Pharmacological Properties of Myrtacine® and Its Potential Value in Acne Treatment

Authors

Christel Fiorini-Puybaret¹, Marie-Françoise Aries², Bernard Fabre¹, Stelianos Mamatas³, Joëlle Luc⁴, Arnaud Degouy², Marco Ambonati⁵, Carine Mejean⁵, Florence Poli⁶

Affiliations

The affiliations are listed at the end of the article

Key words

- Myrtus communis
- Myrtaceae
- acne
- inflammation
- antibacterial activity
- myrtucommulones
- keratinocyte proliferation

Abstract

This study aimed at evaluating the antiproliferative, antibacterial, and anti-inflammatory properties of an ethanolic myrtle extract (Myrtacine®) in vitro, characterising its potential active compounds (myrtucommulones A and B) by structural analysis, and evaluating their biological activity. Antiproliferative activity was assessed by the BrdU incorporation assay in HaCat keratinocytes and inhibitory and bactericidal activities against P. acnes strains by measuring the minimal inhibitory concentration (MIC) and D value. Anti-inflammatory effect was evaluated by measuring 6-keto-prostaglandin F1α and [3H]-arachidonic acid metabolite production in keratinocytes stimulated for inflammation. Myrtacine® inhibited keratinocyte proliferation by 27% and 76% at 1 and 3 µg/mL, respectively (p < 0.001). A comparable effect, though less marked, was observed with 5 µg/mL myrtucommulone A and B (~36% and ~28%, respectively). Myrtacine® inhibited erythromycin-sensible and -resistant P. acnes strains growth with MICs of 4.9 µg/mL and 2.4 µg/mL, respectively. Myrtucommulone B and myrtucommulone A displayed a similar inhibitory activity against both strains (for both strains, MIC = 1.2 µg/mL and about 0.5 µg/mL, respectively). At 3 and 10 µg/mL, Myrtacine® significantly decreased all metabolite production from cyclooxygenase (81% and 107%, p < 0.0001) and lipoygenase (52% and 95%, p < 0.001) pathways. Finally, Myrtacine® exhibited a concentration-dependent anti-lipase activity at 100 µg/mL and 1 mg/mL, as it decreased lipase activity by respectively 53% and 100% (p < 0.01 for both). In conclusion, in vitro, Myrtacine® demonstrated antiproliferative, antibacterial, and anti-inflammatory properties that may be of value to exert a global action in the treatment of acne lesions.

Supporting information available online at http://www.thieme-connect.de/ejournals/toct/plantamedica

Introduction

Acne is a common disease whose pathogenesis is not fully understood. At least four factors are known to promote the development of acne: hyperseborrhea, hyperkeratosis and ductal cornification, Propionibacterium acnes colonisation of pilosebaceous ducts, and inflammation, which is rather a consequence of the other three factors [1, 2]. Most patients only suffer from mild to moderate acne comedonica or papulopustulosa Grade I–II, whose first-line treatment generally consists of topical agents whereas systemic treatment is indicated for higher grades of acne [1]. Currently, no topical treatment showed a significant activity against all the pathogenic factors of acne, whether it be retinoids, antibiotics, or benzoyl peroxide [1]. Therefore, treatment strategies combining two or three agents are currently recommended by the national and international guidelines for the management of mild to moderate acne, due to their higher tolerance and efficacy [3, 4]. Studies on pharmacological properties of Myrtus communis (Myrtaceae) mainly deal with its specific compounds, nonprenylated acylphloroglucinols. They have been reported to possess antibacterial activity against certain microorganisms [5–7], but also antifungal [8] and antioxidant properties [9]. Furthermore, a study recently showed that myrtucommulones from myrtle might possess anti-inflammatory potential [10]. However, their antibacterial activity against P. acnes has never been evaluated.

