. [49]
95	Coumaroyl feruloyl glycerol (isomer 1)[a,*]	Serbia	Ristivojević et al. [49]
96	Coumaroyl feruloyl glycerol (isomer 2)[a,*]	Serbia	Ristivojević et al. [49]
97	Dicaffeoyl coumaroyl glycerol[a]	Serbia	Ristivojević et al. [49]
98	Dicaffeoyl feruloyl glycerol[a]	Serbia	Ristivojević et al. [49]
Phenolic acid esters			
99	(*E*)-cinnamyl-(*Z*)-cinnamate[a,1]	Honduras	Lotti et al. [36]
100	Decyl caffeate[a]	Egypt	El-Hady et al. [61]
101	Caffeic acid phenacetyl ester[a,*]	United Kingdom	Saleh et al. [56]
102	Caffeic acid sesquiterpene ester (isomer 1)[a,*]	United Kingdom	Saleh et al. [56]
103	Caffeic acid sesquiterpene ester[a,*]	United Kingdom	Saleh et al. [56]
104	Methylgalangin hydroxypropionyl ester[a,*]	United Kingdom	Saleh et al. [56]
105	Caffeic acid monoterpene(geranyl) ester[a,*]	United Kingdom	Saleh et al. [56]
106	Methyl methylene dioxy kaempferol hexanoyl ester (isomer 1)[a,*]	United Kingdom	Saleh et al. [56]
107	Methyl methylene dioxy kaempferol hexanoyl ester (isomer 2)[a,*]	United Kingdom	Saleh et al. [56]
108	Caffeic acid sesquiterpene ester (isomer 2)[a,*]	United Kingdom	Saleh et al. [56]
Xanthones			
109	α-Mangostin[b]	Thailand	Sanpa et al. [4]

(*Continued*)

Table 2 | Phenolic compounds identified in propolis for the first time since 2011—*Continued*

