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## ► To cite this version:

Floriane Rischard, Amandine Flourat, Léa Broche, Abdouramane Dosso, Blandine Godon, et al.. Novel Biobased Multifunctional Emollients for Cosmetic Applications: Toward the Ingredient-List Reduction. ACS Sustainable Chemistry & Engineering, 2023, 11 (48), pp.16955-16964. 10.1021/acssuschemeng.3c04259 . hal-04295931

**HAL Id: hal-04295931**

**<https://hal.science/hal-04295931>**

Submitted on 15 Jul 2024

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# Novel bio-based multifunctional emollients for cosmetic applications: toward the ingredients-list reduction

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## ABSTRACT

The use of several ingredients in cosmetic formulations can often result in long ingredient lists, which can be daunting for consumers. While each of these particular ingredients serves a purpose, some are petroleum-based and may have adverse effects on the environment or human health. Ferulic acid, a *para*-hydroxycinnamic acid present in numerous agro-industrial by-products, exhibits anti-microbial, antioxidant and UV-filtering properties. In this work, ferulic acid was functionalized through chemo-enzymatic reaction steps (80 to 93% isolated yields) applying green chemistry principles, by using various natural fatty alcohols. The resulting compounds have demonstrated good emollient properties through physico-chemical and spreading evaluations. Two

green metrics (Mass Intensity and Ecoscale) were used to assess the synthesis of these novel emollients, which were found to have a very low environmental impact. The findings of this study could provide a novel solution for multifunctional, bio-based ingredients in cosmetic formulations while reducing the environmental impact of the products.

## KEYWORDS

Ferulic acid, Green Chemistry, Multifunctional emollients, Cosmetic ingredients, Texture properties

## INTRODUCTION

Cosmetic formulations are complex systems composed of multiple ingredients. Each of these ingredients has a particular function in the final formulation and is thus essential. For example, antioxidants protect the formulation from oxidation and preservatives from the growth of microorganisms. UV-filters protect the consumer's skin when exposed to sunlight.<sup>1</sup> Emollients are essential for the protecting, conditioning, softening and smoothing effects of the skin.<sup>2,3</sup> However, this long list of ingredients can be alarming for the consumer. Moreover, these ingredients are often petroleum-based and sometimes suspected as potential endocrine disruptors (like some UV-filters or preservatives for example),<sup>4-7</sup> or having adverse effects on the environment (like octinoxate, a commonly used UV-filter, that can have adverse effects on some coral species, or silicones that can be persistent and accumulate in the environment).<sup>8-10</sup> The cosmetic industry is looking for competitive multifunctional ingredients, on the one hand, in order to reduce the list of ingredients and for bio-based ingredients, on the other hand, to propose more natural products.

Ferulic acid is present in non-neglectable quantities in some agricultural co-products<sup>11-13</sup> and has been proven to have anti-microbial and antioxidant properties.<sup>14-19</sup> Several studies have

shown that ferulic acid-derivatives can exhibit both aforementioned activities, as well as UV-filtering properties.<sup>20-22</sup> In addition, endocrinian disruption tests conducted on ferulic acid derivatives has proven negative.<sup>23</sup> All these advantages make ferulic acid the perfect synthon for the design of multifunctional ingredients.

Emollients are not only essential to the structure of the formulation but also have complex sensory properties that can be linked to multiple characteristics, such as an ease of spreading, softness during and after application, filmogenic properties, etc. Unfortunately, ferulic acid does not have the textural properties to be used as an emollient and the challenge of this study was its modification into a multifunctional emollient suitable for cosmetic formulations. For the modification of ferulic acid into corresponding emollients, different synthetic pathways have been considered. Fisher or Steglich esterifications would have required intensive distillation to remove excess of fatty alcohol or unsustainable conditions and delicate purification step (i.e. removing urea derivatives) respectively, and were discarded.<sup>24</sup> Starting from the corresponding aldehyde, vanillin, Wittig reaction<sup>25</sup> or Knoevenagel condensation<sup>21,26</sup> could be envisaged. The first one using triphenyl phosphonium salt presented a poor atom economy profile, whereas the second one could be sustainable but purification step was needed to eliminate the remaining aldehyde. Thus, a chemo-enzymatic pathway was preferred to decrease the environmental impact of the synthesis, while achieving total conversions and reaching excellent yields.

Several studies have been carried out on the extraction and/or modification of bio-based molecules to be used as high added value compounds for cosmetic applications, such as UV filtering,<sup>27-29</sup> antioxidant,<sup>22,30,31</sup> antimicrobial<sup>32,33</sup> or antityrosinase<sup>34,35</sup> activities. In 2022, Goussard *et al*<sup>36</sup> published a review on bio-based alternatives to volatile silicones. This review presents emollients such as hydrocarbons and oxygenated oils (e.g., fatty esters) that can either

be petroleum- or bio-based. Most hydrocarbons are petroleum-based, like paraffin oil for example which is composed of a mixture of ramified alkanes, obtained after distillation and fractionation of crude petroleum,<sup>37,38</sup> but some hydrocarbons can also be obtained from renewable resources.<sup>39,40</sup> Fatty esters, which can be bio-based, are also largely used as silicone-like emollients.<sup>41,42</sup>

The originality of this study is the association of (1) the development of a new family of bio-based molecules from ferulic acid with respect to green chemistry principles, and (2) the characterization of these molecules from their protective properties to their complex and various emollient characteristics in term of texture and interaction with skin.