Our in vitro studies aimed at determining whether Myrtacine®, ethanolic myrtle extract, was an active agent in the treatment of acne, i.e.,
whether it was able to show activity against the main pathogenic factors of acne. Therefore, our objective was first to evaluate the antiproliferative activity of Myrtacine® on human keratinocytes, then to determine its antibacterial activity on P. acnes and to assess its anti-inflammatory properties in a cellular model of inflammation. Another aim was to characterise potential active compounds of Myrtacine® by structural analysis and to evaluate their biological activity.

### Material and Methods

#### Plant material
Leaves of *Myrtus communis* L. (Myrtaceae) were collected in the Messinia area (Greece) in 2008 and identified by Dr. S. Mamatas (Institut de Recherche Pierre Fabre). A voucher specimen (N° JGF1311) is deposited at the Conservatoire Botanique Pierre Fabre (Cambounet-sur-Sor, France).

#### Extraction and isolation
Myrtacine® is an ethanol extract prepared from myrtle leaves and standardised to 0.75% of myrtucommulones. One kg of dry and powdered myrtle leaves was extracted with 5 L of 100% EtOH for 1 h under agitation. After filtration and rinsing of the pomace with 1 volume of EtOH, the filtrate was collected. After removal of chlorophyll using activated charcoal (8 g/kg of plant), the filtrate was dried on maltodextrin and a yellow-orange powder was obtained. The residue (11 g/100 g of dry myrtle leaves) yielded the myrtle extract named Myrtacine® and standardised to 0.75% of myrtucommulones. Myrtucommulone A (1) and B’ (2) were separated by dissolution of 15 g of Myrtacine® in 750 mL of MeOH, then 3 extractions with cyclohexane. Myrtucommulone A was contained in the cyclohexane fraction and myrtucommulone B’ in the MeOH fraction.

**Myrtucommulone A**: The cyclohexane phase (1 L) was extracted three times with ammonium hydroxide (500, 250, and 250 mL). The cyclohexane phase was discarded and the aqueous phase was acidified with 5 N HCl and extracted successively with 500, 250, and 250 mL. The cyclohexane phase (1 L) was extracted thrice with cyclohexane. MeOH was evaporated, and the dry residue (350 mg) was redissolved in MeOH. Crystals of myrtucommulone A (17.3 mg, yield: 0.1%) were obtained by crystallisation of the solution for 48 h at 6°C. The IR, UV, MS, and NMR spectral studies confirmed that the isolated product was myrtucommulone A (1) as a yellow powder with purity of 92% by HPLC.

**Myrtucommulone B’**: pale yellow powder, [α]D20 = 17.6 (c 0.102, CHCl3); UV (MeOH) λmax (log ε) 208 (4.36), 232 (4.28), 292 (4.50) nm; 1H-NMR (125 MHz) (Table 1); Formula C38H52O10, UV (MeOH) λmax (log ε) 208 (4.36), 232 (4.28), 292 (4.50) nm, purity of 92% by HPLC. As myrtucommulone B’ was the main acylphloroglucinol in Myrtacine®, the content in myrtucommulones was expressed in myrtucommulone B’ and described by ourselves in a patent [12].

### Table 1

1H and 13C NMR data of myrtucommulone B’ in CDCl3.

