

HETEROCYCLES, Vol. 78, No. 6, 2009, pp. 1413 - 1426. © The Japan Institute of Heterocyclic Chemistry  
Received, 28th November, 2008, Accepted, 26th January, 2009, Published online, 28th January, 2009  
DOI: 10.3987/REV-08-651

## THE DITERPENOIDS FROM THE GENUS *HYPTIS* (LAMIACEAE)

**Franco Piozzi,\* Maurizio Bruno, Sergio Rosselli, and Antonella Maggio**

Dipartimento di Chimica Organica, Università degli Studi di Palermo, Viale delle Scienze, Parco d'Orleans II, I-90128 Palermo, Italy.

Fax +39-091-596825 e-mail: fpiozzi@unipa.it

**Abstract** – The genus *Hyptis* (family Lamiaceae) is known mainly for the essential oils isolated from the aerial parts of several species. Less known are the diterpenoids, extracted from a limited number of species. In consideration of the interest for the structures of this class of compounds, largely occurring in the whole Lamiaceae family, the present paper means to review and update their chemistry. Also the use of many species of *Hyptis* in folk-medicine is reported.

### INTRODUCTION

The genus *Hyptis*, family Lamiaceae (Labiatae) comprises about 400 species, and is one of the largest genera of the family. It is native of Central and South America, including the southern part of United States.<sup>1,2</sup> Now several species were introduced in Western and Central Africa (for instance Cameroon, Nigeria, Burkina Faso, Ivory Coast), and even in India, China, Thailand and Fiji Islands, where they are cultivated specially for the production of essential oils. Moreover, they are important for the ethnopharmacologic point of view.

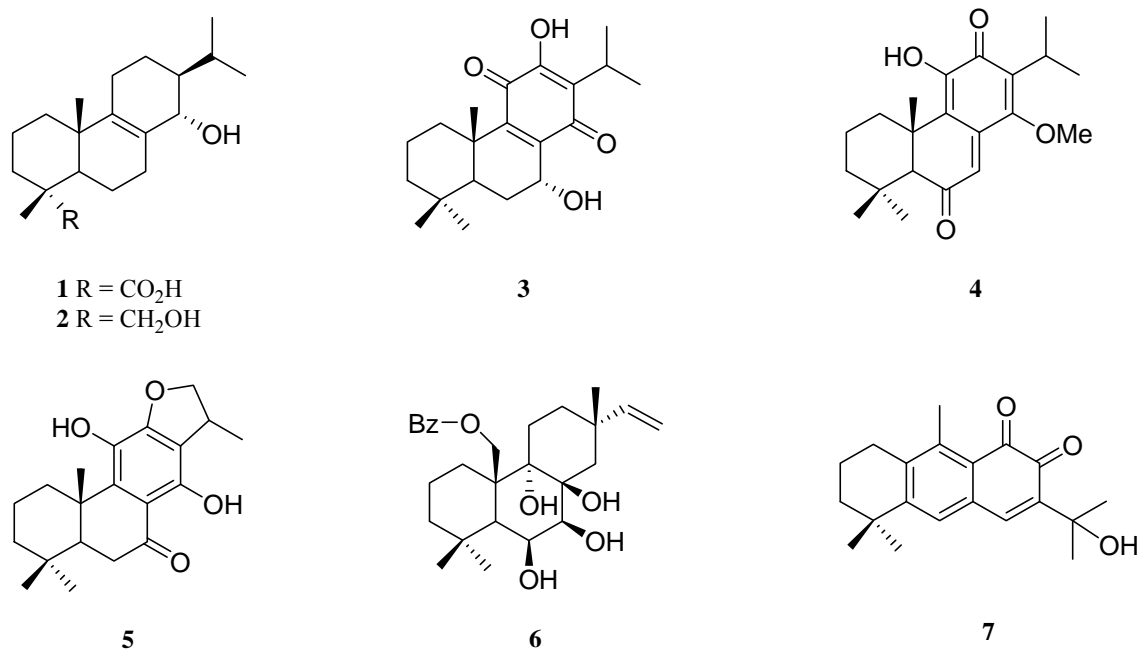
For this reason, a large number of species was investigated for their content of essential oils, and minor attention was given to other constituents. For instance, the occurrence of diterpenoids was reported only in nine species.

### CHEMICAL INVESTIGATIONS

The present paper means to review the isolation and the structures of these products. A total of 66 diterpenoids occurs in the genus, and 26 of them show heterocyclic structures.

The first paper concerning this investigation was published in 1974 and reported the isolation of two novel diterpenoids with the abietane skeleton from the aerial parts of *Hyptis suaveolens* collected in Trinidad<sup>3</sup>: suaveolic acid **1** and suavelol **2**.

Two years later, three diterpenoids were isolated from the root extract of *Hyptis fructicosa* harvested in Brazil.<sup>4</sup> The first one was identified with the already known horminone **3**;<sup>5</sup> the second product was new, and was attributed the structure **4** of 14-methoxy-taxodione. The structure of the third product was elucidated the following year<sup>6</sup> as **5**: it is a new natural compound and was given the name huptol. All these three diterpenoids have the abietane skeleton, and huptol **5** show an  $\alpha,\beta$ -unsaturated furanic ring fused with the C-ring of the abietane skeleton.



A diterpenoid with a different skeleton was isolated in 1990 from the leaves of *Hyptis salzmanii*, growing in Brasil.<sup>7</sup> It was given the name salzol and the structure **6** of 6,7,8-trihydroxy-20-benzoyloxy-isopimarane.

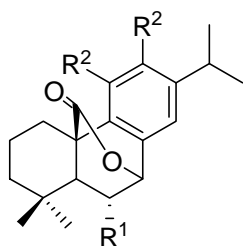
In the same year the roots of *Hyptis umbrosa* from Brazil<sup>8</sup> yielded an unusual product, with a rearranged abietane skeleton, named umbrosone. The elucidation of the structure **7** rested on deep NMR investigations.

