

Ethnobotany, Chemical Constitution and Biological Activities of *Moquilea* Genus: A Systematic Review

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ABSTRACT

Moquilea (Chrysobalanaceae) is a taxon recently separated from previous *Licania* genus. Several plants from *Moquilea* genus have been studied for the evaluation of their biological properties and chemical constitution analysis, especially those used as edible material and as a medicinal agent in several countries from tropical zones of America where the plants are endemic. Considering these facts, the present systematic review has the aim to summarize available information about ethnobotany, chemical components and biological effects investigated for *Moquilea* plants. For this purpose, eight data bases (Pubmed, ACS publications, EBSCOhost, ScienceDirect, SciELO, SpringerLink, Taylor and Francis Online and Wiley Online Library) were searched and 2116 results corresponding to full-text articles and book chapters were screened using defined inclusion criteria. Finally, information from 45 documents were included in the review. According to compiled information, there are few species with available data related to their ethnobotanical applications. However, there is a wide variety of biological activities reported for extracts and isolated components obtained from *Moquilea* plants, including antioxidant, antimicrobial, cytotoxic and gastroprotective effects. Polyphenols and triterpenes are the major secondary metabolites reported among *Moquilea* plants.

Key words: Activities, Ethnobotany, Extracts, Metabolites, *Moquilea*.

INTRODUCTION

Plants from current *Moquilea* taxon were former members of *Licania* genus.^[1] This recent accepted taxonomic classification of *Licania* based on genetic data established that *Moquilea* plants must be classified as a separate genus from *Licania*.^[1-3] According to this division, *Moquilea* genus is integrated by 54 species of trees original from Neotropics and several of them have been studied for the characterization of their biological activities and secondary metabolites.^[1-4]

Some *Moquilea* plants have reported ethnobotanical applications. For example, *M. platypus* have been used in Central America to treat stomach ache, diarrhea and snake bites.^[5,6] The leaves and fruits of this tree are consumed as food in the regions where the plant is endemic.^[7-10] In Brazil, *M. tomentosa* fruits are considered as edible and their seeds are source of vegetal oil.^[11,12] This kind of information has inspired several investigations of the chemical characterization and biological activity of *Moquilea* plants.

Studied biological effects for *Moquilea* plants are varied, ranging from *in vitro* antioxidant activity analysis to the observation of the gastroprotective effect *in vivo*.^[13,14] In the case of secondary metabolites characterization, polyphenols and triterpenes are the major groups of compounds studied among *Moquilea* plants.^[4,13] Considering these backgrounds, the aim

of the present review is to summarize the available information related to ethnobotanical applications, biological activities and secondary metabolites identified in *Moquilea* species using a systematic approach for the search of relevant literature in the topic.

METHODS

Moquilea is now considered as a separated genus derived from a previous taxon corresponding to *Licania* genus, this in accordance to the current taxonomic classification.^[1-3] Therefore, most species from *Moquilea* genus retain *Licania* as the first term of their scientific name in literature due to previous taxonomic classification. Taking into account this fact, the search terms “*Licania*” and “*Moquilea*” were employed in the following data bases: Pubmed, ACS publications, EBSCOhost, ScienceDirect, SciELO, SpringerLink, Taylor and Francis Online and Wiley Online Library. A total number of 2116 results were found corresponding to full-text articles and book chapters. Then, the content of the found documents were screened and 2077 titles were excluded according to following criteria: content irrelevant to the scope of the review ($n=1860$), plants not included in *Moquilea* genus according to the current taxonomic definition of the genus^[1] ($n=185$), repeated results among data bases ($n=15$), incomplete information ($n=15$) and not

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recognized species name ($n=2$). According to this, 39 articles and book chapters from consulted data bases were included in the review. Additionally, we added six known references important to the topic that are not included in the searched data bases. Finally, the review includes 45 references published between 1992 and 2021.