No.	Chemical name	Geographic location	References
110	γ-Mangostin[b]	Thailand	Sanpa et al. [4]
111	Mangostanin[b]	Thailand	Sanpa et al. [4]
112	8-Deoxygartanin[b]	Thailand	Sanpa et al. [4]
113	Gartanin[b]	Thailand	Sanpa et al. [4]
114	Garcinone B[b]	Thailand	Sanpa et al. [4]
115	Furofuran lignan methylpinoresinol[b]	Thailand	Sanpa et al. [4]
Phenylpropanoids			
116	2-Acetyl-1-feruloyl-3-caffeoylglycerol[a,1]	China	Shi et al. [37]
117	(+)-2-Acetyl-1-caffeoyl-3-cinnamoylglycerol[a,1]	China	Shi et al. [37]
118	(−)-2-Acetyl-1-caffeoyl-3-cinnamoylglycerol[a,1]	China	Shi et al. [37]
119	(+)-2-Acetyl-1-(*E*)-coumaroyl-3-(*E*)-cinnamoylglycerol[a,1]	China	Shi et al. [37]
120	(+)-2-Acetyl-1-(*E*)-feruloyl-3-(*E*)-cinnamoylglycerol[a,1]	China	Shi et al. [37]
121	(−)-2-Acetyl-1-(*E*)-feruloyl-3-(*E*)-cinnamoylglycerol[a,1]	China	Shi et al. [37]
122	2-Acetyl-1,3-dicinnamoylglycerol[a,1]	China	Shi et al. [37]
123	(−)-2-Acetyl-1-(*E*)-cinnamoyl-3-(3″(ζ),16″)-dihydroxy-palmitoylglycerol[a,1]	China	Shi et al. [37]
124	2-Acetyl-1,3-dicaffeoylglycerol[a]	China	Shi et al. [37]
125	2-Acetyl-1-caffeoyl-3-coumaroylglycerol[a]	China	Shi et al. [37]
126	2-Acetyl-1-feruloyl-3-coumaroylglycerol[a]	China	Shi et al. [37]
127	2-Acetyl-1,3-diferuloylglycerol[a]	China	Shi et al. [37]
128	6-*O*-*p*-coumaroyl-*D*-galactopyranose[b,1]	Brazil	De Souza et al. [13]
129	6-*O*-cinnamoyl-1-*O*-*p*-coumaroyl-β-*D*-glucopyranose[b]	Brazil	De Souza et al. [13]
130	Dicoumaroyl glycero[a,*]	United Kingdom	Saleh et al. [56]
131	Acetylcoumaroyl glycerol[a,*]	United Kingdom	Saleh et al. [56]
132	Boropinic acid[a]	Italy	Taddeo et al. [62]
133	4′-Geranyloxyferulic acid[a]	Italy	Taddeo et al. [62]
134	7-Isopentenyloxycoumarin[a]	Italy	Taddeo et al. [62]
135	Auraptene[a]	Italy	Taddeo et al. [62]
Phenylpropanoid glycosides			
136	Scopolin[a]	Algeria	Soltani et al. [31]
Phenolic glycosides			
137	Torachrysone-*O*-hexose[b,*]	Malaysia	Zhao et al. [63]
138	Torachrysone-*O*-(acetyl)-hexose[b,*]	Malaysia	Zhao et al. [63]
139	Torachrysone-*O*-(galloyl)-hexose[b,*]	Malaysia	Zhao et al. [63]
140	Gallic acid-hexose[b,*]	Malaysia	Zhao et al. [63]
Stilbenes			
141	(*E*)-4-(3-methyl-2-buten-1-yl)-3,4′,5-trihydroxy-3′-methoxystilbene[a,1]	Australia	Duke et al. [64]
142	(*E*)-2-(3-methyl-2-buten-1-yl)-3,4′,5-trihydroxystilbene (2-prenylresveratrol)[a]	Australia	Duke et al. [64]
143	(*E*)-2,4-bis(3-methyl-2-buten-1-yl)-3,3′,4′,5-tetrahydroxystilbene[a,1]	Australia	Duke et al. [64]
144	(*E*)-2-(3-methyl-2-buten-1-yl)-3-(3-methyl-2-butenyloxy)-3′,4′,5-trihydroxystilbene[a,1]	Australia	Duke et al. [64]
145	(*E*)-2,6-bis(3-methyl-2-buten-1-yl)-3,3′,5,5′-tetrahydroxystilbene[a,1]	Australia	Duke et al. [64]
146	(*E*)-2,6-bis-(3-methyl-2-buten-1-yl)-3,4′,5-trihydroxy-3′-methoxystilbene[a,1]	Australia	Duke et al. [64]
147	(*E*)-5-(2-(8-hydroxy-2-methyl-2-(4-methylpent-3-en-1-yl)-2*H*-chromen-6-yl) vinyl)-2-(3-methylbut-2-en-1-yl)benzene-1,3-diol[a,1]	Ghana	Almutairi et al. [65]
148	5-((*E*)-3,5-dihydroxystyryl)-3-((*E*)-3,7-dimethylocta-2,6-dien-1-yl)benzene-1,2-diol[a,1]	Ghana	Almutairi et al. [65]
149	Schweinfurthin C[a]	Nigeria	Zhang et al. [66]
150	Mappain[a]	Nigeria	Zhang et al. [66]
151	Geranyl stilbenoid[a,*]	Nigeria	Zhang et al. [66]
152	Solomonin B[a,1]	Fiji	Trusheva et al. [59]
153	Solomonin C[a,1]	Fiji	Trusheva et al. [59]
Lignans			
154	Meso-(rel 7S,8S,7′R,8′R)-3,4,3′,4′-tetrahydroxy-7,7′-epoxylignan[a]	Argentina	Agüero et al. [35]
155	(7S,8S,7′S,8′S)-3,3′,4′-trihydroxy-4-methoxy-7,7′-epoxylignan[a]	Argentina	Agüero et al. [35]
Phenolic acids			
156	Caffeic acid derivative 1[a,*]	Portugal	Falcão et al. [52]
157	Caffeic acid derivative 1 (isomer)[a,*]	Portugal	Falcão et al. [52]
158	Caffeic acid derivative 2[a,*]	Portugal	Falcão et al. [52]
159	Ferulic acid derivative[a,*]	Portugal	Falcão et al. [52]
160	Sandaracopimaric acid[a]	Saudi Arabia	Jerz et al. [67]
161	(*E*)-3-hydroxy-1,7-diphenylhept-1-ene-5-acetate[a]	Chile	Nina et al. [68]
162	(*E*)-5-hydroxy-1,7-diphenylhept-1-ene-3-acetate[a]	Chile	Nina et al. [68]

(*Continued*)

Table 2 | Phenolic compounds identified in propolis for the first time since 2011—*Continued*