The aerial parts of *Hyptis dilatata*, collected in Panama,<sup>9</sup> proved to be very rich in diterpenoids. The paper published in 1998, based on extensive chromatographic fractioning, reported the isolation of three known abietane compounds from the first fraction: carnosol **8**,<sup>10</sup> rosmanol **9**,<sup>11,12</sup> methylrosmanol **10**.<sup>13,14</sup>

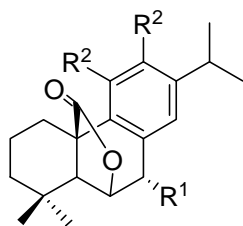
The treatment of the following fractions required acetylation and diazomethane treatment: many known abietane derivatives were isolated: diacetyl-carnosol **11**,<sup>10,11</sup> triacetyl-rosmanol **12**,<sup>11,13</sup> diacetyl-methylrosmanol **13**,<sup>13</sup> diacetyl-ethylrosmanol **14**,<sup>14</sup> triacetyl-isorosmanol **15**,<sup>15</sup> triacetyl-epirosmanol **16**,<sup>12</sup> diacetyl-carnosic acid **17**,<sup>14,16</sup> diacetyl-carnosic acid methylester **18**,<sup>17</sup>

acetyl-pisiferic acid methylester **19**.<sup>16,18</sup> Two not previously described derivatives were identified: diacetyl-epimethylrosmanol **20** and diacetyl-epiethylrosmanol **21**.

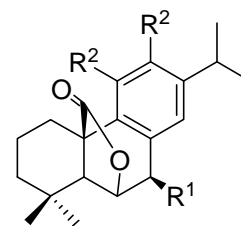
It must be evidenced that the nine abietane **11-21** are not authentic natural products, but derivatives originating from the acetylation/diazomethane treatment: the diterpenes originally occurring before the treatment are carnosol **8**, rosmanol **9**, methylrosmanol **10**, but evidently also ethylrosmanol **22**, isorosmanol **23**, epirosmanol **24**, epimethylrosmanol **25**, epiethylrosmanol **26**, carnosic acid **27**, pisiferic acid **28**, all not acetylated or partially acetylated products. These true natural products **22-28** were not isolated.



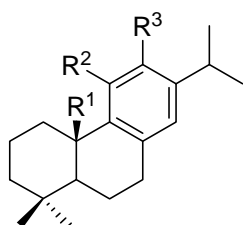
- 8** R<sup>1</sup> = H    R<sup>2</sup> = OH  
**11** R<sup>1</sup> = H    R<sup>2</sup> = OAc  
**15** R<sup>1</sup> = OAc R<sup>2</sup> = OAc  
**23** R<sup>1</sup> = OH    R<sup>2</sup> = OH



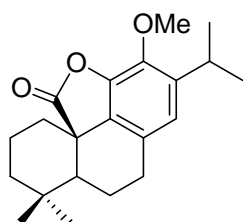
- 9** R<sup>1</sup> = OH    R<sup>2</sup> = OH  
**10** R<sup>1</sup> = OMe    R<sup>2</sup> = OH  
**12** R<sup>1</sup> = OAc    R<sup>2</sup> = OAc  
**13** R<sup>1</sup> = OMe    R<sup>2</sup> = OAc  
**14** R<sup>1</sup> = OEt    R<sup>2</sup> = OAc  
**22** R<sup>1</sup> = OEt    R<sup>2</sup> = OH



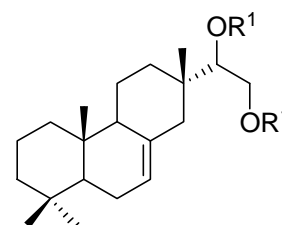
- 16** R<sup>1</sup> = OAc    R<sup>2</sup> = OAc  
**20** R<sup>1</sup> = OMe    R<sup>2</sup> = OAc  
**21** R<sup>1</sup> = OEt    R<sup>2</sup> = OAc  
**24** R<sup>1</sup> = OH    R<sup>2</sup> = OH  
**25** R<sup>1</sup> = OMe    R<sup>2</sup> = OH  
**26** R<sup>1</sup> = OEt    R<sup>2</sup> = OH



- 17** R<sup>1</sup> = CO<sub>2</sub>H    R<sup>2</sup> = OAc    R<sup>3</sup> = OAc  
**18** R<sup>1</sup> = CO<sub>2</sub>Me    R<sup>2</sup> = OAc    R<sup>3</sup> = OAc  
**19** R<sup>1</sup> = CO<sub>2</sub>Me    R<sup>2</sup> = H    R<sup>3</sup> = OAc  
**27** R<sup>1</sup> = CO<sub>2</sub>H    R<sup>2</sup> = OH    R<sup>3</sup> = OH  
**28** R<sup>1</sup> = CO<sub>2</sub>H    R<sup>2</sup> = H    R<sup>3</sup> = OH



**29**

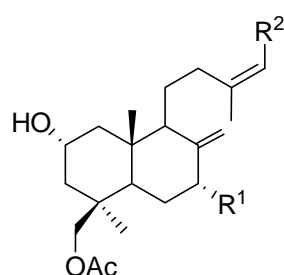


- 30** R<sup>1</sup> = Ac  
**31** R<sup>1</sup> = H

Many of the diterpenoids isolated from *Hyptis dilatata* show heterocyclic rings of 20,6- and 20,7-lactones. Also the known<sup>19</sup> heterocyclic 20,11-lactone **29** was isolated. All the **8-29** products show the abietane skeleton. Another known compound, diacetyl-esquirolin B **30**<sup>20</sup> was also isolated, but it has an isopimarane skeleton (not pimarane, as written in the original paper). Probably, also in this case, the plant contained the non-acetylated esquirolin B **31**.

Seven new products have been isolated from the aerial parts of *Hyptis spicigera* occurring in Mexico,<sup>21</sup> and popularly known as "hierba del burro". It is remarkable that these compounds show a different skeleton, as they are labdane derivatives. They were not given trivial names. On the basis of spectroscopic determinations and functional groups chemical modifications they were attributed the following structures.

The first product has the structure **32** of 19-acetoxy-2 $\alpha$ ,7 $\alpha$ ,15-trihydroxy-labda-8(17),(13Z)-diene. The other new products are 15,19-diacetoxy-2 $\alpha$ ,7 $\alpha$ -dihydroxy-labda-8(17),(13Z)-diene **33**; 7 $\alpha$ ,15,19-triacetoxy-2 $\alpha$ -hydroxy-labda-8(17),(13Z)-diene **34**; 19-acetoxy-2 $\alpha$ ,7 $\alpha$ -dihydroxy-labda-8(17),(13Z)-dien-15-al **35**; 19-acetoxy-7 $\alpha$ ,15-dihydroxy-labda-8(17),(13Z)-dien-2-one **36**; 19-acetoxy-2 $\alpha$ ,7 $\alpha$ -dihydroxy-labda-14,15-dinor-labd-8(17)-en-13-one **37**; 2 $\alpha$ ,7 $\alpha$ ,15,19-tetrahydroxy-*ent*-labda-8(17),(13Z)-diene **38**. It is remarkable that product **38** has the *ent*-labdane skeleton, whereas the **33-37** products have the normal labdane backbone.