ETHNOBOTANICAL APPLICATIONS

There are few species from *Moquilea* genus that have reported ethnobotanical applications according to the information obtained from consulted data bases. The most reported specie is *M. platypus*. The fruits of this tree are used as food in Belize. In this country, the decoction made of *M. platypus* seeds combined with garlic skin is used to treat diarrhea, while seed powder is swallowed and applied as poultice to treat snake bites.^[5,15] In Nicaragua, decoction and infusions made of bark, leaves and fruits of *M. platypus* are used to treat stomach ache and diarrhea.^[6] In Mexico, the concoction made of leaves of *M. platypus* is eaten as an appetizer and the fruit is also eaten. Ground seeds are used in the same country to treat dysentery and diarrhea.^[7-9,16] In Panama, fruits of *M. platypus* are used as fodder for livestock.^[10] *M. platypus* fruits are considered as edible material in Colombia.^[17] In Brazil, *M. salzmannii* and *M. tomentosa* fruits are consumed as food. In this country, *M. tomentosa* seeds are used as source of vegetal oil.^[11,12]

BIOLOGICAL ACTIVITIES

There is a wide variety of biological activities studied for *Moquilea* plant extracts and metabolites. However, only four species have been studied. Most studies used *in vitro* approaches to measure their antioxidant potential, antimicrobial activity and cytotoxicity against tumoral cell lines among other effects. Moreover, there are studies using *in vivo* assays to observe the effect of plant extracts on gastrointestinal motility. The biological activities investigated for *Moquilea* plants are summarized in Table 1. Details about results of those studies are described below.

Moquilea kallunkiae

Methanol extract from *M. kallunkiae* stems inhibited the growth of chloroquine-resistant *Plasmodium falciparum* strain (W2 Indochina) at concentration of 100 µg/mL with an inhibition percentage of 85.8 %.^[18,19]

Moquilea platypus

The aqueous and ethanol extracts obtained from the leaves of *M. platypus* have demonstrated gastroprotective activity in models of gastric ulcer induction in rats by the administration of ethanol and indomethacin. The aqueous and ethanol extracts showed a protective index (PI) ranging from 80 % to 94 % against stomach ulcer formation induced with ethanol and indomethacin when they are oral administered at dose of 1000 mg/kg and 500 mg, respectively. Histological observation of stomach tissue isolated from control and treatment groups of those models showed that the extracts reduce tissue inflammation, necrosis, and leucocyte infiltration. Results obtained by pyloric ligation model of ulcer induction showed that the extracts promote the secretion of gastric mucus and, in the case of the aqueous extract, it reduces the acid and thiobarbituric acid reactive substances (TBARS) contents in gastric mucosa.^[14,20] The aqueous extract does not affect intestinal motility but promotes a decrease in gastric empty according to red phenol model using rats as experimental animals.^[20]

The methanol extract from *M. platypus* seeds has shown antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Proteus mirabilis* and *Pseudomonas aeruginosa* with average zones of inhibition in the range of 14 to 18 mm according to agar diffusion assay.^[21]

Table 1: Biological activities studied for *Moquilea* species.

Species	Evaluated substance (plant section)*	Studied biological activities	References
<i>M. kallunkiae</i>	Methanol extract (St)	Antimalarial	[18,19]
<i>M. platypus</i>	Ethanol extract (L)	Gastroprotective	[14]
	Aqueous extract (L)	Gastroprotective and gastrointestinal motility reduction	[20]
<i>M. pyrifolia</i>	Methanol extract (S)	Antibacterial	[21]
	Methanol extract (L)	Molluscicidal and piscicidal	[22,23]
<i>M. tomentosa</i>	Ethanol extract (L)	Acaricidal	[24-27]
	Ethanol extract (S)	Antioxidant	[28]
	Ethanol extract and fractions (S)	Antioxidant and cytotoxicity	[13]
	Ethanol extract (S)	Antioxidant and antibacterial	[29]
	Extract obtained by successive extraction with methanol 50 %, acetone 70 % and water (F)	Antioxidant	[12]
	Ethanol extract (L)	Antioxidant	[30]
	Aqueous saline extract: sodium chloride 0.85 % (S)	Antiviral and cytotoxicity	[31-33]
	Dichloromethane fraction from methanol extract (L)	Cytotoxicity	[34-36]
	Betulinic acid and oleanolic acid (F,L)		
	Mixture of triterpenic acids; 79 % betulinic, 13.1 % ursolic and 7.9 % tormentic (L)		
	Dichloromethane, ethanol, and ethyl acetate extracts (L)	Antileishmanial	[37]

*F: fruits, L: leaves, S: seeds, St: stems.