The best way to assess these novel emollients would have been to set up *in vivo* sensory analysis on a trained expert panel, nevertheless this method requires a prior innocuity testing of all novel ingredients. Thus, in addition of anti-UV, antiradical and antimicrobial tests, our compounds were characterized through physico-chemical and *in vitro* texture tests, leading to 4 properties: viscosity, density, surface activity and spontaneous spreadability. Several studies showed that those particular properties are linked to functional emollients performances: Douguet *et al*<sup>43</sup> developed predictive models to predict the spreading behavior of emollients based on those physico-chemical measurements; Chao *et al*.<sup>44</sup> established a correlation between sensory analyses results and physico-chemical ones; Goussard *et al*<sup>36</sup> reviewed various previous works that established relationships between physicochemical properties and functional emollients performances. All these criteria will give a roadmap for selecting compound(s) matching a defined application. Finally, the environmental impact of the novel bio-based emollients was assessed through the calculation of two green metrics: MI and Ecoscale.<sup>45,46,46</sup>

## RESULTS AND DISCUSSIONS

### Synthesis and sustainability assessment of novel bio-based emollients

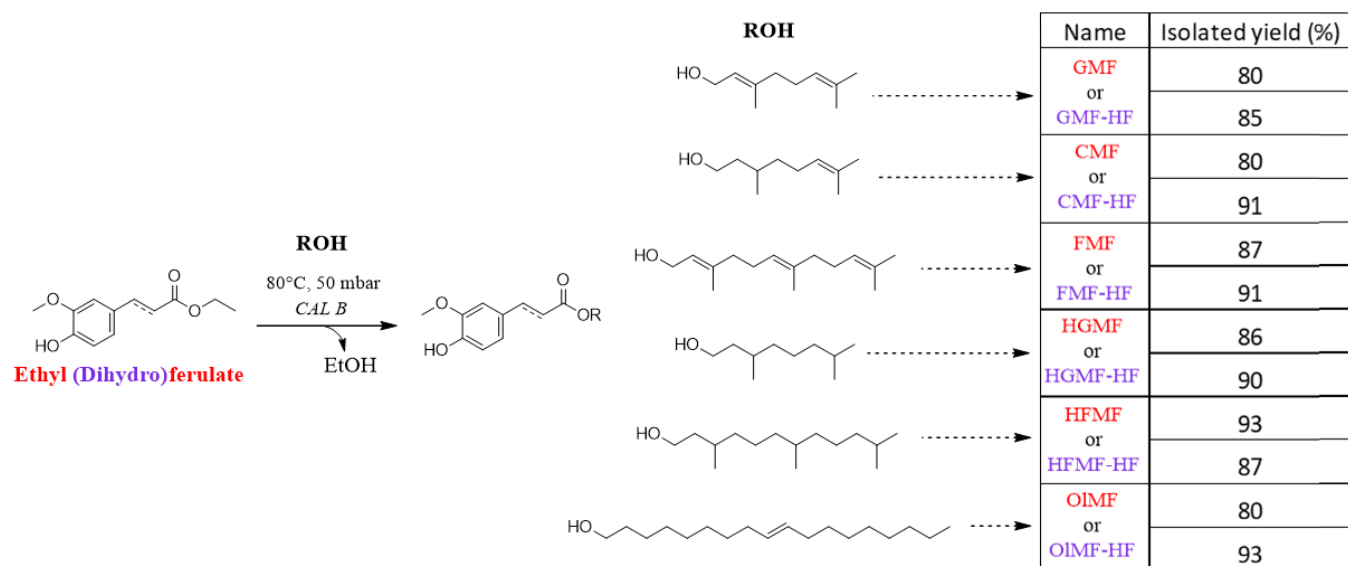
The synthesis of the novel bio-based emollients is based on the work of Pion *et al.*<sup>47</sup> who developed a new chemo-enzymatic pathway to obtain bis- and trisphenols as building blocks for polymer chemistry. Here the cited method was adapted to the synthesis of monophenols from renewable ferulic acid and natural alcohols. The goal was to (1) provide ferulic acid with new emollient characteristics while taking advantage of its multifunctionality, as well as (2) determine structure-activity relationships.

Firstly, ferulic acid was esterified into ethyl ferulate (**EtFe**) through Fischer esterification followed or not by the reduction of the double bond between the ester and the aromatic cycle, to obtain ethyl dehydroferulate (**EtHFe**). These two first steps allow to enhance the reactivity of ferulic acid towards a lipase-mediated transesterification, as shown by Reano *et al.*<sup>48</sup> It also decreases the fusion temperature of ferulic acid (which has a melting point of about 170°C), to 56 and 45°C for EtFe and EtHFe respectively. The enzymatic transesterifications were then performed at a temperature of 75°C, without adding any organic solvent, as EtFe or EtHFe were liquids.

Scheme 1 summarizes the enzymatic transesterification of **EtHFe** or **EtFe** into different monophenols using the corresponding fatty alcohols (ROH). Monophenols are named as follows: the first G, C, F or Ol stands for the corresponding fatty alcohols (respectively geraniol, citronellol, farnesol or oleyl alcohol) with an eventual H first if the fatty alcohol is saturated (hydrogenated), MF for mono ferulate and HF for hydrogenation of the ferulate (if relevant). For example, HGMF-HF stands for Hydrogenated Geraniol Mono Ferulate – with Hydrogenated Ferulate (EtHFe).

Six monophenols with a double C-C conjugated bond with their aromatic cycle were obtained from equimolar quantities of **EtFe** and the different bio-based alcohols. This first group of molecules will further be referred to as the conjugated monophenols. Six analogues to the first monophenols (without any double C-C conjugated bond with their aromatic cycle) were obtained from equimolar quantities of **EtHFe** and the same alcohols. The second group will further be referred to as the non-conjugated monophenols. All reactions were performed at multigram scale.

**Scheme 1.** Chemo-enzymatic synthesis of ferulic acid-based monophenols



With respect to previously published data<sup>47,49,50</sup> for the synthesis of bis- or trisphenols, our synthesis does not require any excess of EtFe or EtHFe to achieve their full conversion (follow by H-NMR, Figures S25 and S26) into the corresponding monophenols, while observing very good to excellent isolated yields after 24 to 48 h. Indeed, we obtained yields from 80 to 93% while using equimolar quantities of both reagents (EtFe or EtHFe and the alcohol) and 10 to 20 % w/w of *Candida antarctica* lipase B (CAL B) immobilized on resin. This allowed to avoid the time and money consuming step of purification by flash chromatography. The immobilized

enzyme was simply filtered off and could be further reused. It is to notice that reactions carried on **EtFe** led globally to slightly lower yield than those on **EtHFe** due to already known lower reactivity of the conjugated ester.