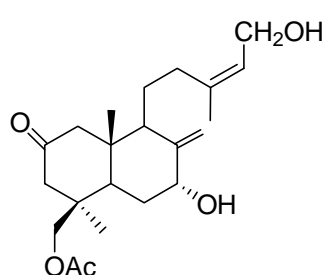


**32** R<sup>1</sup> = OH R<sup>2</sup> = CH<sub>2</sub>OH

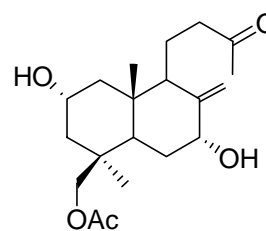
**33** R<sup>1</sup> = OH R<sup>2</sup> = CH<sub>2</sub>OAc

**34** R<sup>1</sup> = OAc R<sup>2</sup> = CH<sub>2</sub>OAc

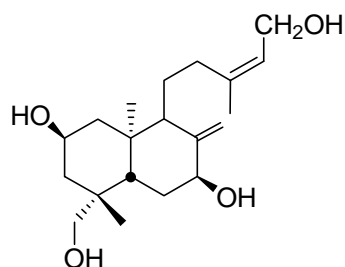
**35** R<sup>1</sup> = OH R<sup>2</sup> = CHO



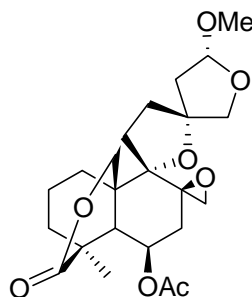
**36**



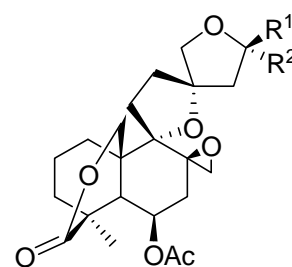
**37**



**38**



**39**

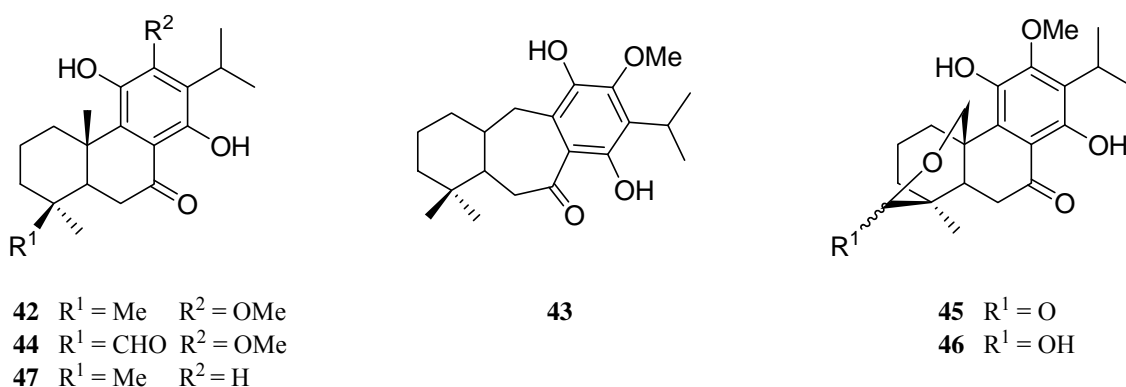


**40** R<sup>1</sup> = OMe R<sup>2</sup> = H

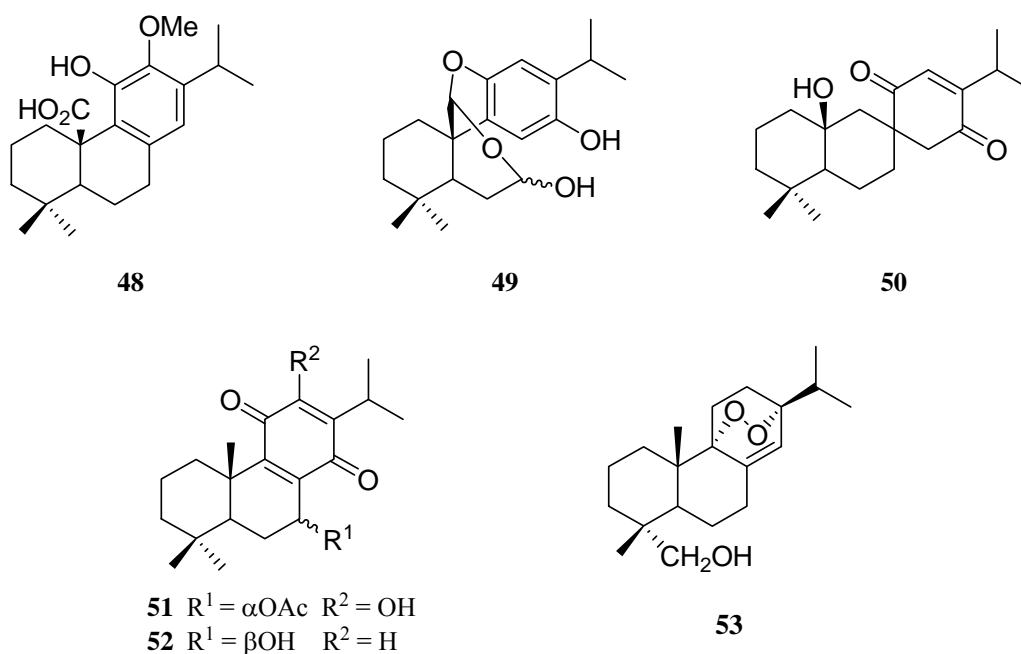
**41** R<sup>1</sup> = H R<sup>2</sup> = OMe

Three diterpenoids, also in this case with the labdane skeleton, have been found in the aerial parts of *Hyptis fasciculata* collected in Brazil.<sup>22</sup> The first product was identified as the known<sup>23</sup> methoxynepetaefolin **39**, showing four oxygenated rings, whilst the others are new natural products, 15 $\beta$ -methoxyfasciculatin **40** and 15 $\alpha$ -methoxyfasciculatin **41**, both also rich in oxygenated rings.