No.	Chemical name	Geographic location	References
163	Caffeic acid hextrieneoate[a,*]	United Kingdom	Saleh et al. [56]
164	Benzoyl dihydroxyphenylpropionic acid[a,*]	United Kingdom	Saleh et al. [56]
165	Benzoyl hydroxyphenylacetic acid[a,*]	United Kingdom	Saleh et al. [56]
166	Hydroxy phenyl acetyl dihydroxyphenylacetic acid[a,*]	United Kingdom	Saleh et al. [56]
167	Pinobanksin phenyl propionate (isomer 1)[a,*]	United Kingdom	Saleh et al. [56]
168	Dimethyl pinocembrin benzoate[a,*]	United Kingdom	Saleh et al. [56]
169	Pentenoyl hydroxyphenylpropionic acid[a,*]	United Kingdom	Saleh et al. [56]
170	Pinobanksin phenyl propionate (isomer 2)[a,*]	United Kingdom	Saleh et al. [56]
171	Pinobanksin benzoate[a,*]	United Kingdom	Saleh et al. [56]
172	Pinobanksin phenyl propionate (isomer 3)[a,*]	United Kingdom	Saleh et al. [56]
173	Methyl pinobanksin acetate[a,*]	United Kingdom	Saleh et al. [56]
174	Pinobanksin caffeate[a,*]	United Kingdom	Saleh et al. [56]
175	Caffeoyldimethyl pinocembrin[a,*]	United Kingdom	Saleh et al. [56]
176	Methyl chrysin acetate derivative[a,*]	United Kingdom	Saleh et al. [56]
177	Pinobanksin dimethyl cinnamate[a,*]	United Kingdom	Saleh et al. [56]
178	(4*R*,5*R*,9*R*,10*R*)-13-hydroxypodocarp-8(14)-en-19-oic acid[b]	Brazil	Cisilotto et al. [47]
Other phenols			
179	Nordihydroguaiaretic acid[a]	Argentina	Agüero et al. [35]
180	3′-Methyl-nordihydroguaiaretic acid[a]	Argentina	Agüero et al. [35]
181	4′-Methyl-nordihydroguaiaretic acid[a]	Argentina	Agüero et al. [35]
182	(*E*)-cinnamyl-(*E*)-cinnamylidenate[a,1]	Thailand	Athikomkulchai et al. [45]
183	Kaempferol-dimethyl ether[a]	Portugal	Falcão et al. [52]
184	5-Hexadecylresorcinol[a]	Cameroon	Kardar et al. [69]
185	5-(10′*Z*-pentadecenyl)-resorcinol[a]	Cameroon	Kardar et al. [69]
186	5-(12′*Z*-heptadecenyl)-resorcinol[a]	Cameroon	Kardar et al. [69]
187	5-(14′*Z*-heptadecenyl)-resorcinol[a,1]	Cameroon	Kardar et al. [69]
188	5-(14′*Z*-nonadecenyl)-resorcinol[a]	Cameroon	Kardar et al. [69]
189	3-Undecyl phenol[a]	Cameroon	Kardar et al. [69]
190	3-Tetradecylphenol[a]	Cameroon	Kardar et al. [69]
191	3-Pentadecylphenol[a]	Cameroon	Kardar et al. [69]
192	3-Hexadecylphenol[a]	Cameroon	Kardar et al. [69]
193	3-Heptadecylphenol[a]	Cameroon	Kardar et al. [69]
194	3-Nonadecylphenol[a]	Cameroon	Kardar et al. [69]
195	3-(10′*Z*-pentadecenyl)-phenol[a]	Cameroon	Kardar et al. [69]
196	3-(12′*Z*-pentadecenyl)-phenol[a,1]	Cameroon	Kardar et al. [69]
197	3-(8′*Z*-heptadecenyl)-phenol[a]	Cameroon	Kardar et al. [69]
198	3-(12′*Z*-heptadecenyl)-phenol[a]	Cameroon	Kardar et al. [69]
199	3-(14′*Z*-heptadecenyl)-phenol[a]	Cameroon	Kardar et al. [69]
200	3-(13′*Z*-nonadecenyl)-phenol[a,1]	Cameroon	Kardar et al. [69]
201	3-(14′*Z*-nonadecenyl)-phenol[a,1]	Cameroon	Kardar et al. [69]
202	Deperoxidized derivative of plukenetione C[a,1]	Cameroon	Almutairi et al. [65]
203	1,3-Dihydroxy-5-heptadecenylbenzene[a]	Egypt	El-Hady et al. [61]
204	1,3-Dihydroxy-5-heptadecylbenzene (C17:0) derivate[a]	Egypt	El-Hady et al. [61]
205	1,3-Dihydroxy-5-heptadecenylbenzene (C19:1) derivate[a]	Egypt	El-Hady et al. [61]
206	(*E*)-4-(3′-ethoxyprop-1′-enyl)phenol (Ethyl *p*-coumaroyl ether)[a]	United States	Savka et al. [70]
207	Coumaric acid cinnamyl ether[a,*]	United Kingdom	Saleh et al. [56]
208	Dimethyl kaempferol phenethyl ether[a,*]	United Kingdom	Saleh et al. [56]
209	Dihydroxy propionyl pinocembrin methyl ether[a,*]	United Kingdom	Saleh et al. [56]
210	Pinocembrin methyl ether (isomer 1)[a,*]	United Kingdom	Saleh et al. [56]
211	Dimethyl galangin phenacetyl ether[a,*]	United Kingdom	Saleh et al. [56]
212	Pinocembrin methyl ether (isomer 2)[a,*]	United Kingdom	Saleh et al. [56]
213	Hexadieneoyl dimethyl pinobanksin[a,*]	United Kingdom	Saleh et al. [56]
214	Pinobanksin-5-methylether-3-*O*-propanoate[a]	Mexico	Alday et al. [71]
215	Pinobanksin-5-methylether-3-*O*-butyrate[a]	Mexico	Alday et al. [71]
216	Tetragocarbone A[b,1]	Australia	Nishimura et al. [72]
217	Tetragocarbone B[b,1]	Australia	Nishimura et al. [72]
218	3-(2-Hydroxy-4-methoxybenzyl)-6-methoxy-2,3-dihydrobenzofuran (Riverinol)[a,1]	Nigeria	Omar et al. [60]