<table>
<thead>
<tr>
<th>Position</th>
<th>δH</th>
<th>δC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>/</td>
<td>109.23</td>
</tr>
<tr>
<td>2</td>
<td>16.60 s</td>
<td>163.65</td>
</tr>
<tr>
<td>3</td>
<td>/</td>
<td>102.59</td>
</tr>
<tr>
<td>4</td>
<td>16.85 s</td>
<td>164.17</td>
</tr>
<tr>
<td>5</td>
<td>5.90 s</td>
<td>97.93</td>
</tr>
<tr>
<td>6</td>
<td>11.55 s</td>
<td>158.18</td>
</tr>
<tr>
<td>7</td>
<td>3.76, d, (10.9 Hz)</td>
<td>39.05</td>
</tr>
<tr>
<td>8</td>
<td>3.00, hept, (6.5 Hz)</td>
<td>25.90</td>
</tr>
<tr>
<td>9</td>
<td>0.85, d (6.3 Hz)</td>
<td>21.96</td>
</tr>
<tr>
<td>10</td>
<td>0.76, d (6.5 Hz)</td>
<td>21.76</td>
</tr>
<tr>
<td>1’</td>
<td>/</td>
<td>114.09</td>
</tr>
<tr>
<td>2’</td>
<td>/</td>
<td>202.88</td>
</tr>
<tr>
<td>3’</td>
<td>/</td>
<td>54.88</td>
</tr>
<tr>
<td>4’</td>
<td>/</td>
<td>212.57</td>
</tr>
<tr>
<td>5’</td>
<td>/</td>
<td>48.72</td>
</tr>
<tr>
<td>6’</td>
<td>10.36, s</td>
<td>178.08</td>
</tr>
<tr>
<td>7’</td>
<td>/</td>
<td>210.91</td>
</tr>
<tr>
<td>8’</td>
<td>3.91, hept</td>
<td>38.95</td>
</tr>
<tr>
<td>9’</td>
<td>1.22, d (6.85 Hz)</td>
<td>19.31</td>
</tr>
<tr>
<td>10’</td>
<td>1.20, d (6.85 Hz)</td>
<td>19.24</td>
</tr>
<tr>
<td>11’</td>
<td>1.42, s</td>
<td>26.54</td>
</tr>
<tr>
<td>12’</td>
<td>1.32, s</td>
<td>23.33</td>
</tr>
<tr>
<td>13’</td>
<td>1.35, s</td>
<td>25.93</td>
</tr>
<tr>
<td>14’</td>
<td>1.50, s</td>
<td>24.81</td>
</tr>
</tbody>
</table>

Myrtucommulone B’ (2): pale yellow powder, [α]D20 = 17.6 (c 0.102, CHCl3); UV (MeOH) λmax (log ε) 208 (4.36), 232 (4.28), 292 (4.50) nm; 1H-NMR (CDCl3) 500 MHz and 13C-NMR (125 MHz) (Fig. 1S, Table 1); Formula C38H52O10, UV (MeOH) λmax (log ε) 208 (4.36), 232 (4.28), 292 (4.50) nm, purity of 92% by HPLC. As myrtucommulone B’ was the main acylphloroglucinol in Myrtacine®, the content in myrtucommulones was expressed in myrtucommulone B’ and was standardised to 0.75% (w/w) of the dry extract.

Myrtucommulones were titrated by analytical HPLC (Fig. 3S, Supporting Information).
anthraquinone was used as an internal standard. Solutions of 2-methylanthraquinone and Myrtacine® were prepared in EtOH to 0.1 mg/mL and 5 mg/mL, respectively. A solution test was prepared with 5 mL of each, and 20 µL of the solution was injected. Under these conditions, myrtucommulones A and B were eluted at 17 min and 6 min, respectively (Fig. 3S, Supporting Information).

Myrtacine® and myrtucommulones antiproliferative activity
Myrtacine® and myrtucommulone antiproliferative activity was assessed by BrdU incorporation assay. Myrtacine® and myrtucommulone stock solutions prepared in DMSO were diluted in DMEM with 1% foetal calf serum (FCS). DMSO final concentration (< 0.01%) was previously shown not modifying 6-keto PGF1α production. HaCat human keratinocytes were incubated either with Myrtacine® or without (negative control) or with myrtucommulones or positive controls (transforming growth factor β1, TGFβ1, 2 ng/mL, and mitomycin C, 0.3 µg/mL; see Supporting Information for further details).