A recent paper<sup>24</sup> reports on the investigation of the roots of *Hyptis platanifolia*, again from Brasil. Five abietane derivatives were isolated: two of them are the known inuroyleanol **42**<sup>25</sup> and coulterone **43**,<sup>25</sup> whilst new products are 19-oxo-inuroyleanol **44**, 11,14-dihydroxy-12-methoxy-7-oxo-8,11,13-abietatrien-19,20 $\beta$ -olide **45** and 19,20-epoxy-12-methoxy-11,14,19-trihydroxy-7-oxo-8,11,13-abietatriene **46**, the last as a diastereoisomeric mixture at the 19-hydroxy group. No trivial names were given to these new products. Both products **45** and **46** have a lactone or lactol 20,19-ring.



Another species from Northeastern Brazil is *Hyptis martiusii*, popularly known as “cidreira-do-mato”, whose roots were investigated. A paper<sup>26</sup> reported the isolation of two known diterpenoids: carnosol **8**<sup>10</sup> and 11,14-dihydroxy-8,11,13-abietatrien-7-one **47**.<sup>27</sup> In a second paper<sup>28</sup> some new diterpenes were described: 12-O-methyl-carnosic acid **48**, the structurally interesting 7-seco-7(20),11(20)-diepoxy-7,14-dihydroxy-abieta-8,11,13-triene **49**, and a product **50** with a rearranged abietane skeleton, designated as martiusane. In continuation<sup>29</sup> two more abietane diterpenes were found: the known 7 $\alpha$ -acetoxy-royleanone **51**<sup>30</sup> and the new 7 $\beta$ -hydroxy-11,14-dioxo-abieta-8,12-diene **52**.

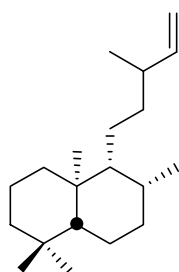
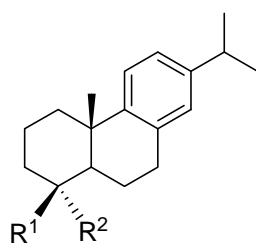
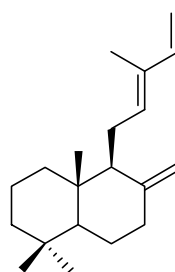
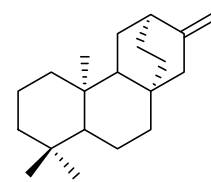
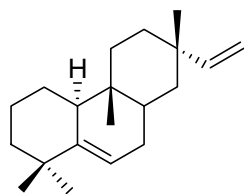
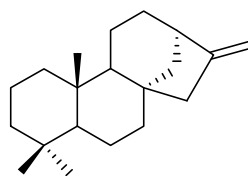
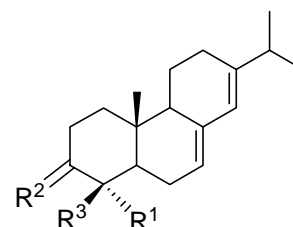
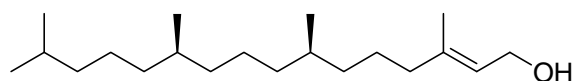
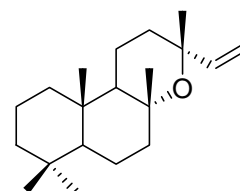


An abietane diterpenoid with high antiplasmodial activity was isolated<sup>31</sup> from the leaves of *Hyptis suaveolens* collected in Nigeria. It has the structure **53** of 9 $\alpha$ ,13 $\alpha$ -*epi*-dioxiabiet-8(14)-en-18-ol. The same product had been isolated from *Cedrus atlantica*.<sup>32</sup>

The **1-53** diterpenoids here listed were isolated from the aerial parts or from the roots or from the whole plant. A large number of investigations on the essential oils of this genus was performed for the

identification of their components, almost exclusively mono- and sesquiterpenes. However in one case also the occurrence of minor amounts of some diterpenes was detected.

This the case of the oil from *Hyptis suaveolens*, largely studied. A first paper<sup>33</sup> on material collected in Venezuela quoted the presence of three unidentified diterpenes. In a sample of the oil from Malaysia the GC analysis indicated the occurrence of six unidentified diterpenes.<sup>34</sup> In a sample of oil from Nigeria<sup>35</sup> the occurrence of a diterpene hydrocarbon was reported, indicated as 5 $\beta$ H,8 $\beta$ H,9 $\beta$ H,10 $\alpha$ -labd-14-ene **54** but no structural formula was given. Two diterpenes, 8,11,13-abietatriene **55** and 8,11,13-abietatrien-18-ol **56** (syn. dehydroabietol, dehydroabietinol) were identified in the oil from Kumaon, India.<sup>36</sup> Particularly rich in diterpenoids was the oil from Cameroon:<sup>37</sup> biformene **57**, atisirene **58**, rimuene **59**, abietatriene **55**, phyllocladene **60**, abietinol **61** (syn. abietol), dehydroabietol **56** and the linear diterpene phytol **62** were identified. The oil from North India<sup>38</sup> contained abietadiene **63**, abietatriene **55** and dehydroabietol **56**. Many products occurred in the oil from Alfenas (Brazil).<sup>39,40</sup> abietatriene **55**, abietadiene **63**, abieta-7,13-dien-3-one **64**, abietinol **61**, 4-epi-abietinol **65**,<sup>41, 42</sup> dehydroabietol **56**, manoyloxide **66**. Remarkable differences were observed in the content of diterpenes (and also of monoterpenes and sesquiterpenes) depending on the geographical origin of the oil and on the season of harvesting.

**54****55** R<sup>1</sup> = Me R<sup>2</sup> = Me**56** R<sup>1</sup> = Me R<sup>2</sup> = CH<sub>2</sub>OH**57****58****59****60****61** R<sup>1</sup> = CH<sub>2</sub>OH R<sup>2</sup> = H,H R<sup>3</sup> = Me**63** R<sup>1</sup> = Me R<sup>2</sup> = H,H R<sup>3</sup> = Me**64** R<sup>1</sup> = Me R<sup>2</sup> = O R<sup>3</sup> = Me**65** R<sup>1</sup> = Me R<sup>2</sup> = H,H R<sup>3</sup> = CH<sub>2</sub>OH**62****66**

As far as we know, no occurrence of diterpenoids in other oils is reported in the literature.

Concerning the structure of these diterpenoids, it can be remarked that they show the abietane or the labdane skeleton prevalently; only few have different skeleta.