To evaluate the environmental impact of the novel bio-based obtained emollients, the Ecoscale<sup>45</sup> of each reaction step was calculated. This tool has been designed to give chemical reactions a score ranking from 0 to 100 (the latter representing an ideal reaction), based on 6 parameters that can give penalty points to the assessed reaction: the yield, the price of each reaction components, the general safety of the reaction, the technical setup that is used, the time and temperature necessary and the workup/ purification needed to recover the product. The Ecoscale is thus calculated as follows: 100 points minus the sum of individual penalties for each category. A score superior to 75 is considered *excellent*, between 75 and 50 is *acceptable* and below 50 is *inadequate*. This green metric allows to evaluate how the assessed reactions follow or not several green chemistry principles, such as principles 3 (less hazardous synthesis), 5 (benign solvents and auxiliaries) and 12 (inherently benign chemistry for accident prevention) with the assessment of the safety of the reaction; principle 6 (design for energy efficiency) is also evaluated through other parameters.

Details of Ecoscale calculation for every reaction are available in supporting information (Tables S1 to S15). For the transesterification reactions, the technical setup was a reduced pressure of 50 mbar, which needs a little more equipment than a common setup; therefore a 1-point penalty was attributed to this category. Some extra penalties have been given for the use of acetone which is a flammable solvent, and for the duration and temperature of the reaction. No penalty was given for the workup/purification, as a simple filtration was needed since the reaction was done with equimolar quantities. Finally, the very good yields of the reaction only



gave a 3.5 to 10-points penalty. This adds up to the overall penalty of 12.5 to 19, giving Ecoscale values between 81 to 87.5, which is considered *excellent* (Table 1). The synthesis of EtFe, EtHFe and H-Farnesol ranked at 83, 72 and 76.5, respectively, which can be considered as *very good* to *excellent* scores.

**Table 1.** Ecoscale and MI (mass intensity) values for every reaction

| Name       | Ecoscale | Mass Intensity |                  |
|------------|----------|----------------|------------------|
|            |          | With solvents  | Without solvents |
| EtFe       | 83       | 24.5           | 4,4              |
| EtHFe      | 72       | 13.3           | 3,1              |
| H-Farnesol | 76.5     | 10.7           | 3,1              |
| GMF        | 81       | 10.9           | 2,8              |
| CMF        | 81       | 10.8           | 2,8              |
| FMF        | 84.5     | 8.5            | 2,4              |
| HGMF       | 84.5     | 9.9            | 2,6              |
| HFMF       | 87.5     | 7.9            | 2,2              |
| OIMF       | 81       | 8.4            | 2,5              |
| GMF-HF     | 83.5     | 10             | 2,5              |
| CMF-HF     | 86.5     | 9.3            | 2,4              |
| FMF-HF     | 86.5     | 8              | 2,2              |
| HGMF-HF    | 86       | 9.7            | 2,5              |
| HFMF-HF    | 85       | 8.1            | 2,2              |
| OIMF-HF    | 87.5     | 7.1            | 2                |

The Ecoscale can be used as a quick tool for the evaluation of a process, but it has some flaws. Especially, it does not consider the atom economy of the process (principle 2 of green chemistry principles). In addition, the mass intensity (MI)<sup>46,51</sup> of the reactions were calculated. It considers the mass of all matter (reagents, solvents, catalysts, treatment solutions), except water, that is necessary to obtain 10 mmol of product. This sum is then divided by the mass of 10 mmol of product. We can thus consider that the closer to 1 the MI, the better the atom economy. Syntheses were given MI scores ranging from 7.1 to 10.9 for the enzymatic transesterifications,

which are quite good scores. The synthesis of EtFE, EtHFe and H-Farnesol have MI scores of 24.5, 13.3 and 10.7, respectively. Since the solvents used in the process (acetone, AcOEt and EtOH) could be recovered and further reused, we also calculated the MI of the reactions by removing the solvent masses: 2 to 2.8 for the monophenols, and between 4.4 and 3.1 for the other reactions. These results are in accordance with principle 2 of green chemistry principles as mentioned, but also with principle 1 (prevent waste). All results of MI are available in the supporting information (Tables S1 to S15).

Based on the aforementioned data, we can conclude that the sustainability of the synthetic routes can be considered as *very good to excellent*. Indeed, the synthesis of the novel emollients follows several green chemistry principles as mentioned above. Four other principles were considered while designing the syntheses: principles 4 (design benign chemicals), 7 (use of renewable feedstock), 8 (reduce derivatives) and 9 (catalysis).

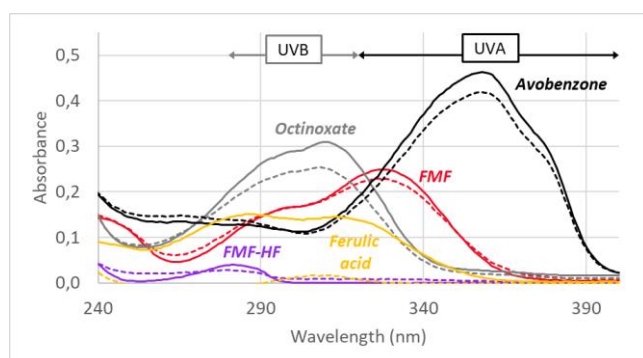
## Characterization of the novel emollients

### UV-filtering results

The absorbance of all monophenols and two commercial UV-filters (avobenzone and octinoxate) was measured before and after a 1-hour irradiation ( $\lambda = 300$  nm,  $P = 8.32$  W/m<sup>2</sup>). As references, the same protocol was applied to EtFe, EtHFe and Ferulic acid. The conjugated monophenols show a maximum of absorbance at about 327 nm, with a relative absorbance between 0.20 and 0.27. After 1-h of irradiation, their maximum of absorbance decreases by 8% to 27%. While EtFe has the same maximum wavelength, it has been found to have a much lower absorbance (0.14), that decrease by 94% after 1 hour of irradiation. EtFe absorbs less than conjugated monophenols and is totally unstable unlike corresponding monophenols.