Moquilea pyrifolia

Methanol extract from the leaves of *M. pyrifolia* has molluscicidal activity against the snails of *Biomphalaria glabrata*. The extract killed all the snails used in the test at concentration of 50 ppm, but it did not have piscicidal activity at concentration of 10 000 mg/L against *Poecilia reticulata* nor *Carassius auratus*.^[22,23]

Moquilea tomentosa

Acaricidal activity has been reported for *Moquilea tomentosa* leaves against *Rhipicephalus microplus* larvae. Ethanol extract caused a mortality rate of 40,26 % of treated larvae at concentration of 600 mg/mL.^[24-27]

Lima de Medeiros *et al.* reported results for the investigation of *M. tomentosa* fruits with the purpose of determine their nutritional and antioxidant potentials. According to this study, dry pulp has higher values for protein, fat, and dietary fiber (values up to 4.59 %, 4.06 % and 41.70 %, respectively) than dry seeds. However, dry seeds have more digestible carbohydrates (up to 69.01 %). Seeds also have higher contents of total tocopherols (1.76 mg/100 g). Ethanol extract from seeds of *M. tomentosa* has higher values for total phenolics (203 mg of gallic acid equivalents (GAE)/mg) and total flavonoids (29.88 mg of quercetin equivalents (QE)/mg) than pulp ethanol extract. Only the extract obtained from seeds has antioxidant activity with an inhibitory concentration (IC_{50}) of 10.03 µg/mL on DPPH

radical scavenging assay. The extract from seeds has shown IC_{50} values of 18 $\mu\text{g/mL}$ without iron stress and 88 $\mu\text{g/mL}$ with iron stress on thiobarbituric acid reactive substances (TBARS) assay. According to the ferric reducing antioxidant power (FRAP) assay, extracts from seeds have FRAP values up to 0.309 mM FeSO_4/mg .^[28]

The fractionation of an ethanol extract of *M. tomentosa* seeds with different solvents and the chemical analysis of the extract and their fractions indicate that ethyl acetate fraction had the highest values for total phenolics (201.83 mg GAE/g) and flavonoids (90.81 mg QE/g), but aqueous fraction had the highest tannins content (0.182 mg tannic acid equivalents/g). However, the evaluation of the antioxidant activity of the extract and its fractions shows that the methanol fraction was the most potent according to DPPH scavenging (IC_{50} of 26.30 $\mu\text{g/mL}$) and TBARS assays (IC_{50} of 105.72 and 8.55 $\mu\text{g/mL}$ without iron stress and with iron stress, respectively). Ethyl acetate and methanol fractions have iron chelating activity with an iron complexation percentage near to 30 % at concentration of 1000 $\mu\text{g/mL}$. The ethanol extract has not shown cytotoxicity at test concentration of 250 $\mu\text{g/mL}$ against human breast adenocarcinoma cell line (MCF-7) nor human colon adenocarcinoma cell line (Caco-2).^[13]

Farias *et al.* reported the study of biological activities from another ethanol extract made of *M. tomentosa* seeds. According to this report, the extract has shown antioxidant activity under DPPH radical scavenging assay (IC_{50} of 216.72 $\mu\text{g/mL}$). The extract also had antibacterial activity against *Staphylococcus aureus* (minimal inhibitory concentration: 6.49 mg/mL) and inhibitory activity against acetylcholinesterase (inhibition percentage of 13.9 % at concentration 0.5 mg/mL).^[29]