## BIOLOGICAL ACTIVITY AND PHARMACOLOGY

The most diffused utilization of species belonging to the *Hyptis* genus is related to their essential oils, obtained, also in industrial scale, from several species. Such oils are largely used in cosmetics and flavouring and as insecticides and insect repellents. Dried whole plants are used for pest control. Oils, parts of plants and extracts find diffused application in ethnopharmacology of tropical countries.

About the biological activities and related pharmacology, wide information is reported in a review<sup>2</sup> and references therein. Rarely such activities were attributed to single diterpenoids<sup>2,21,26,29</sup> or to the whole mixtures of terpenoids, but usually to the oils or to the extracts in different solvents. In the case of *H. martiusii*, the cytotoxic and antimitotic activity was tested on the pure diterpenoids.<sup>26,29</sup> The diterpenoids from *H. spicigera* inhibit the larval growth of the European corn borer.<sup>21</sup>

Therefore, many reports are concerned with activities as expectorant, antihelminthic, antibacteric, antimicrobial, antiviral, antibiotic, antimicrobial, antiseptic, antimalaric, antidolorific, anticonvulsive, antioxidant, cytotoxic, anti-tumour. Preparations are used against gastrointestinal disorders, fevers, grippe, cough, asthma, cramps, conjunctivitis, depression, and the most various ailments.

The extract of *H. spicigera* shows antimicrobial, phytotoxic and antifungine properties, and cytotoxic activity on KB cells.<sup>45,21</sup> The powdered plant is used as insecticide in Africa.<sup>43</sup>

The ethanolic extract of *H. umbrosa* has a significant antimicrobial activity.<sup>8</sup> Also the methanolic extract of *H. salzmanii* is active against *Staphylococcus aureus*, *Bacillus subtilis*, *Candida albicans* and *Mycobacterium smegmatis*.<sup>7</sup> The methanolic extract of *H. albida* is active against *C. albicans* and other Gram-positive and Gram-negative bacteria,<sup>44</sup> and used in Mexico against gastroenteric diseases.<sup>45</sup>

Some *Hyptis* species are active against schistosomiasis.<sup>46</sup>

The essential oil of *H. mutabilis* has antiulcerogenic activity,<sup>47</sup> and the essential oil of *H. lanceolata* shows antifungine properties.<sup>48</sup> Extracts of leaves of *H. mutabilis* are used in Mexico and Brazil against malaria and numberless ailments.<sup>47,49</sup>

The oil from *H. pectinata* has insecticide<sup>50</sup> and antiseptic<sup>51</sup> activity. Extracts of *H. pectinata* have antimicrobial, antibacteric activity<sup>44,51</sup> and are cytotoxic against various cancer cells;<sup>51</sup> the aqueous extract is antinociceptive and antiedematogenic.<sup>52</sup> It is widely used in Mexico and West Africa.<sup>53</sup>

The methanolic extract of the roots of *H. fruticosa* shows antibacteric and anti-tumour activity.<sup>4,54</sup>

Terpenoids from *H. emoryi* have been investigated as antifertilizing agents<sup>55</sup> and tumour-inhibitors.<sup>56</sup> A triterpene from *H. rombooides* is cytotoxic in vitro against cells of human hepatome HS-G2.<sup>57</sup>

Extracts of the whole plant of *H. capitata* are reported to be active against HIV, leucemia, many species of cancer, and to have anti-inflammatory, anti-arthritic, anti-diabetic, anti-ulcera, anti-atherosclerosis properties.<sup>58</sup>

*H. verticillata* has various activities: insecticide, acaricide,<sup>59</sup> anticancer,<sup>60</sup> anti-inflammatory, cytotoxic, antimitotic,<sup>61</sup> antimicrobial.<sup>44</sup>

The most investigated species is certainly *H. suaveolens*, largely employed in ethnomedicine of Mexico, Brazil, Central and South America, West Africa, India. Roots, leaves, flowers are commonly used. The oil is active as antimicrobial,<sup>35,62,63</sup> antibacterial,<sup>64</sup> fungicide,<sup>35,48,65</sup> larvicide against *Aedes aegypti*, and also against *Vibrio cholerae*.<sup>66</sup> A tea prepared from the roots is used as stomachic<sup>67</sup> in India. The aqueous extract has antinociceptive activity.<sup>68</sup>

A recent paper<sup>69</sup> reported the anti-inflammatory activity of suaveolic acid (**1**) and suavelol (**2**) occurring in *Hyptis suaveolens* collected in El Salvador; these diterpenoids had been isolated previously<sup>3</sup> from the same species.

Table 1 Diterpenes from genus *Hyptis*

No	name	taxa	Ref.
1	suaveolic acid	<i>H. suaveolens</i> (A)	3
2	suavelol	<i>H. suaveolens</i> (A)	3
3	horminone	<i>H. fruticosa</i> (R)	4
4	14-methoxy-taxodione	<i>H. fruticosa</i> (R)	4
5	hyptol	<i>H. fruticosa</i> (R)	6
6	salzol	<i>H. salzmanii</i> (A)	7
7	umbrosone	<i>H. umbrosa</i> (R)	8
8	carnosol	<i>H. dilatata</i> (A)	9
		<i>H. martiusii</i> (R)	26
9	rosmanol	<i>H. dilatata</i> (A)	9
10	methylrosmanol	<i>H. dilatata</i> (A)	9
11	diacetyl-carnosol	<i>H. dilatata</i> (A)	9
12	triacetyl-rosmanol	<i>H. dilatata</i> (A)	9
13	diacetyl-methylrosmanol	<i>H. dilatata</i> (A)	9
14	diacetyl-ethylrosmanol	<i>H. dilatata</i> (A)	9
15	triacetyl-isorosmanol	<i>H. dilatata</i> (A)	9
16	triacetyl-epirosmanol	<i>H. dilatata</i> (A)	9
17	diacetyl-carnosic acid	<i>H. dilatata</i> (A)	9