As expected, as it has been demonstrated by Dean *et al*<sup>52</sup> that the aromatic conjugation plays an important role in the UV properties of hydroxycinnamic acid derivatives, the UV absorbance of the conjugated monophenols was far better than their non-conjugated analogues that exhibit a maximum of absorbance around 282 nm and have a relative absorbance between 0.03 and 0.06. EtHFe was found to have similar absorbance than non-conjugated monophenols, but showed 100% of degradation after 1 hour of irradiation.

A representative example is given in Figure 1, the conjugated monophenol (FMF) absorbs in a broad range of wavelengths, covering a part of the UVA as well as the UVB. Although lower than that of the synthetic references (which have maximums of absorbance of 0.46 and 0.31), its absorbance remains good (0.25), while its non-conjugated analogue (FMF-HF) has a small absorbance in the UVB range. Ferulic acid has two maximums of absorbance almost corresponding to the ones of FMF and FMF-HF, but experienced an almost total degradation after 1 hour of irradiation. Comparison with starting materials (EtFe, EtHFe and Ferulic acid) showed that modifications allowed the obtention of more stable and more effective compounds towards UVs. Overall, compared to the references, all monophenols have been found to have good stability after 1 h of irradiation. All numerical values can be found in Table S17.

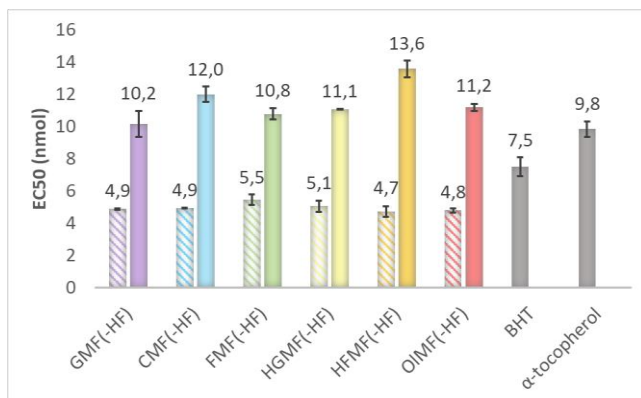


**Figure 1.** Absorbance spectra of FMF (in red), FMF-HF (in purple), Ferulic acid (in yellow), octinoxate (in grey) and avobenzone (in black) before (plain curves) and after (dotted curves) 1-h irradiation ( $\lambda = 300$  nm,  $P = 8.32$  W/m<sup>2</sup>) for solutions at 10  $\mu$ M in ethanol.

#### Antiradical activities results

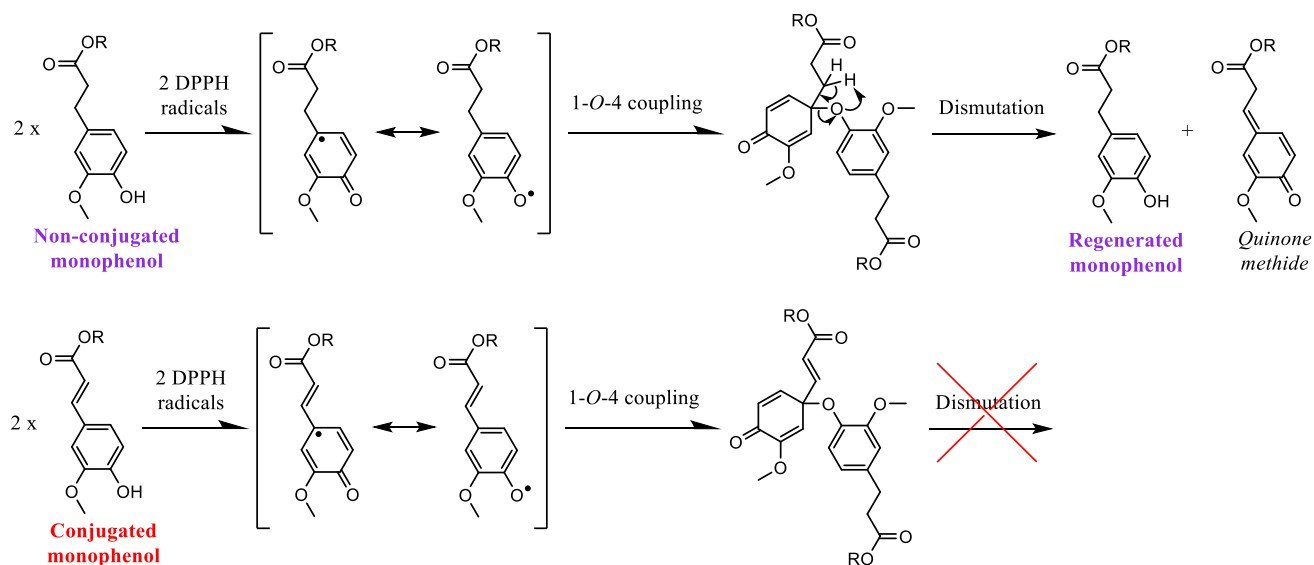
DPPH assays<sup>53</sup> were used to assess the antiradical properties of the new compounds. BHT, a commercial synthetic antioxidant used in cosmetic formulation, and  $\alpha$ -tocopherol ( $\alpha$ T), which can be a natural alternative to synthetic antioxidants, were used as benchmarks. EtFe, EtHFe and Ferulic acid were also evaluated by following the same protocol. For every sample, we calculated EC<sub>50</sub> that correspond to the minimal quantity of compound necessary to reduce 50 % of the free radical DPPH°.

As a general trend, unlike what was observed for the UV absorbance, the antiradical activity of the non-conjugated monophenols is statistically higher than their conjugated counterparts (Figure 2). This phenomenon has been explained by Reano *et al.*<sup>48</sup>: after the coupling of two radical hydroxycinnamic acid derivatives, the saturated ones can regenerate part of the phenol through dismutation, whereas the unsaturated ones cannot undergo dismutation (Scheme 2).