M. tomentosa fresh fruits have values for total phenolics, total anthocyanins and total carotenoids of 1236.42 mg of GAE/100 g, 2.96 mg of cyanidin 3-*O*-glucoside equivalents/100 g and 2.43 mg of β -carotenoids equivalents/100 g, respectively. The fruits have a total antioxidant activity of 14 271.69 μmol trolox equivalents/100 g according to DPPH scavenging activity assay.^[12] The ethanol extract from *M. tomentosa* leaves also have antioxidant activity according to this assay (IC_{50} of 67.03 $\mu\text{g/mL}$).^[30]

Extract of *M. tomentosa* seeds made using 0.85 % sodium chloride solution as extractant has shown a maximum non-toxic concentration on human larynx epidermoid tumor cell line (HEp-2) of 625 $\mu\text{g/mL}$ and an IC_{50} of 7.66 mg/mL against cell viability. This extract inhibited the proliferation of acyclovir-resistant herpes simplex virus type 1 (ACVr-HSV1) on HEp-2 cultures with a IC_{50} value of 9 $\mu\text{g/mL}$ giving a selective index of 851. The extract also can inactivate viral particles when they are set in direct contact before their addition to HEp-2 cultures (viral index of 2.46).^[31-33]

Cytotoxicity evaluation of pentacyclic triterpenes isolated from *M. tomentosa* fruits and leaves indicates that betulinic acid and oleanolic acid are capable to inhibit the growth of human erythroleukemia cells lines, corresponding to K562 and multidrug resistant K562-Lucena 1 (K562/VCR). The compounds induce apoptosis and DNA fragmentation in exposed cell cultures. Similar results are reported for the dichloromethane fraction obtained from the methanolic extract of *M. tomentosa* leaves and the mixture of triterpenic acids (79% betulinic, 13.1%, ursolic and 7.9%, tormentic) obtained from it.^[34-36]

Dichloromethane, ethanol, and ethyl acetate extracts from *M. tomentosa* leaves have not shown inhibitory activity against *Leishmania amazonensis*.^[37]

CHEMICAL CONSTITUTION

Around ninety compounds have been detected or isolated from *Moquilea* plants. Polyphenols and triterpenes are the groups most frequently reported among studied species of the genus.

Polyphenols

The following compounds have been isolated from *M. pyrifolia* leaves using chloroform-methanol mixture 9:1 and methanol as extraction solvents: kaempferol (1), kaempferol-3-rhamnoside (2), kaempferol-3-arabinoside (3), kaempferol-3-(2''-xylosyl) rhamnoside (4), hypolaetin (5), 8-hydroxyeriodictyol (6), 8-hydroxyarnigenin (7), myricetin (8), myricetin-3-rhamnoside (9), myricetin-3-(2''-xylosyl)rhamnoside (10), quercetin (11), quercetin-3-rhamnoside (12), quercetin-3-arabinoside (13) and quercetin-3-(2''-xylosyl)rhamnoside (14).^[4,22,38,39]

Phytochemical screening of the ethanol extracts from *M. tomentosa* seeds and leaves indicates the presence of hydrolysable tannins, flavonols, flavononols, flavones, flavonones, catechins and saponins.^[13,30] The extract was fractionated with solvents of different polarities for their analysis through high-performance liquid chromatography coupled to diode array detector (HPLC-DAD), these analyses demonstrate the presence of 1, 11, gallic acid (15), catechin (16), chlorogenic acid (17), caffeic acid (18), epicatechin (19), ellagic acid (20), kaempferol glycoside (21) and rutin (22) in the extract and all its fractions. Ethyl acetate fraction had the highest quantities of these compounds (ranging from 7.81 to 46.59 mg/g) except for methanol fraction that had the highest content of kaempferol (5.41 mg/g).^[13]