[*]The molecular structure of the compound is not completely defined. [a]Constituent isolated from the honeybee propolis (from the genus *Apis* sp.). [b]Constituent isolated from the stingless bee propolis (from genera *Scaptotrigona* sp., *Melipona* sp., *Tetragonula* sp., *Trigona* sp., *Tetrigona* sp., or. *Heterotrigona* sp.). [1]Newly discovered compound. Compounds already mentioned in Huang et al. [8] are excluded.

2.1. Terpenoids

Terpenes and terpenoids are the biggest and most diverse group of secondary plant metabolites, which include more than 25,000 compounds. They are molecules composed from one or more isoprene (C_5) units. Term terpene refers to a hydrocarbon molecule, whereas term terpenoid refers to hydrocarbon molecule that has been modified (e.g., addition of oxygen). Terpenes are further divided into seven classes: hemiterpenes (C_5), monoterpenes (C_{10}), sesquiterpenes (C_{15}), diterpenes (C_{20}), triterpenes (C_{30}), tetraterpenes (C_{40}), and polyterpenes (C_{45} or more) [73]. They are the second biggest and most important group of compounds and also the most abundant volatile components of propolis [74]. As mentioned before, they are one of the main biologically active substances in propolis and they play a major role in determining its quality. Terpenes were found mainly in tropical propolis, being rarer in poplar propolis type, yet some of them were also isolated from the Mediterranean propolis. Sesquiterpenes are the main group of terpenes found in propolis and are further divided into acyclic, monocyclic, dicyclic, and tricyclic sesquiterpenes. Other important terpenes from propolis are monoterpenes, triterpenes, and diterpenes, latter being the most important terpene from the pharmacological point of view [8,20,40,75].

Walker and Crane [24] mentioned 18 isolated terpenoids from propolis and Marcucci [6] added another 11. Between 2000 and 2012 Huang et al. [8] reported 58 terpenoids isolated from propolis for the first time, whereas between 2013 and 2018 another 46 were reported. In total, at least 133 terpenes were isolated from propolis until 2018. Terpenes isolated between 2013 and 2018 were found in propolis samples from Africa (Cameroon, Algeria, Egypt, and Nigeria), Asia (Malaysia and Thailand), South America (Chile, Brazil, and Bolivia), Middle East (Saudi Arabia), and Oceania (Australia and Pitcairn Island). Otherwise, most of the newly isolated terpenoids after 2013 belong to the group of triterpenes. Newly isolated terpenoids are listed in Table 3.

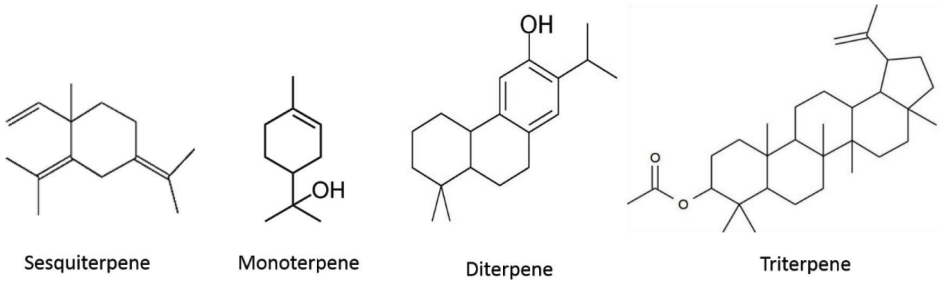

Figure 2 | Terpenoid groups/classes isolated from different propolis samples around the world.