**Figure 2.** EC<sub>50</sub> of conjugated monophenols (plain areas) and their non-conjugated analogues (hatched areas), compared to two references (grey areas).

All non-conjugated monophenols have significantly higher antiradical activities than the two benchmarks (lower EC<sub>50</sub>), while some of the conjugated monophenols exhibit antiradical activities that are non-significantly (*p*-value > 0.134) different than that of αT (GMF, FMF, HGMF and OIMF). All monophenols have antiradical activities that are 3 to 17 times lower than the ones of EtFE, EtHFe and Ferulic acid that were found to have EC<sub>50</sub> of 80.4±1.9, 41.5±2.3 and 60.8±8.4 nmol respectively. All tested monophenols have good to excellent antiradical activities (EC<sub>50</sub> < 15 nmol), that have been enhanced compared to starting materials, and could be a bio-based alternative to synthetic antioxidants, such as BHT.



**Scheme 2.** Hypothetical formation of quinone methide and regeneration of monophenol through dismutation of saturated monophenol (adaptation of scheme 3 by Reano *et al.*<sup>48</sup>)

## Results of physico-chemical characterizations

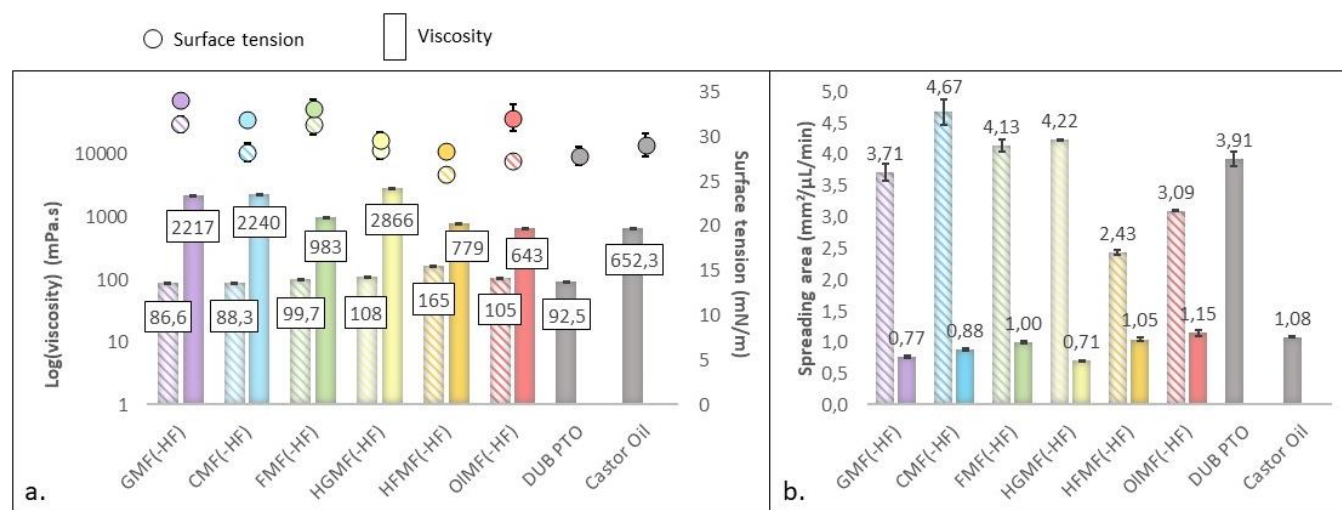
Previous studies have linked density, surface tension, viscosity and spreadability to functional emollient performances.<sup>36,43,44</sup> The novel emollients were then assessed for these four characteristics and compared to two reference emollients: pentaerythrityl tetraethylhexanoate (DUB PTO) and castor oil. DUB PTO is a star-shaped ramified fatty ester used to give consistency and structure to cosmetic creams,<sup>36,43,54</sup> and castor oil is a vegetable oil which is known for its high viscosity.<sup>43</sup> Those two references are frequently used in skincare products for their various functionalities,<sup>55-58</sup> and will thus enable to discover the potential of the novel emollients.

The density of all monophenols was found at about  $1.02 \pm 0.03$ , which is significantly higher than typically used emollients,<sup>36,43</sup> such as castor oil or DUB PTO (that both have a density of 0.96). Direct emulsions are more stable if the density of the fatty phase is close to that of the aqueous phase, preventing creaming or sedimentation. For example, one can suppose that an emulsion prepared with FMF-HF (density =  $1.01 \pm 0.001$ ) as part of the dispersed phase will exhibit better stability over time than the same emulsion prepared with castor oil.

The surface tension of the novel monophenols was found between 25 and 34 mN/m<sup>2</sup>, which is in the range of other emollients: Douguet *et al*<sup>43</sup> found that mineral oils exhibit an average surface tension of  $29.1 \pm 2.9$ , for vegetable oils, they found a surface tension of  $32.8 \pm 0.9$  and  $29.1 \pm 2.1$  for esters; DUB PTO and Castor Oil surface tensions are in the same range, respectively  $27.8 \pm 1.00$  and  $29.0 \pm 1.3$  (Figure 3a). Some monophenols (HFMF-HF, CMF, HGMF and OIMF for example) have surface tensions that are not significantly different than the two chosen references (p-value > 0.829). Numerical values for surface tension and density, as well as all protocols, are available in S.I.

During rheological measurements, all samples presented a Newtonian behavior. The dynamic viscosity at the Newtonian plateau is correlated to the tackiness, stickiness and spreadability of emollients: the lower the viscosity, the better the spreading and the lower the tackiness and stickiness.<sup>43,59</sup>

The viscosity of non-conjugated monophenols has been found between 86 and 165 mPa.s (Figure 3a). Douguet *et al*<sup>43</sup> studied the properties of 53 typically used emollients and established ranges for their viscosities, depending on their structural family: the non-conjugated monophenols exhibit viscosities in the range of some vegetable and mineral oils, and long chain and/or ramified silicones and esters.<sup>36,44</sup> The less viscous of the conjugated monophenols (OIMF, HFMF, FMF) have a viscosity between 643 and 983 mPa.s, comparable to long-chain dimethicone, castor oil, or glycerine, whereas GMF, CMF, HGMF present the highest viscosities.