The analysis of the ethanol extract of *M. tomentosa* seeds using ultrahigh-performance liquid chromatography system coupled to mass spectrometry (UHPLC-MS) has shown the presence of the following components: galocatechin (23), coumaric acid (24) and ferulic acid (25). Other compounds reported through the same analysis, which specific configuration and constitution must be defined in further research, are galocatechin dimer isomer, naphthalenedicarboxylic acid hexoside, hydroxyjasmonic acid-*O*-hexoside, larciresinol hexoside and quercetin pentosyl hexoside.^[28]

M. platypus seeds have prodelphinidins and flavonoids according to UHPLC-MS analysis. This material has a total phenolics amount of 92 mg of GAE/g.^[40] The structures of reported polyphenols in *Moquilea* plants are shown in Figure 1.

Diterpenes and Triterpenes

Tinospinoside D (26) is a diterpene detected by UHPLC-MS analysis of the ethanol extract obtained from *M. tomentosa* seeds.^[28] On the other

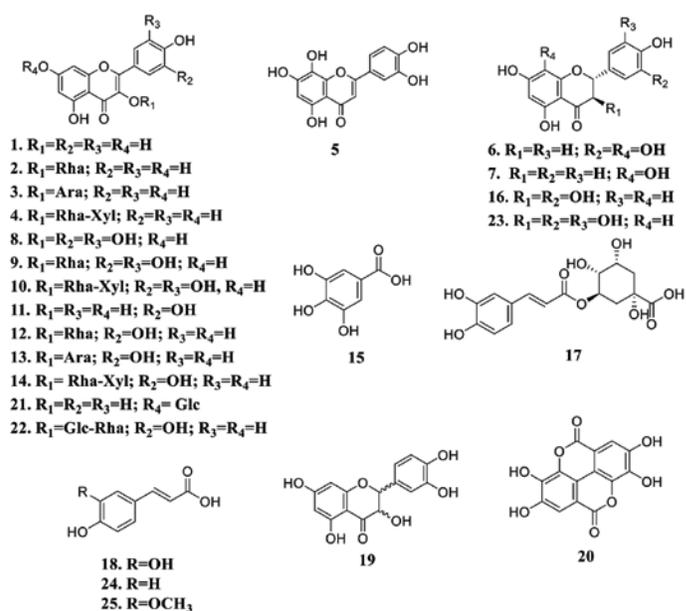


Figure 1: Polyphenols detected in *Moquilea* species.

hand, triterpenes corresponding to betulinic acid (27) and licanolide (28) are compounds isolated from hexane extract of *M. tomentosa* fruits. Oleanolic acid (29) has been obtained from methanol extract of the same fruits. Compounds corresponding to 27, lupeol (30), stigmaterol (31) and β -sitosterol (32) are substances isolated from hexane extract of *M. tomentosa* leaves, while 27, tormentic acid (33) and ursolic acid (34) are reported components of the methanol extract of the same plant material.^[4,39,41,42] The ethyl acetate fraction from *M. tomentosa* fruits methanol extract contains 29. Dichloromethane fraction obtained from methanol extract of leaves of the same plant have 27, 33 and 34.^[34]

The extraction of *M. pyrifolia* with chloroform and the further chromatographic fractionation of the extract have allowed the isolation of 27, 29, 30, 32, 34, α -amyrin (35), betulin (36) and uvaol (37). A similar procedure with the same plant material, using chloroform-methanol 9:1 mixture as extraction solvent, has yielded 33, 2 α -hydroxy ursolic acid (38), maslinic acid (39), β -sitosterol-3-O-glucoside (40), 11 α -hydroxybetulinic acid (41), 6 β -hydroxybetulinic acid (42), 2 α ,3 β -dihydroxyup-12-en-28-oic acid 3-(3',4'-dihydroxybenzoyl ester) (43), 2 α ,3 β ,27-trihydroxyup-12-en-28-oic acid 3-(3',4'-dihydroxybenzoyl ester) (44), ursolic acid 3- α -L-arabinoside (45), euscaptic acid 28- β -D-glucopyranosyl ester (46), tormentic acid 28- β -D-glucopyranosyl ester (47), 2 α ,3 α -dihydroxyurs-12-ene-28-oic acid (48) and euscaptic acid (49).^[22,39,43] Figure 2 summarizes the structure of diterpenes and triterpenes identified in *Moquilea* genus.