18	diacetyl-carnosic acid methyl ester	<i>H. dilatata</i> (A)	9
19	acetyl-pisiferic acid methyl ester	<i>H. dilatata</i> (A)	9
20	diacetyl-epimethylrosmanol	<i>H. dilatata</i> (A)	9
21	diacetyl-epiethylrosmanol	<i>H. dilatata</i> (A)	9
22	ethylrosmanol	<i>H. dilatata</i> (A)	9
23	isorosmanol	<i>H. dilatata</i> (A)	9
24	epirosmanol	<i>H. dilatata</i> (A)	9
25	epimethylrosmanol	<i>H. dilatata</i> (A)	9
26	epiethylrosmanol	<i>H. dilatata</i> (A)	9
27	carnosic acid	<i>H. dilatata</i> (A)	9
28	pisiferic acid	<i>H. dilatata</i> (A)	9
29	lactone	<i>H. dilatata</i> (A)	9
30	diacetyl-esquirolin B	<i>H. dilatata</i> (A)	9
31	esquirolin B	<i>H. dilatata</i> (A)	9
32	19-acetoxy-2 $\alpha$ ,7 $\alpha$ ,15-trihydroxy-labda-8(17),(13Z)-diene	<i>H. spicigera</i> (A)	21
33	15,19-diacetoxy-2 $\alpha$ ,7 $\alpha$ -dihydroxy-labda-8(17),(13Z)-diene	<i>H. spicigera</i> (A)	21
34	19,7 $\alpha$ ,15-triacetoxy-2 $\alpha$ -hydroxy-labda-8(17),(13Z)-diene	<i>H. spicigera</i> (A)	21
35	19-acetoxy-2 $\alpha$ ,7 $\alpha$ -dihydroxy-labda-8(17),(13Z)-diene-15-al	<i>H. spicigera</i> (A)	21
36	19-acetoxy-7 $\alpha$ ,15-dihydroxy-labda-8(17),(13Z)-dien-2-one	<i>H. spicigera</i> (A)	21
37	19-acetoxy-2 $\alpha$ ,7 $\alpha$ -dihydroxy-labda-14,15-dinor-labd-8(17)-en-13-one	<i>H. spicigera</i> (A)	21
38	2 $\alpha$ ,7 $\alpha$ ,15,19-tetrahydroxy- <i>ent</i> -labda-8(17),(13Z)-diene	<i>H. spicigera</i> (A)	21
39	methylnepetaefolin	<i>H. fasciculata</i> (A)	22
40	15 $\beta$ -methoxyfasciculatin	<i>H. fasciculata</i> (A)	22
41	15 $\alpha$ -methoxyfasciculatin	<i>H. fasciculata</i> (A)	22
42	inuroyleanol	<i>H. platanifolia</i> (R)	24
43	coulterone	<i>H. platanifolia</i> (R)	24
44	19-oxo-inuroyleanol	<i>H. platanifolia</i> (R)	24
45	11,14-dihydroxy-12-methoxy-7-oxo-8,11,13-abietatrien-19,20- $\beta$ -olide	<i>H. platanifolia</i> (R)	24
46	19,20-epoxy-12-methoxy-11,14,19-trihydroxy-7-oxo-8,11,13-abietatriene	<i>H. platanifolia</i> (R)	24
47	11,14-dihydroxy-8,11,13-abietatrien-7-one	<i>H. martiusii</i> (R)	26
48	12-O-methyl-carnosic acid	<i>H. martiusii</i> (R)	28
49	7-seco-7(20),11(20)-diepoxy-7,14-dihydroxy-abieta-8,11,13-triene	<i>H. martiusii</i> (R)	28
50	martiusane	<i>H. martiusii</i> (R)	28
51	7 $\alpha$ -acetoxy-royleanone	<i>H. martiusii</i> (R)	29
52	7 $\beta$ -hydroxy-11,14-dioxo-abieta-8,12-diene	<i>H. martiusii</i> (R)	29

53	9 $\alpha$ ,13 $\alpha$ - <i>epi</i> -dioxiabiet-8(14)-en-18-ol	<i>H. suaveolens</i> (A)	31
54	5 $\beta$ H,8 $\beta$ H,9 $\beta$ H,10 $\alpha$ -labd-14-ene	<i>H. suaveolens</i> (EO)	35
55	8,11,13-abietatriene	<i>H. suaveolens</i> (EO)	36-40
56	8,11,13-abietatrien-18-ol	<i>H. suaveolens</i> (EO)	36,38-40
57	biformene	<i>H. suaveolens</i> (EO)	37
58	atisirene	<i>H. suaveolens</i> (EO)	37
59	rimuene	<i>H. suaveolens</i> (EO)	37
60	phyllocladene	<i>H. suaveolens</i> (EO)	37
61	abietinol	<i>H. suaveolens</i> (EO)	37,39-40
62	phytol	<i>H. suaveolens</i> (EO)	37
63	abietadiene	<i>H. suaveolens</i> (EO)	38,39-40
64	abieta-7,13-dien-3-one	<i>H. suaveolens</i> (EO)	39,40
65	4- <i>epi</i> -abietinol	<i>H. suaveolens</i> (EO)	39,40
66	manoyloxide	<i>H. suaveolens</i> (EO)	39,40

R = roots. A = aerial parts. EO = essential oil.

## REFERENCES

1. J. C. Willis (1966), "A dictionary of the flowering plants and ferns", 7<sup>th</sup> edition, Cambridge University Press, 1966.
2. D. Q. Falcao and F. S. Menezes, *Rev. Bras. Farm.*, 2003, **84**, 69.
3. P. S. Manchand, J. D. White, J. Fayos, and J. Clardy, *J. Org. Chem.*, 1974, **39**, 2306.
4. F. Marletti, F. Delle Monache, G. B. Marini-Bettolo, M. De Araujo, M. Cavalcanti, I. L. De Albuquerque, and O. G. De Lima, *Gazz. Chim. Ital.*, 1976, **106**, 119.
5. M. M. Janot and P. Poitier, *Ann. Pharm. Fr.*, 1964, **22**, 387.
6. F. Delle Monache, F. Marletti, G. B. Marini-Bettolo, J. F. De Mello, and I. L. De Albuquerque, *Gazz. Chim. Ital.*, 1977, **107**, 319.
7. I. Messana, F. Ferrari, M. A. De Moraes Souza, and E. Gàcs-Baitz, *Phytochemistry*, 1990, **29**, 329.
8. F. Delle Monache, G. Delle Monache, E. Gàcs-Baitz, J. S. De Barros Coelho, J. L. De Albuquerque, A. De Andrade Chiappeta, and J. F. De Mello, *Phytochemistry*, 1990, **29**, 3971.
9. J. G. Urones, I. S. Marcos, D. Diez, and L. R. Cubilla, *Phytochemistry*, 1998, **48**, 1035.
10. C. H. Brieskorn, A. Fuchs, J. B. Bredenberg, J. D. McChesney, and E. Wenkert, *J. Org. Chem.*, 1964, **29**, 2293.
11. R. Inatani, N. Nakatani, H. Fuwa, and H. Seto, *Agric. Biol. Chem.*, 1982, **46**, 1661.
12. B. M. Fraga, A. G. Gonzalez, J. R. Herrera, J. G. Luis, and A. G. Ravelo, *Phytochemistry*, 1985, **24**, 1853.