**Figure 3a.** Viscosity at the Newtonian plateau (histogram, at the bottom) and surface tension (dots, at the top) of conjugated monophenols (plain areas) and their non-conjugated analogues (hatched areas), and of 2 commercial references (grey areas). Viscosity values are shown in a

logarithmic scale. **3b.** Spreading area of conjugated monophenols (plain areas) and their non-conjugated analogues (hatched areas) compared to two commercial references (grey areas).

The ease of spreading of emollients is directly linked to applicative properties and distribution of product on the skin.<sup>43,54</sup> The spontaneous spreading area was obtained on Vitroskin®, a non-biological skin substrate that can mimic the topography, pH, critical surface tension, chemical reactivity and ionic strength of the human skin.<sup>60</sup> 10  $\mu$ L of each sample were deposited at the center of a 6.5 cm side square of a hydrated Vitro-skin®. This square piece of Vitro-skin® was then kept in the hydration chamber for 10 minutes to allow the spreading of the sample. Spontaneous spreading values were then determined by calculating the area of the spreading zone using the Image J software (spreading area, divided by the quantity of sample and the spreading time).

Three of the non-conjugated monophenols (*ie* GMF-HF, FMF-HF, HGMF-HF) have spreadability between 3.70 and 4.70  $\text{mm}^2/\mu\text{L}/\text{min}$  (Figure 3b), which is not significantly different to that of DUB PTO ( $p$ -value  $> 0.446$ ). CMF-HF has the highest spreadability, which is significantly higher than that of DUB PTO. The last two non-conjugated monophenols (*ie* HFMF-HF, OIMF-HF) have lower spreadability, between that of DUB PTO and Castor Oil. The conjugated monophenols have spreadability between 71 and 115  $\text{mm}^2$  that are not significantly different to that of Castor Oil ( $p$ -values between 0.160 and 1.000).

Several studies have shown that surface tension is linked to spreading properties: the higher the surface tension, the lower the spreadability.<sup>36,43</sup> The results recorded herein are in accordance with this observation (Figure 3). The non-conjugated monophenols have been found to have higher spontaneous spreadability and lower surface tension than their conjugated analogues.



For all tested physico-chemical characteristics, corresponding monophenols are competitive to emollients like DUB PTO or castor oil, while bringing additional active properties (UV-filtering and/or antiradical activities) as mentioned previously. Those results could be an interesting tool to help choosing appropriate emollients for further formulation analyses, according to the desired textural properties, and depending on the targeted application and the skin area to cover (body milk for a large area or eye cream, for example, for a small area).

### Antimicrobial assays

Cosmetic products are commonly formulated with synthetic preservatives such as parabens or phenoxyethanol, that efficiently prevent the growth of microorganisms. Unfortunately, some studies show their negative impacts on human health.<sup>5,6</sup> In this respect, bio-based alternatives to synthetic preservatives, with a broad spectrum of inhibition toward several types of microorganisms are of considerable interest to the cosmetic sector. As ferulic derivatives can exhibit such inhibition, a preliminary study was conducted on the growth of two bacteria, a gram -: *Escherichia coli* (*E. coli*) and a gram +: *Bacillus subtilis* (*B. subtilis*) at different concentrations of monophenols. As references, the inhibition of ethyl paraben as well as starting materials (*i.e.* EtFe, EtHFe and Ferulic acid) was studied towards the same microorganisms.

Ethyl paraben showed really good inhibition towards both microorganisms (for a concentration of less than 2.5% w/v, see Table 2). All starting materials showed really good inhibitions too, for concentrations of 2.5 or less than 2.5% w/v.

Unfortunately, GMF and CMF were not soluble in the solution used for the tests so we could not determine their antimicrobial properties. The other tested molecules either exhibited an inhibition toward *B. subtilis* or *E. coli*, except for OIMF-HF that exhibited no inhibition. CMF-HF was the only monophenol exhibiting an inhibition toward both bacteria, but at least 5% w/v

was necessary. Four other monophenols exhibited good inhibition (for < 2.5% w/v) toward *B. subtilis*: HGMF, HFMF and their non-conjugated analogues. The common feature of the four molecules being the saturated fatty alcohol, one can assume that this chemical structure is a key feature for higher antimicrobial activity. Overall, monophenols showed less inhibition than the reference and the starting materials, probably due to solubility and diffusion issues.

It is important to note that this assay is only the first step for the characterization of antimicrobial properties. It allows to make a first selection between different molecules that could exhibit potential inhibition but does not show the effect of the tested molecules toward the bacteria, *i.e.* bactericidal or bacteriostatic effect. It could be interesting to further investigate those effects with the four monophenols that exhibited the best anti-bacterial effect, as well as the role of the saturation.