Myrtacine® and myrtucommulone antibacterial and bactericidal activity
Myrtacine® and myrtucommulone antibacterial activity was determined in erythromycin sensible (EryS) and resistant (EryR) P. acnes strains by assessing minimal inhibitory concentration (MIC) using a micromethod. Erythromycin was taken as positive control. Assays were performed in duplicate. Results were considered valid when the MIC value differed from no more than one dilution for both assays. Myrtacine® bactericidal activity was assessed by measuring the D value. Myrtacine® samples were inoculated with each microbial solution, collected after 5, 10, 30, and 60 minutes of incubation, neutralised and cultivated in agar medium for 48 h. The residual bacteria were counted, and logarithmic reduction was calculated (see Supporting Information for further details).

Anti-inflammatory activity of Myrtacine® and myrtucommulones
Firstly, 6-keto prostaglandin F1α (6-keto PGF1α) production from A23187-stimulated human keratinocytes was immunoassayed. Myrtacine® and myrtucommulone stock solutions were diluted in culture medium, without FCS. Final DMSO concentration (< 0.01%) was previously shown not modifying 6-keto PGF1α production. HaCat keratinocytes were preincubated for 60 min with extract dilutions or indomethacin (positive control) or with extract dilutions or indomethacin (positive control) then stimulated with 1 µM A23187 for 5 h, and 6-keto PGF1α was assayed by ELISA in culture media. The same experiment was performed with SVK14 keratinocytes and 5 µM A23187 to test the effect of myrtucommulones. Secondly, cyclooxygenase (COX) and lipoxygenase (LOX) metabolite production from ionomycin-stimulated human keratinocytes was assessed by chromatography and scanner analysis. Keratinocytes prelabelled with [3H]-arachidonic acid ([3H]-AA), as previously described [13], were preincubated with or without Myrtacine®, or with indomethacin, then incubated with ionomycin. Cellular lipids were extracted and separated by thin-layer liquid chromatography [14]. [3H]-AA metabolite production was analysed by chromatography, radioactive metabolites were separated as previously described [15], identified and quantified (see Supporting Information for further details).

Myrtacine® anti-lipase activity
Myrtacine® anti-lipase activity was evaluated in tubo by spectrophotometric assay of lipase activity using 1,2-diglyceride as the substrate and DTT as the reference product. All experiments were performed in triplicate. Results were expressed as mean ± SD, difference in OD/min, UI/L of active lipase, and percentage of inhibition compared to the control. Comparisons between groups were performed by one-way analysis of variance followed by a Dunnett’s test (α < 0.1).

Supporting information
Suppliers of reagents and biochemicals, general experimental procedures, spectroscopic data and HPLC profiles, culture of SVK14 and HaCat keratinocyte cell lines, and methods used to determine Myrtacine® and myrtucommulone antiproliferative, antibacterial, anti-inflammatory, and anti-lipase activity are described in more detail as Supporting Information.

Results

Myrtacine® and myrtucommulones inhibited HaCat keratinocyte proliferation in a concentration-dependent manner (Fig. 2 and Fig. 3), the highest concentration inducing a highly significant inhibition (p < 0.001) when cells were incubated with 3 µg/mL of extract or 5 µg/mL of myrtucommulone A or B. Antibiobacterial activity of Myrtacine® and myrtucommulones was then assessed on P. acnes strains, and their MICs were determined. Myrtacine® was active against all P. acnes strains, inhibiting the growth of EryS and EryR strains at 4.9 µg/mL and 2.4 µg/mL.
mL, respectively. Myrtucommulone B′ also exhibited high antibacterial activity against both *P. acnes* strains, with a MIC comparable to that of Myrtacine® (1.2 µg/mL). Myrtucommulone A was similarly efficient, with a MIC of 0.3 and 0.6 µg/mL on EryR and EryS strains, respectively. Compared with erythromycin, Myrtacine® activity was lower on the EryS *P. acnes* strain (4.9 vs. 0.001 µg/mL) but much higher on the EryR strain (2.4 vs. 781.2 µg/mL).