13. M. Arisawa, T. Hayashi, K. Ohmura, K. Nagayama, M. Shimizu, N. Morita, and L. Berganza, *J. Nat. Prod.*, 1987, **50**, 1164.
14. A. G. Gonzalez, S. L. Andrés, J. R. Herrera, J. G. Luis, and A. G. Ravelo, *Can. J. Chem.*, 1989, **67**, 208.
15. N. Nakatani and N. Inatani, *Agric. Biol. Chem.*, 1984, **48**, 2081.
16. A. G. Gonzalez, C. M. Rodriguez, and J. G. Luis, *Phytochemistry*, 1987, **26**, 1471.
17. H. M. G. Al-Hazimi, *Phytochemistry*, 1986, **25**, 1238.
18. J. Geiwiz and E. Haslinger, *Helv. Chim. Acta*, 1995, **78**, 818.
19. Z. Djarmati, R. M. Jankov, A. Djordjevic, B. Ribar, D. Lazar, and P. Engel, *Phytochemistry*, 1992, **31**, 1307.
20. C. Li, Z. Lin, H. Zheng, J. Zhang, and H. Sun, *Chin. Chem. Lett.*, 1991, **2**, 223.
21. M. Fragoso-Serrano, E. Gonzalez-Chimeo, and R. Pereda-Miranda, *J. Nat. Prod.*, 1999, **62**, 45.
22. A. Ohsaki, Y. Kishimoto, T. Isobe, and Y. Fukuyama, *Chem. Pharm. Bull.*, 2005, **53**, 1577.
23. P. S. Manchand, *Tetrahedron Lett.*, 1973, 1907.
24. E. C. C. Araùjo, M. A. S. Lima, E. P. Nunes, and E. R. Silveira, *J. Braz. Chem. Soc.*, 2005, **16**, 1336.
25. B. Frontana, J. Càrdenas, and L. Rodriguez-Hahn, *Phytochemistry*, 1994, **36**, 739.
26. L. V. Costa-Lotufo, E. C. C. Araùjo, M. A. S. Lima, M. E. A. Moraes, C. Pessoa, S. Silveira, and M. O. Moraes, *Pharmazie*, 2004, **59**, 78.
27. Y. H. Kuo, C. H. Chen, and S. L. Huang, *J. Nat. Prod.*, 1998, **61**, 829.
28. E. C. C. Araùjo, M. A. S. Lima, and E. R. Silveira, *Magn. Reson. Chem.*, 2004, **42**, 1049.
29. E. C. C. Araùjo, M. A. S. Lima, R. C. Montenegro, M. Nogueira, L. V. Costa-Lotufo, C. Pessoa, M. O. Moraes, and E. R. Silveira, *Z. Naturforsch. C*, 2006, **61**, 177.
30. M. Hensch, P. Ruedi, and C. H. Eugster, *Helv. Chim. Acta*, 1975, **58**, 1921.
31. J. C. Chukwujekwu, P. Smith, P. H. Coombes, D. A. Mulholland, and J. van Staden, *J. Ethnopharmacol.*, 2005, **102**, 295.
32. A. F. Barrero, J. F. Quilez del Moral, M. Mar Arrador, J. F. Arteaga, M. Akssira, A. Benharref, and M. Dakir, *Phytochemistry*, 2005, **66**, 105.
33. S. E. Flores and J. D. Medina, *Acta Cientif. Venezolana*, 1970, **21**, 161.
34. L. D. Din, Z. Zakaria, M. W. Samsudin, J. Brophy, and R. F. Tota, *Pertanika*, 1988, **11**, 239.
35. M. M. Iwu, C. O. Ezeugwu, C. O. Okunji, D. R. Sanson, and M. S. Tempesta, *Intern. J. Crude Drug Res.*, 1990, **28**, 73.
36. A. K. Pant, A. K. Singh, C. S. Mathela, R. Parihar, and V. Dev, *J. Essent. Oil Res.*, 1992, **4**, 13.
37. M. B. Ngassoum, L. Jirovetz, and G. Buchbauer, *J. Essent. Oil Res.*, 1999, **11**, 283.
38. V. S. Rana, J. P. Juyal, Rashmi, and M. A. Blazquez, *Intern. J. Aromather.*, 2004, **14**, 198.