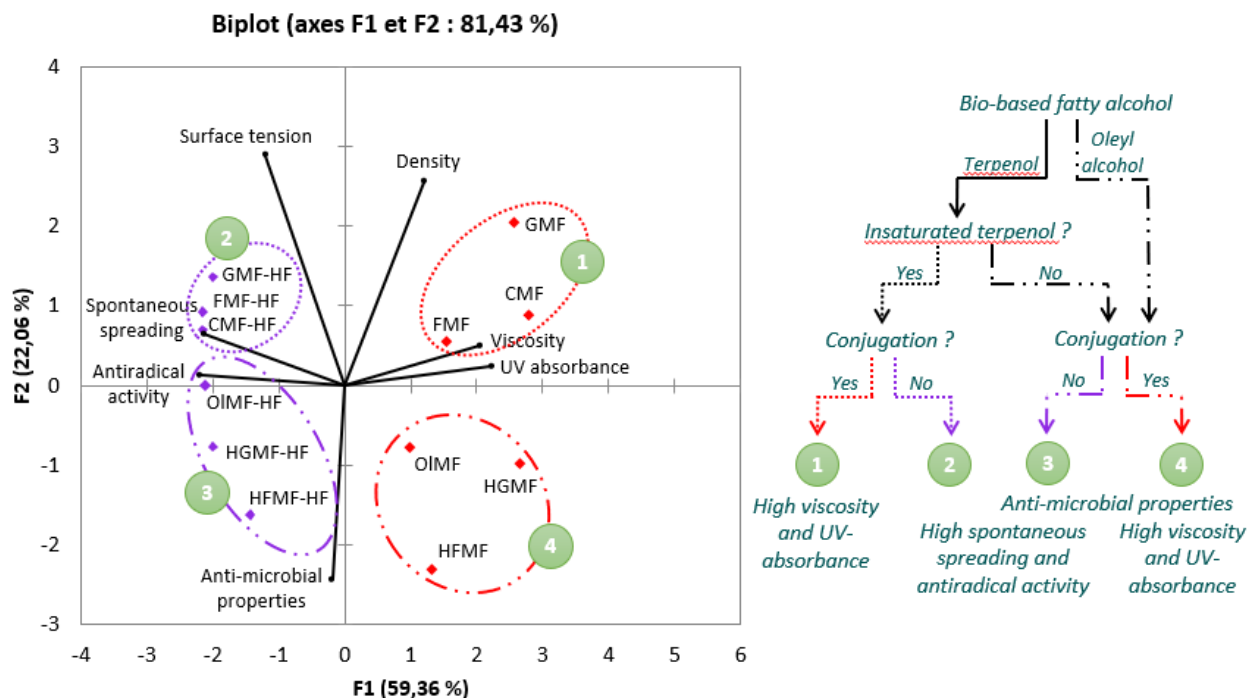
**Table 2.** Relative inhibition of two microorganisms toward the synthesized monophenols, compared to starting materials and a reference

| Name                 | Inhibition <sup>a</sup> |                |
|----------------------|-------------------------|----------------|
|                      | <i>B. subtilis</i>      | <i>E. coli</i> |
| <b>GMF</b>           | N/D <sup>b</sup>        |                |
| <b>CMF</b>           |                         |                |
| <b>FMF</b>           | -                       | ++             |
| <b>HGMF</b>          | +++                     | -              |
| <b>HFMF</b>          | +++                     | -              |
| <b>OIMF</b>          | -                       | +              |
| <b>GMF-HF</b>        | -                       | ++             |
| <b>CMF-HF</b>        | +                       | +              |
| <b>FMF-HF</b>        | -                       | +              |
| <b>HGMF-HF</b>       | +++                     | -              |
| <b>HFMF-HF</b>       | +++                     | -              |
| <b>OIMF-HF</b>       | -                       | -              |
| <b>EtFe</b>          | +++                     | +++            |
| <b>EtHFe</b>         | +++                     | +++            |
| <b>Ferulic acid</b>  | ++                      | +++            |
| <b>Ethyl paraben</b> | +++                     | +++            |

<sup>a</sup>+: inhibition observed for at least 5% w/v of sample; ++: inhibition observed for at least 2.5% w/v of sample; +++: inhibition observed for less than 2.5% w/v of sample; -: no inhibition observed. <sup>b</sup>N/D: non-determined

### Structure/activity relationship of the multifunctional monophenols

A principal component analysis (PCA) was conducted on the 7 properties (UV absorbance, antiradical activity, density, viscosity, surface tension, spontaneous spreading and anti-microbial properties) that were tested to describe the 12 novel monophenols (Figure 4). The benchmarks that were used to compare monophenols to typically used molecules for every given property were not assessed for all 7 properties but only for the ones that they are intended for. For example, DUB PTO is an emollient with interesting physico-chemical properties such as viscosity, surface tension or spreading capabilities, but has no UV-filtering or antiradical activity. On the other hand, octinoxate is a commercial UV-filter but its melting point is above 25°C so its viscosity and spontaneous spreading could not be measured under applied conditions. Finally, the starting materials (*i.e.* EtFe, EtHFe and Ferulic acid) are also solid below 25°C and have thus not been used as references for the physico-chemical properties assessments.



**Figure 4.** Principal component analysis correlating the results of every tested properties on the novel emollients (left side) and structure-activity relationship tree (right side).

This method allows to summarize data in a single biplot which, herein, covers more than 80% of information, and thus describes well the overall results obtained. Each property is represented on the figure, as a vector: for each vector, the farthest from the center of the biplot, the higher the value of the corresponding property. The horizontal and vertical axes of the biplot can represent a given property if its vector is in the same direction as an axis. The vector that represents anti-microbial activity is closed to the vertical axis: antimicrobial properties are then better for the monophenols positioned on the bottom side of the figure, *ie* monophenols synthesized with hydrogenated terpenols. The horizontal axis can be described by high UV absorbance values on the right side and high antiradical activities on the left side. UV absorbance and antiradical activity vectors have almost opposite directions: those two properties are thus anticorrelated. For example, a monophenol that has anti-UV properties has lower antiradical properties and vice-

versa. The same conclusion can be drawn on the viscosity and spontaneous spreading vectors. The higher the viscosity, the lower the spontaneous spreading.

Two vectors forming a right angle represent properties that are independent and not correlated, *e.g.* antiradical activity and anti-microbial properties.

Two groups (red and purple) have been drawn depending on whether the monophenol has a conjugation between its aromatic cycle and the ester. The ACP shows the relation between this chemical structure and the potentially related activities: conjugated monophenols (in red) are positioned on the right side of the PCA and can thus be described by their high viscosity and high UV absorbance. On the other hand, non-conjugated monophenols (in purple) are positioned on the left side of the figure, and can be described by the highest values of spontaneous spreading and the best antiradical activity.