Table 3 | Terpenoids identified in propolis for the first time since 2011

No.	Chemical name	Geographic location	References
Monoterpenes			
219	1,8-Terpineol[a,*]	Cameroon	Papachroni et al. [58]
Sesquiterpenes			
220	*β*-Panasinsene[a]	Malaysia	Tuan et al. [76]
Diterpenes			
221	Cistadiol[a]	Algeria	Piccinelli et al. [48]
222	18-Hydroxy-*cis*-clerodan-3-ene-15-oic acid[a]	Algeria	Piccinelli et al. [48]
223	Propsiadin ((ent)-2-oxo-kaur-16-en-6,18-diol)[a,1]	Saudi Arabia	Almutairi et al. [43]
224	Psiadin[a]	Saudi Arabia	Almutairi et al. [43]
225	Poilaneic acid[a]	Chile	Nina et al. [68]
226	7,8,18-Trihydroxyserrulat-14-ene[a,1]	Australia	Aminimoghadamfarouj and Nematollahi [75]
227	5,18-Epoxyserrulat-14-en-7,8-dione[a,1]	Australia	Aminimoghadamfarouj and Nematollahi [75]
228	(18*RS*)-5,18-epoxyserrulat-14-en-8,18-diol[a]	Australia	Aminimoghadamfarouj and Nematollahi [75]
229	*rel*-(5*S*,6*S*,8*R*,9*R*,10*S*,18*R*,19*S*)-18,19-epoxy-2-oxocleroda-3,12(*E*),14-triene-6,18,19-triol 18,19-diacetate 6-benzoate[a,1]	Brazil	Tazawa et al. [77]
230	Abietinal[a]	Pitcairn Island	Georgieva et al. [78]
Triterpenes			
231	3*β*-Acetoxy-19(29)-taraxasten-20*α*-ol[a]	Saudi Arabia	Jerz et al. [67]
232	Pseudotaraxasterol-3*β*-*O*-acetate[a]	Saudi Arabia	Jerz et al. [67]
233	*β*-Sitosterol[a]	Nigeria	Odiba et al. [79]
234	25-Cyclopropyl-3*β*-hydroxyurs-12-ene[a,1]	Cameroon	Sakava et al. [80]
235	Cycloart-3*β*-hydroxy-12,25(26)-diene[a,1]	Cameroon	Sakava et al. [80]
236	Lup-20(29)-en-3*β*-oate[a]	Cameroon	Sakava et al. [80]
237	Olean-12-en-3*β*,28-diol (erythrodiol)[a]	Cameroon	Sakava et al. [80]
238	*ψ*-Teraxasterol-acetate[a]	Cameroon	Papachroni et al. [58]

(*Continued*)

Table 3 | Terpenoids identified in propolis for the first time since 2011—*Continued*