D value assessment revealed that both Myrtacine® concentrations (1 and 3 mg/mL) induced a time-dependent decrease of the number of UFC/mL, indicating they have a bactericidal activity on EryR and EryS *P. acnes* (Fig. 4). Each concentration had a similar activity on EryR and EryS strains.

To demonstrate the anti-inflammatory activity of Myrtacine®, it revealed a very significant anti-inflammatory activity at the highest concentration, with a 23% inhibition of the A23187-stimulated 6-keto PGF1α production (p < 0.001). In the same way, preincubation of SVK14 keratinocytes with 0.1 and 0.5 µg/mL myrtucommulone A significantly reduced 6-keto PGF1α production (−21% and −17%, respectively, p < 0.05) (Fig. 6a). Myrtucommulone B′ also induced a significant, but lower inhibition of 6-keto PGF1α production (−9%, p < 0.001) (Fig. 6b).

Myrtacine®’s effect on eicosanoid production from COX and LOX pathways is shown in Fig. 7a and b, respectively. The stimulation of HaCat keratinocytes with 0.1 µM ionomycin increased the production of free cellular [3H]-AA by 33% and of its metabolites from COX and LOX pathways by 75% and 69%, respectively (p = 0.0001 for both). Preincubation of keratinocytes with 3 and 10 µg/mL Myrtacine® decreased the ionomycin-triggered eicosanoid production in a dose-dependent manner. The 10 µg/mL dose of Myrtacine® inhibited the production of 6-keto PGF1α, PGE2,
Fig. 5  Activity of Myrtacine® on 6-keto PGF1α production in Ca²⁺ ionophore A23187-stimulated keratinocytes. HaCat keratinocytes were incubated for 1 h with either Myrtacine® dilutions, indomethacin, or without any treatment, then inflammation was stimulated by incubation with 1 µM A23187 for 5 h. The production of 6-keto PGF1α was assayed by ELISA immunoassay. The results are given as mean of 6-keto PGF1α concentration ± standard error and percentage of inhibition. Comparisons between groups were statistically analysed by variance analysis and Bonferonni Dunnett’s test. *** P < 0.001.

Fig. 6a  Activity of myrtucommulones on 6-keto PGF1α production in Ca²⁺ ionophore A23187-stimulated keratinocytes. a  Myrtucommulone A. SVK14 keratinocytes were incubated for 1 h with either myrtucommulone dilutions (hatched bars) or without any treatment (control white and black bars), then inflammation was stimulated by incubation with 5 µM A23187 for 5 h. The production of 6-keto PGF1α was assayed by ELISA immunoassay. The results are given as mean of 6-keto PGF1α concentration ± standard error and percentage of inhibition. Comparisons between groups were statistically analysed by variance analysis and Bonferonni Dunnett’s test. * P < 0.05. *** P < 0.001.

Fig. 6b  Activity of myrtucommulones on 6-keto PGF1α production in Ca²⁺ ionophore A23187-stimulated keratinocytes. b  Myrtucommulone B’. SVK14 keratinocytes were incubated for 1 h with either myrtucommulone dilutions (hatched bars) or without any treatment (control white and black bars), then inflammation was stimulated by incubation with 5 µM A23187 for 5 h. The production of 6-keto PGF1α was assayed by ELISA immunoassay. The results are given as mean of 6-keto PGF1α concentration ± standard error and percentage of inhibition. Comparisons between groups were statistically analysed by variance analysis and Bonferonni Dunnett’s test. * P < 0.05. *** P < 0.001.
PGF2α, PGD2, and PGA2 by 246%, 89%, 64%, and 81%, respectively (p < 0.01 for all) and LTB4 and HETE production by 107% and 87%, respectively (p < 0.01 for all).

To evaluate membrane lipid distribution, the quantity of [3H]-AA incorporated in membrane phospholipids was measured. The preincubation of keratinocytes with 1, 3, and 10 µg/mL Myrtacine® increased this incorporation by respectively 13%, 12%, and 17% (p < 0.001 for all versus control) and decreased the free [3H]-AA cellular pool by respectively −35%, −6%, and −23%. Furthermore, at 10 µg/mL concentration, Myrtacine® increased the content of [3H]-AA in cholesterol esters, with a 40% increase of cholesterol arachidonate.