Essential and Fixed Oils

The essential oil obtained from *M. tomentosa* fruits by hydrodistillation was analyzed by gas chromatography coupled to mass spectrometry (GC-MS). The results of this analysis indicate the presence of the following volatile compounds in the essential oil: hexanal (7.1-16.7 %) (50), ethyl butyrate (2.1-3.1%) (51), 3-hexene-1-ol (2.1-2.5%) (52),

hexanol (11.1-33.5 %) (53), 3-hexanone-2-ol (21.0 %) (54), cyclopentyl ethanone (1.4 %) (55), butyl butyrate (3.4-6.4 %) (56), myrcene (2.1-6.4 %) (57), amyl butyrate (1.5-2.2 %) (58), terpinen-4-ol (0.2-1.0 %) (59), α -terpineol (0.8 %) (60), hexyl butyrate (1.0-3.5 %) (61), vinyl butyrate (2.3 %) (62), isopropyl butyrate (5.1 %) (63), trans-2-hexenal (3.7 %) (64), isoamyl acetate (0.6 %) (65), 4-heptanol (10.5 %) (66), nonane (1.8 %) (67), benzaldehyde (1.0 %) (68), sabinene (0.7 %) (69), 5-methyl-5-hexen-2-one (0.4 %) (70), ethyl hexanoate (1.4 %) (71), hexyl acetate (1.0 %) (72), pentyl isobutyrate (7.4 %) (73), isopentyl butyrate (5.4 %) (74), 1-octanol (0.4 %) (75), 1,2-heptanediol (3.6 %) (76), undecane (0.5 %) (77), *cis*- β -dihydro terpineol (0.1 %) (78), dodecane (0.2 %) (79), pentyl hexanoate (1.0 %) (80), safrol (1.6 %) (81), 2,4-decadienal (0.3 %) (82), hexyl hexanoate (0.2 %) (83), hexadecane (0.1 %) (84) and palmitic acid (0.6 %) (85).^[44,45] Compounds 85 and palmitoleic acid (86) are fatty acids reported in hexane extracts obtained from *M. tomentosa* leaves and fruits, respectively.^[41] Additionally, *M. tomentosa* seeds are known source of vegetal oil with a yield above 30 %.^[46] Figure 3 shows the structure of volatile compounds and fatty acids reported in *Moquilea* species.

CONCLUSION

Few species of the *Moquilea* genus have been studied, however, preliminary results have been obtained from plants investigated, this suggest that further research of more plants of the genus could allow to find new bioactive extracts and compounds. In this sense, it is important to notice that the found information shows that most of the studied bioactive extracts do not have a chemical characterization of their compounds, and more important, in most cases the isolation and identification of major bioactive compounds responsible of the observed effects are pending tasks. Polyphenols, triterpenes and volatile compounds have been detected or isolated, but only few of them have been studied to examine their individual biological properties. Toxicological studies of bioactive extracts and metabolites are also necessary to have a better panorama of their applicability. In summary, *Moquilea* genus is a prom-