No.	Chemical name	Geographic location	References
239	Taraxasterol acetate[a]	Cameroon	Papachroni et al. [58]
240	3α-Hydroxy-olean-12-en-30-ol[a]	Cameroon	Papachroni et al. [58]
241	Bacchara-12,21-dien-3β-ol[a]	Cameroon	Papachroni et al. [58]
242	Betulinaldehyde[a]	Cameroon	Papachroni et al. [58]
243	4,4-Dimethyl-3-oxacholest-5-en-7-one[a,1]	Egypt	El-Hady et al. [61]
244	9,19-Cyclolanostan-3-ol-24-methylene acetate[a,1]	Egypt	El-Hady et al. [61]
245	Dipterocarpol[b]	Thailand	Sanpa et al. [4]
246	3-*O*-acetyl ursolic acid[b]	Thailand	Sanpa et al. [4]
247	Ocotillone I[b]	Thailand	Sanpa et al. [4]
248	Ocotillone II[b]	Thailand	Sanpa et al. [4]
249	Cabralealactone (isomer 1)[b]	Thailand	Sanpa et al. [4]
250	Cabralealactone (isomer 2)[b]	Thailand	Sanpa et al. [4]
251	Ursolic aldehyde[b]	Thailand	Sanpa et al. [4]
252	Oleanolic aldehyde[b]	Thailand	Sanpa et al. [4]
253	Cycloart-24-en-3β,26-diol[a]	Bolivia	Nina et al. [81]
254	Cycloart-24-en-3-one[a]	Bolivia	Nina et al. [81]
255	24(*E*)-cycloart-24-en-26-ol-3-one[a]	Bolivia	Nina et al. [81]
256	Mangiferonic acid methyl ester[a]	Bolivia	Nina et al. [81]
257	Lup-20(29)-en-3-one[a]	Bolivia	Nina et al. [81]
258	Methyl-3β,27-dihydroxycycloart-24-en-26-oate[a,1]	Cameroon	Talla et al. [81]
259	20-Hydroxy-24-dammaren-3-one[b]	Malaysia	Zhao et al. [63]
260	3-Oxo-cycloart-24*E*-en-21,26-diol-21,26-diacetate[a,1]	Pitcairn Island	Georgieva et al. [78]
261	3-Oxo-cycloart-24*E*-en-21,26-diol[a,1]	Pitcairn Island	Georgieva et al. [78]
262	3-Oxo-cycloart-24*E*-en-21,26-diol-21-acetate[a,1]	Pitcairn Island	Georgieva et al. [78]
263	3-Oxo-cycloart-24E-en-21,26-diol-26-acetate[a,1]	Pitcairn Island	Georgieva et al. [78]
264	3-Oxo-cycloart-24-en-26-al[a]	Pitcairn Island	Georgieva et al. [78]

*Compound needs confirmation. [a]Constituent isolated from the honeybee propolis (from the genus *Apis* sp.). [b]Constituent isolated from the stingless bee propolis (from genera *Tetragonula* sp., *Tetrigona* sp., or *Heterotrigona* sp.). [1]Newly discovered compound. Compounds already mentioned in Huang et al. [8] are excluded.

2.2. Fatty Acids

Fatty acids are one of the "waxy" nonpolar parts of propolis, and Heinen and Linskens [83] were one of the first researchers who isolated fatty acids (ranging from C_7 to C_{18}) from propolis. Until 2018, there were many more found in propolis and some authors reported them as long as C_{36} [84]. Despite the fact that fatty acids were discovered in propolis relatively soon, most of the authors do not mention them in their articles. They can be present in propolis as glycosides, free fatty acids, different type of esters, or others [56,84]. There are many different types of fatty acids found in propolis: saturated, monounsaturated, polyunsaturated, and even omega-3 and omega-6 fatty acids [85]. As they are not among the most widely reported compounds in propolis, between 2013 and 2018 only two authors reported fatty acids isolated from propolis for the first time. Among those reported, 13 were free fatty acids and 4 were fatty acid glycosides. All of them were from European samples (Bulgaria and United Kingdom). Details can be found in Table 4.

Table 4 | Fatty acids and their glycosides identified in propolis for the first time since 2011

No.	Chemical name	Geographic location	References
Fatty acids			
265	9-Oxo-10(*E*)-12(*Z*)-octadecadienoic acid[a]	Bulgaria	Bilikova et al. [86]
266	Dihydroxylinoleic acid[a,*]	United Kingdom	Saleh et al. [56]
267	Dihydroxylinolenic acid (isomer 1)[a,*]	United Kingdom	Saleh et al. [56]
268	Dihydroxy eicosenoic acid[a,*]	United Kingdom	Saleh et al. [56]
269	Hydroxylinolenic acid (isomer 1)[a,*]	United Kingdom	Saleh et al. [56]
270	Dihydroxy docosahexenoic acid[a,*]	United Kingdom	Saleh et al. [56]
271	Hydroxylinolenic acid (isomer 2)[a,*]	United Kingdom	Saleh et al. [56]
272	Dihydroxylinolenic acid (isomer 2)[a,*]	United Kingdom	Saleh et al. [56]
273	Hydroxylinoleic acid[a,*]	United Kingdom	Saleh et al. [56]
274	Hydroxyheptadecanoic acid acetate[a,*]	United Kingdom	Saleh et al. [56]
275	Hydroxydocosapentaenoic acid[a,*]	United Kingdom	Saleh et al. [56]
276	Dihydroxylinolenic acid (isomer 3)[a,*]	United Kingdom	Saleh et al. [56]
277	Hydroxydocosahexanoic acid[a,*]	United Kingdom	Saleh et al. [56]
Fatty acid glycosides			
278	Hydroxynonadecanoic acid glucoside[a,*]	United Kingdom	Saleh et al. [56]
279	Octadecatriol glucoside[a,*]	United Kingdom	Saleh et al. [56]
280	Dihydroxy ecosanoic acid glucoside[a,*]	United Kingdom	Saleh et al. [56]
281	Hydroxy ecosanoic acid glucoside[a,*]	United Kingdom	Saleh et al. [56]

*The molecular structure of the compound is not completely defined. [a]Constituent isolated from the honeybee propolis (from the genus *Apis* sp.). Compounds already mentioned in Huang et al. [8] are excluded.