Finally, a spectrophotometric assay of lipase activity was performed with and without Myrtacine®. Compared to the control, DTT at 0.25, 0.5, and 1 mM significantly inhibited the lipase activity by respectively 58%, 58%, and 100%, as shown by the decrease of lipase substrate degradation from 0.094 OD/min to respectively 0.042, 0.006, and −0.003 OD/min (p < 0.01). Myrtacine® exhibited a similar dose-dependent inhibitory effect at 100 µg/mL and 1 mg/mL, decreasing lipase activity by 53% and 100%, respectively (p < 0.01 for both).
Discussion

Overall, our results suggest that Myrtacine® may be an active agent potentially interesting in the treatment of acne. Firstly, it demonstrated a strong dose-dependent inhibitory activity of keratinocyte proliferation in vitro. Although the precise pathological process of comedogenesis is not fully understood, an increase in proliferating basal keratinocytes and their subsequent retention may be the main contributory factor [16,17]. Acne treatments such as topical retinoids are known to exhibit a frequent retention may be the main contributory factor [16, 17]. Furthermore, the susceptibility of keratinocytes to vitamin A analogues action in vitro seems to be markedly different depending on the type and origin [18], they have been shown to inhibit HaCaT keratinocyte proliferation in high seeding densities of cells [19].

In the same conditions of high proliferation, Myrtacine® exerted a similar antiproliferative effect by decreasing keratinocyte proliferation by more than 75% when it was tested in the millimolar concentration range. The same experiment performed with myrtucommunol A and B revealed a similar, though less marked inhibitory effect of the 2 compounds, indicating they may constitute part of Myrtacine® activity. Other compounds of Myrtacine® such as ursoic acid or β-sitosterol may also be involved in its antiproliferative activity and may explain its stronger efficacy compared to myrtucommunolones. To our knowledge, such an antiproliferative effect has never been observed in vitro with other myrtle extracts.

Besides keratinocyte proliferation and keratinisation, acne pathogenesis is characterised by an elevated proliferation of P. acnes in microcomedones with a range of 10^5–10^6 cells/cm^2 recovered per follicle [20], which may activate the synthesis of proinflammatory molecules and trigger inflammatory responses. Myrtacine® demonstrated strong inhibitory and bactericidal activity in vitro against all P. acnes strains, with MICs in the micromolar range and a time-dependent decrease of P. acnes population with 1 and 3 mg/mL Myrtacine® concentrations. Compared to benzyol peroxide, which has proven its clinical efficacy despite a poor inherent antibacterial activity in vitro with MIC against P. acnes ranging from 100 to 800 µg/mL [21], our results suggest that Myrtacine® could also have a comparable antibacterial efficacy in vivo, by reducing P. acnes population within the follicles. However, this hypothesis needs further evaluation in an in vivo study. The results of Myrtacine® MIC tests are consistent with literature data which showed the antibacterial effect of myrtle extracts on gram+ bacteria [5–7]. However, none specifically described an antimicrobial activity of these extracts on P. acnes strains. Myrtucommunolone A and B showed a similar inhibitory activity, suggesting that they may constitute the largest part of its antibacterial activity.