39. F. T. Martins, M. H. Santos, M. Polo, and L. C. A. Barbosa, *Quim. Nova*, 2006, **29**, 1203.
40. F. T. Martins, M. H. Santos, M. Polo, and L. C. A. Barbosa, *Flavour Fragr. J.*, 2007, **22**, 123.
41. C. Tabacik and C. Poisson, *Phytochemistry*, 1971, **10**, 1639.
42. B. Marongiu, S. Porcedda, A. Caredda, A. Pira, L. Vargiu, V. Massa, S. Cadeddu, and R. Loddo, *J. Essent. Oil Res.*, 2004, **16**, 256.
43. J. P. Aycard, F. Kini, B. Kam, E. M. Gaydou, and R. Faure, *J. Nat. Prod.*, 1993, **56**, 1171.
44. A. Rojas, L. Hernandez, R. Pereda-Miranda, and R. Mata, *J. Ethnopharmacol.*, 1992, **35**, 275.
45. R. Pereda-Miranda, and G. Delgado, *J. Nat. Prod.*, 1990, **53**, 182.
46. B. Gilbert, J. P. De Souza, M. Fascio, M. Kitagawa, S. S. C. Nascimento, C. C. Fortes, A. P. Seabra, and J. Pellegrino, *An. Acad. Bras. Cienc.*, 1970, **42**, 397.
47. P. P. P. Barbosa and C. P. Barbosa, *Phytother. Res.*, 1992, **6**, 114.
48. P. H. A. Zollo, L. Biyiti, F. Tchoumboungang, C. Menut, G. Lamaty, and P. H. Bouchet, *Flav. Fragr. J.*, 1998, **13**, 107.
49. R. Pereda-Miranda and M. Gascon-Figueroa, *J. Nat. Prod.*, 1988, **53**, 182.
50. M. Pietschmann, O. Vostrowsky, H. J. Bestmann, A. K. Pant, and C. S. Mathela, *J. Essent. Oil Res.*, 1998, **10**, 550.
51. R. Pereda-Miranda, L. Hernandez, M. J. Villavicencio, M. Novelo, P. Ibarra, H. Chai, and J. M. Pezzuto, *J. Nat. Prod.*, 1993, **56**, 583.
52. M. D. Bispo, R. H. V. Mourao, E. M. Franzotti, K. B. R. Bomfim, M. D. Arrigoni-Blank, M. P. N. Moreno, M. Marchioro, and A. R. Antonioli, *J. Ethnopharmacol.*, 2001, **76**, 81.
53. K. A. Malan, Y. Pelissier, J. M. Bessiere, and F. Pellerin, *Plant Med. Phytother.*, 1989, **23**, 86.
54. M. C. M. Araujo, M. S. B. Cavalcanti, J. F. Mello, I. L. Albuquerque, O. G. Lima, F. Delle Monache, G. M. Maciel, and A. L. Lacerda, *Rev. Inst. Antibiot.*, 1974, **14**, 101.
55. B. D. Tanowitz, S. A. Junak, and D. M. Smith, *J. Nat. Prod.*, 1984, **47**, 739.
56. K. Sheth, S. Jolad, R. Wiedhopf, and J. R. Cole, *J. Pharm. Sci.*, 1972, **61**, 1819.
57. Y. L. Lin, H. P. Lee, R. L. Huang, J. C. Ou, and Y. H. Kuo, *Zhonghua Yaoxue Zazhi*, 1993, **45**, 61.
58. K. H. Lee, Y. M. Lin, T. S. Wu, D. C. Zhang, T. Yamagishi, T. Hayashi, I. H. Hall, J. J. Chang, R. Y. Wu, and T. H. Yang, *Planta Med.*, 1988, **54**, 308.
59. R. B. R. Porter, P. B. Reese, and D. J. Williams, *Phytochemistry*, 1995, **40**, 735.
60. M. Kuhnt, A. Proebstle, H. Rimpler, R. Bauer, and M. Heinrich, *Planta Med.*, 1995, **61**, 227.
61. V. E. A. German, *J. Pharm. Sci.*, 1971, **60**, 649.
62. B. G. V. N. Rao, and S. Adinarayana, *Riechst. Aromen Koerperpflagem.*, 1970, **20**, 220.
63. O. T. Asekun, O. Ekundayo, and B. A. Adeniyi, *Fitoterapia*, 1999, **70**, 440.
64. S. R. Jain, P. R. Jain, and M. R. Jain, *Planta Med.*, 1974, **26**, 196.

65. H. B. Singh, R. K. Handique, and G. P. Rao, *Fitoterapia*, 1992, **63**, 462.
  66. A. Kar and S. R. Jain, *Qual. Plant Mater. Veg.*, 1971, **20**, 231.
  67. T. N. Misra, R. S. Singh, T. N. Ojha, and J. Upadhyay, *J. Nat. Prod.*, 1981, **44**, 735.
  68. T. C. Santos, M. S. Marques, I. A. C. Menezes, K. S. Dias, A. B. L. Silva, I. C. M. Mello, A. C. S. Carvalho, S. C. H. Cavalcanti, A. R. Antonioli, and R. M. Marcal, *Fitoterapia*, 2007, **78**, 333.
  69. P. Grassi, T. S. Urias Reyes, S. Sosa, A. Tubaro, O. Hofer, and K. Zitterl-Eglseer, *Z. Naturforsch. C*, 2006, **61**, 165.
- 



**Franco Piozzi** was born in Milan in 1928. He obtained a BSc in Industrial Chemistry in 1949 (University of Milan), a BSc in Pharmacy in 1952 (University of Pavia) and the PhD in 1958 under the guidance of Prof. Adolfo Quilico at the Polytechnic School of Milan, where he was lecturer and then assistant professor (1951-1965). In 1965 he was appointed at the University of Palermo, as professor of Organic Chemistry until 2003. Formally retired November 2003, he is still active in research at the Department of Organic Chemistry. Research fields: in the 1950-1970 period he was interested in heterocyclic chemistry, in the chemistry of some alkaloids, and in the structure elucidation of natural terpenoids. After 1970 he is interested exclusively in the chemistry of natural products, especially diterpenoids. He is the author of more than 290 scientific publications. In the 1978, 1979, 1981, 1983, 1989 years he was lecturer for semestral courses of Organic Chemistry at the Somali National University in Mogadishu.



**Prof. Maurizio Bruno** was born in Rome in 1957. Degree in Chemistry in 1980. From 1983 to 1992 assistant professor at the Department of Organic Chemistry, University of Palermo. From 1985 to 1986 he worked at the Florida State University with Prof. Werner Herz and from 1987 to 1988 at the Imperial College, London, with Prof. Steven Ley. He was appointed to the faculty of Engineering (University of Palermo) as associated professor (1992-2000) and then as full professor of Organic Chemistry (2000-present). From 2002 he has been included in the ISI list as one of the most cited researcher in the world. In 2005 the President of the Italian Republic appointed him as “Commendatore dell’Ordine al Merito della Repubblica Italiana” for his contributions to the scientific research. He works in natural organic products chemistry on natural and semisynthetic terpenoids with antifeedant activity. Lately he is interested in sesquiterpenes from Compositae, in natural and semisynthetic compounds with anti-HIV and cytotoxic activity and in the extraction and analysis of essential oils with antibacterial properties. He is author of more than 170 papers on international journals.



**Dr. Sergio Rosselli** was born in Palermo in 1970. In 1995 He obtained the degree in chemistry with honour. In 1996, he attended the PhD course in Technology of Biological Active Compounds working on the developing of new drug carriers. Since December 1997, he is assistant professor in organic chemistry in the faculty of science of Palermo University, and he works in Organic Chemistry Department. His research field concerns the study of secondary metabolites from plants: isolation, structural elucidation, synthesis and chemical modification of bioactive compounds. He is mainly interested in terpenoids with antifeedant, antibacterial and cytotoxic activities.



**Dr. Antonella Maggio** was born in Erice (TP) in 1971. Degree in Chemistry in 1995. PhD in Organic Chemistry in 1999. From 1996 to 1998 she worked at CSIC (Spain) with prof. Benjamin Rodriguez. From 1999 to 2003 she works to contract with prof. Franco Piozzi. From 2004 she is assistant professor at the Department of Organic Chemistry, University of Palermo.

She works in natural organic products chemistry. She is interested in sesquiterpenes, terpenoids and flavones from Mediterranean plants. The research deals with natural and semisynthetic compounds with anti-HIV, cytotoxic and antifeedant activity. She is author of 30 papers on international journals.