2.3. Alcohols

Propolis, among other things, also contains different types of alcoholic compounds, such as simple alcohols, fatty alcohols, sugar alcohols, sterols, and others [8,24,84]. Between 2013 and 2018, two new alcohols were isolated from propolis samples from Africa (Cameroon) and Middle East (Oman). Table 5 includes only alcohols that were not included in the previous tables.

2.4. Alkaloids and their Derivatives

One of the most surprising discoveries regarding propolis in the recent years is definitely the discovery of alkaloids and their derivatives in propolis samples. Neither alkaloids nor nitrogenous compounds (except some vitamins from only a few samples) as such were reported from propolis before 2011–2012 [8,87]. To the best of our knowledge, alkaloids and their derivatives were first isolated from propolis in 2015 [57], when they were isolated from Brazilian propolis. They were later reported again, when they were isolated from Algerian propolis in 2017 [31] and from Brazilian propolis in 2018 [47]. Altogether 16 alkaloids and 5 alkaloid derivatives were isolated from propolis samples from two different countries. Specifics are listed in Table 6.

Table 5 | Alcohols and related compounds identified in propolis for the first time since 2011

No.	Chemical name	Geographic location	References
Alcohols			
282	Pinitol[a]	Oman	Popova et al. [42]
283	1′-*O*-eicosanyl glycerol[a,1]	Cameroon	Talla et al. [82]

[a]Constituent isolated from the honeybee propolis (from the genus *Apis* sp.). [1]Newly discovered compound. Compounds already mentioned in Huang et al. [8] are excluded.

2.5. Other Compounds

Researchers also reported some new compounds in propolis that do not belong to any of the previously mentioned groups but were still isolated from propolis for the first time. Nineteen new compounds were isolated between 2013 and 2018, with the addition of one compound isolated in 2011 [35], which was not included in the review article by Huang et al. [8]. The newly isolated compounds were found in propolis from South America (Argentina), Africa (Algeria), and Europe (United Kingdom). Specifics are listed in Table 7.

Besides compounds mentioned above, there might be some that were not included in this review, either because their structures were not determined [47,60,66], because authors did not pay enough attention to their novelty and they were not specifically labelled as new [13,31,47,53,63,64,67,88], or simply because they were overlooked. In conclusion, actual number of compounds isolated in the recent years could be even higher.

Table 6 | Alkaloids and their derivatives identified in propolis for the first time since 2011

No.	Chemical name	Geographic location	References
Alkaloids			
284	7(3-Methoxy-2-methylbutyryl)-9-echimidinylretronecine derivative (1)[b,*]	Brazil	Coelho et al. [57]
285	7(3-Methoxy-2-methylbutyryl)-9-echimidinylretronecine derivative (2)[b,*]	Brazil	Coelho et al. [57]
286	Pagicerine[a]	Algeria	Soltani et al. [31]
287	Demecolcine[a]	Algeria	Soltani et al. [31]
288	Papaverine[a]	Algeria	Soltani et al. [31]
289	Aspidospermidine[a]	Algeria	Soltani et al. [31]
290	Morphinan-6-one-2-ol[a]	Algeria	Soltani et al. [31]
291	Thebaine[a]	Algeria	Soltani et al. [31]
292	N,O-dimethyl stephine[a]	Algeria	Soltani et al. [31]
293	Morpholine[a]	Algeria	Soltani et al. [31]
294	Lelobanonoline[b]	Brazil	Cisilotto et al. [47]
295	2-[6-(2-Hydroxy-propyl)-1-methyl-[2]-piperidyl]-1-phenylethanone[b]	Brazil	Cisilotto et al. [47]
296	Norlobelanidine[b]	Brazil	Cisilotto et al. [47]
297	Norlobeline[b]	Brazil	Cisilotto et al. [47]
298	Lobeline[b]	Brazil	Cisilotto et al. [47]
299	Lobelanidine[b]	Brazil	Cisilotto et al. [47]
Alkaloid derivatives			
300	5(4*H*)-thebenidinone[a]	Algeria	Soltani et al. [31]
301	4-(Phenylthioxomethyl)morpholine[a]	Algeria	Soltani et al. [31]
302	4-Methyl-2,6-bis(4-morpholylmethyl)phenol[a]	Algeria	Soltani et al. [31]
303	3-[(Trimethylsilyl)oxy]4,5α-epoxy-14- hydroxy-17-(2-propenyl)morphinan-6-one[a]	Algeria	Soltani et al. [31]
304	Nicotinaldehydesemicarbazone[a]	Algeria	Soltani et al. [31]