Inflammation is another important part of acne pathogenesis. Although some authors suggested that inflammatory events were involved in the very early stages of acne lesion development [22], P. acnes is thought to be the main effector of the inflammatory response by the production and release of proinflammatory mediators and chemokines, as well as degradation enzymes such as lipases and proteases [20,21]. By suppressing various responses of keratinocytes to inflammation induced in vitro, Myrtacine® demonstrated very significant anti-inflammatory properties, which might reduce inflammation in acne lesions. First, it significantly inhibited the A23187-induced production of 6-keto-PGF1α. Experiments performed with the isolated active acyl-phloroglucinols showed that myrtucommunolone A, and myrtucommunolone B to a lesser extent, were also able to inhibit this production, suggesting that myrtucommunolone A is the main active substance responsible for this inhibition. Furthermore, Myrtacine® decreased the synthesis of eicosanoids by potently inhibiting cyclooxygenase and lipoxygenase pathways. However, according to the results of the membrane lipid distribution analysis, it seems to have an indirect inhibitory effect on eicosanoid synthesis. In fact, preincubation of ionomycin-stimulated keratinocytes with Myrtacine® induced a modification of AA distribution by increasing its incorporation in membrane phospholipids and decreasing the cellular pool of free AA. Myrtacine® may have an inhibitory effect on keratinocyte phospholipase A2 or, as suggested by membrane lipid analysis, may promote AA incorporation in cholesterol esters such as cholesterol arachidonate. A further study in keratinocytes non-stimulated with ionomycin may explain the actual effect of Myrtacine® on AA metabolism and membrane lipid distribution.

Our results are in agreement with those of a previous study [10], which evaluated the anti-inflammatory effect of myrtle non-prenylated acylphloroglucinols in human polymorphonuclear leucocytes, although the authors hypothesised a different mode of action for anti-inflammatory compounds. Feisst et al. [10] demonstrated that myrtucommunolone A and semimyrtucommulone to a lesser extent were able to compromise cellular proinflammatory responses, suggesting they may possess important anti-inflammatory properties. They identified myrtucommunolone A and semimyrtucommulone as direct inhibitors of cyclooxygenase- and lipooxygenase at IC50 values ranging from 1.8 to 29 µM, thus potently suppressing eicosanoid biosynthesis in vitro and in vivo. The efficacy of myrtucommunolone A as an anti-inflammatory compound in vivo has recently been shown in models of inflammation in vivo, such as mouse carrageenan-induced paw oedema and pleurisy [23]. The study of the effect of Myrtacine® on gene expression and enzymatic activity of COX and LOX should give further information about its mode of action on eicosanoid synthesis and its anti-inflammatory effect on keratinocytes.

Finally, in vitro Myrtacine® anti-lipase activity suggests that it might also reduce perifollicular inflammation promoted by free fatty acids in vivo [24]. Indeed, the latter are produced by P. acnes lipase from sebum lipids, an important substrate for P. acnes growth [20].

In conclusion, our results suggest that Myrtacine® may be an interesting agent for the treatment of comedones and inflammatory acne lesions, as it demonstrated in vitro the antiproliferative, antibacterial, and anti-inflammatory properties required to target the main pathogenic factors of the disease and exert a global action on the development of acne lesions. Further studies are needed to confirm these properties in vivo.

Acknowledgements

We thank Marielle Romet who provided medical writing assistance on behalf of Ducray Laboratory, Bruno David for his contribution to the elaboration of this manuscript, and C. Long for HR-MS and UV spectra realisation. This work was supported by the Pierre Fabre Group.
Affiliations
1 Laboratoire des Produits Végétaux, Institut de Recherche Pierre Fabre, Centre de R & D Pierre Fabre 3, Toulouse, France
2 Laboratoire de Pharmacologie Cellulaire, Pierre Fabre Dermocosmétique, Centre de R & D Pierre Fabre 3, Toulouse, France
3 Institut de Recherche Pierre Fabre, Centre de R & D Pierre Fabre 3, Toulouse, France
4 Laboratoire de Bactériologie, Pierre Fabre Dermocosmétique, Vigoulet, France
5 Laboratoires Pierre Fabre Dermocosmétique, Les Cauquillous, Lavaur, France
6 Cabinet de Dermatologie, Paris, France

References

Please note: This article was changed according to the following erratum on April 20, 2011: In this article affiliation 6 was corrected after e-first online publication.