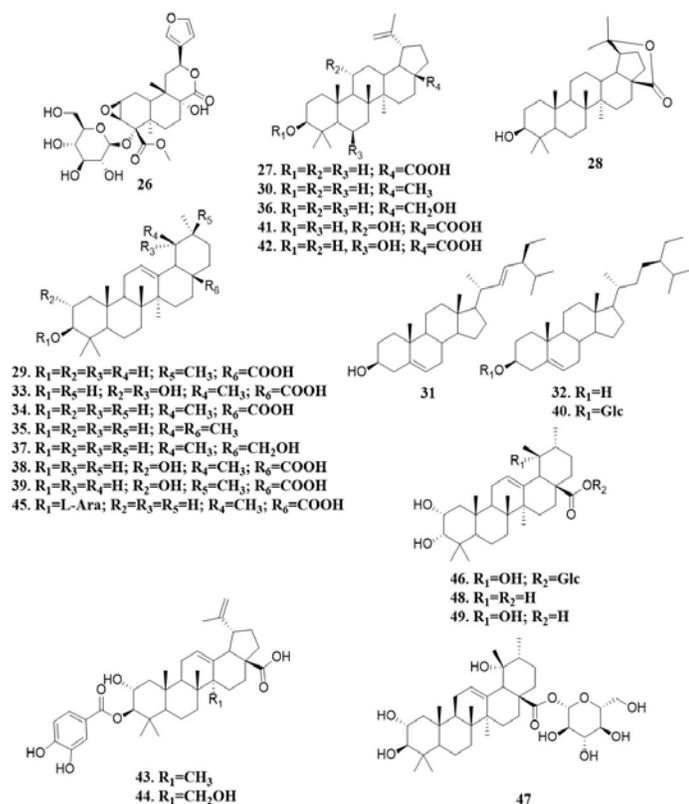


Figure 2: Triterpenes isolated from *Moquilea* species.

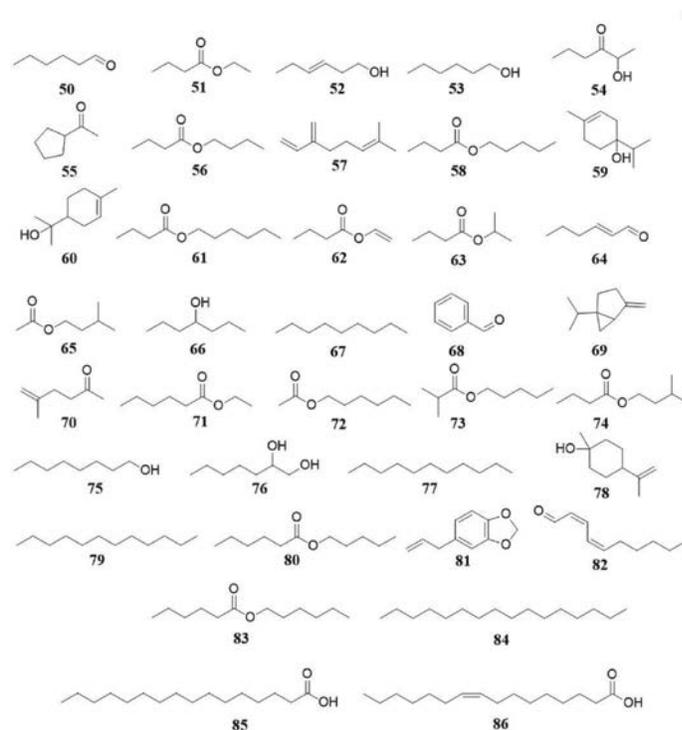


Figure 3: Volatile compounds and fatty acids present in *Moquilea* species.

ising source of bioactive extracts and compounds, thus, further research, especially of less studied species, will help to get a better understanding in this topic.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

ACVr-HSV1: Acyclovir-resistant herpes simplex virus type 1; **Caco-2:** Human colon adenocarcinoma cell line; **DPPH:** 2,2-diphenyl-1-picrylhydrazyl; **FRAP:** Ferric reducing antioxidant power; **GAE:** Gallic acid equivalents; **Hep-2:** human larynx epidermoid tumor cell line; **HPLC-DAD:** High-performance liquid chromatography coupled to diode array detector; **IC₅₀:** Half-maximal inhibitory concentration; **K562/VCR:** Human erythroleukemia cells line; **MCF-7:** Human breast adenocarcinoma cell line; **PI:** Protective index; **QE:** Quercetin equivalents; **TBARS:** Thiobarbituric acid reactive substances; **UHPLC-MS:** Ultrahigh-performance liquid chromatography coupled to mass spectrometry.

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