[*]The molecular structure of the compound is not completely defined. [a]Constituent isolated from the honeybee propolis (from the genus *Apis* sp.). [b]Constituent isolated from the stingless bee propolis (from genera *Scaptotrigona* sp. or *Melipona* sp.). Compounds already mentioned in Huang et al. [8] are excluded.

Table 7 | Compounds, not belonging to any previously mentioned groups, identified in propolis for the first time since 2011

No.	Chemical name	Geographic location	References
305	4-[4-(4-Hydroxy-phenyl)-2,3-dimethyl-butyl]-benzene-1,2-diol[a]	Argentina	Agüero et al. [35]
306	Ethoxy sulfonate[a,*]	United Kingdom	Saleh et al. [56]
307	3,4,5-Triphenylpyrazole[a]	Algeria	Soltani et al. [31]
308	3-(4-Methoxyphenyl)benzo[*f*]quinazoline[a]	Algeria	Soltani et al. [31]
309	2-(4-Methoxyphenyl)-4-[(2-propyn-1-yl)thio]quinazoline[a]	Algeria	Soltani et al. [31]
310	4-Aminobenzo[*g*]quinazoline[a]	Algeria	Soltani et al. [31]
311	5-(4-Diethylaminobenzylidene)rhodanine[a]	Algeria	Soltani et al. [31]
312	Carbamazepine[a]	Algeria	Soltani et al. [31]
313	1-(3*H*-imidazol-4-yl)-ethanone[a]	Algeria	Soltani et al. [31]
314	Nifenazone[a]	Algeria	Soltani et al. [31]
315	Podofilox[a]	Algeria	Soltani et al. [31]
316	Brallobarbital[a]	Algeria	Soltani et al. [31]
317	Cyclobarbital[a]	Algeria	Soltani et al. [31]
318	6,7,8-Trimethoxy-isoquinoline[a]	Algeria	Soltani et al. [31]
319	1-Butyl-isoquinoline[a]	Algeria	Soltani et al. [31]
320	1-(Phenylthioxomethyl)-2,5-pyrrolidinedione[a]	Algeria	Soltani et al. [31]
321	2-(4-Methoxyphenyl)-2-methyl-1,3-dioxolane[a]	Algeria	Soltani et al. [31]
322	1′*H*-cholesta-3,5-dieno-[3,4-*b*]indol[a]	Algeria	Soltani et al. [31]
323	3-(3,4-Dimethoxyphenyl)-6-nitro-coumarin[a]	Algeria	Soltani et al. [31]
324	10-Butyl-3,7-dinitro-10*H*-phenothiazine[a]	Algeria	Soltani et al. [31]

[*]The molecular structure of the compound is not completely defined. [a]Constituent isolated from the honeybee propolis (from the genus *Apis* sp.). Newly discovered compound. Compounds already mentioned in Huang et al. [8] are excluded.

3. CONCLUSION

Until 2000 at least 300 compounds were reported from propolis [6,11] and Huang et al. [8] reported another 241 between 2000 and 2012. Despite these numbers, just between 2013 and 2018 at least 305 compounds were isolated from propolis for the first time, including the first isolation of alkaloids. This number excludes 19 compounds isolated between 2011 and 2012, which were excluded from the previously mentioned review by Huang et al. [8] and were thus included in this article, bringing the total number to 324. Altogether, until 2018 more than 850 compounds are reported from propolis.

Compounds included in this article were isolated from 6 different continents and from 29 different countries (including the 19 added compounds isolated in 2011–2012 mentioned above). New compounds were isolated on more than one occasion from propolis of some countries, most often from Brazil (6×). Most of the compounds belong to the groups of flavonoids (92), phenols (126), and terpenes (46), whereas fatty acids (17), alcohols (2), alkaloids (21), and other compounds (20) represent a minor fraction. Despite the fact that propolis has been intensely studied for at least 30–40 years, new discoveries are being made on a yearly basis and it is not yet known how many more will be discovered in the upcoming years.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

The informations were gathered and the bulk of the article was written by Luka Šturm, while the critical revision and final approval were done by dr. Nataša Poklar Ulrih, whom also submitted the article.

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