Amongst the first two colored groups of molecules, four subsidiary groups can be drawn in total, depending on the nature of the bio-based alcohol. Four groups have finally been created, that are composed of monophenols with similar structures: at the right top of the biplot, group 1 which is composed of conjugated monophenols synthesized with unsaturated alcohols; at the left top, group 2 with the non-conjugated analogues of group 1; at the left bottom, group 3 with the three other non-conjugated monophenols, synthesized either with a saturated terpenol or oleyl alcohol; and group 4 at the right bottom with the conjugated analogues of group 3. This analysis clearly shows the relation between the chemical structure of the monophenols and their properties.

Finally, this mapping can be used as a formulation tool to select the best candidates depending on the specifications needed. Thus, OIMF-HF may be chosen for an important antiradical

activity and a low viscosity whereas CMF will be selected for its high viscosity and UV absorbance. Also, a structure-activity relationship tree has been drawn (Figure 5) to help the prediction of potential properties of a monophenol depending on its structure. Moreover, formulators may choose to associate several emollients according to the expected properties.

## CONCLUSION

Following several green chemistry principles, twelve novel bio-based emollients were successfully synthesized from diverse bio-sourced fatty alcohols enzymatically esterified to ferulic-based synthons, with very good to excellent scores for two green metrics (MI and Ecoscale). Six monophenols with a C-C bond conjugated with their aromatic cycle, and their 6 non-conjugated analogues were obtained in excellent yield (80-93%).

The twelve novel emollients were characterized to assess their multifunctional properties: seven characteristics were evaluated and were compared to commercially available referents typically used for each tested property. UV-filtering and antiradical properties were found to be anti-correlated: conjugated monophenols are the best UV-filters with very good stability (LoA between 8 and 27%) and non-conjugated ones have the best antiradical properties, with  $EC_{50}$  below 15 mmol. Monophenols bearing saturated fatty alcohols exhibited the highest anti-microbial inhibition. Density and surface tension exhibit values close to commercial emollients. Conjugated monophenols display the highest viscosity, whereas the non-conjugated ones have the highest spontaneous spreading, those two properties being anti-correlated.

Finally, the mapping of the twelve novel bio-based emollients as a function of the various tested properties, represented as a PCA, made it possible to choose the best candidates depending on the specification for the formulation of cosmetic products. In the future, it will be interesting

to incorporate these emollients in complex media in order to investigate their behaviors with other ingredients and to put forward certain emollients.

## SUPPORTING INFORMATION

Experimental details, materials and methods, including spectra and experimental data.

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### Author Contributions

FR performed investigations, validation and formal analysis of the results and write the original draft. LB and FR performed spontaneous spreading measures. AD performed HRMS analyses. BG performed additional antimicrobial analyses. AF, EG and GS conceptualized and supervised the work. AF, EG, GS and FA reviewed the manuscript. GS and FA acquired funding and provided resources.

## ACKNOWLEDGMENTS

This work was financially supported by the Région Normandie and the URD Agro-Biotechnologies Industrielles (ABI) through the financial support of the Grand Reims, the Région Grand Est and the Conseil Départemental de la Marne.

## REFERENCES

- (1) Egambaram, O. P.; Kesavan Pillai, S.; Ray, S. S. Materials Science Challenges in Skin UV Protection: A Review. *Photochemistry and Photobiology* **2020**, *96* (4), 779–797. <https://doi.org/10.1111/php.13208>.

- (2) Purnamawati, S.; Indrastuti, N.; Danarti, R.; Saefudin, T. The Role of Moisturizers in Addressing Various Kinds of Dermatitis: A Review. *Clin Med Res* **2017**, *15* (3–4), 75–87. <https://doi.org/10.3121/cm.2017.1363>.
- (3) Lawton, S. Practical Issues for Emollient Therapy in Dry and Itchy Skin. *Br J Nurs* **2009**, *18* (16), 978–984. <https://doi.org/10.12968/bjon.2009.18.16.43964>.
- (4) Wang, J.; Pan, L.; Wu, S.; Lu, L.; Xu, Y.; Zhu, Y.; Guo, M.; Zhuang, S. Recent Advances on Endocrine Disrupting Effects of UV Filters. *International Journal of Environmental Research and Public Health* **2016**, *13* (8), 782. <https://doi.org/10.3390/ijerph13080782>.
- (5) Wang, J.; Liu, Y.; Kam, W. R.; Li, Y.; Sullivan, D. A. Toxicity of the Cosmetic Preservatives Parabens, Phenoxyethanol and Chlorphenesin on Human Meibomian Gland Epithelial Cells. *Experimental Eye Research* **2020**, *196*, 108057. <https://doi.org/10.1016/j.exer.2020.108057>.
- (6) Ma, X.; Wang, H.; Song, Y.; Pan, Y. Skin Irritation Potential of Cosmetic Preservatives: An Exposure-Relevant Study. *Journal of Cosmetic Dermatology* **2021**, *20* (1), 195–203. <https://doi.org/10.1111/jocd.13502>.
- (7) Pop, A.; Berce, C.; Bolfa, P.; Nagy, A.; Catoi, C.; Dumitrescu, I.-B.; Silaghi-Dumitrescu, L.; Loghin, F. Evaluation of the Possible Endocrine Disruptive Effect of Butylated Hydroxyanisole, Butylated Hydroxytoluene and Propyl Gallate in Immature Female Rats. *Farmacia* **2013**, *61* (1), 202–211.
- (8) Ouchene, L.; Litvinov, I. V.; Netchiporouk, E. Hawaii and Other Jurisdictions Ban Oxybenzone or Octinoxate Sunscreens Based on the Confirmed Adverse Environmental Effects of Sunscreen Ingredients on Aquatic Environments. *J Cutan Med Surg* **2019**, *23* (6), 648–649. <https://doi.org/10.1177/1203475419871592>.
- (9) Downs, C. A.; Kramarsky-Winter, E.; Segal, R.; Fauth, J.; Knutson, S.; Bronstein, O.; Ciner, F. R.; Jeger, R.; Lichtenfeld, Y.; Woodley, C. M.; Pennington, P.; Cadenas, K.; Kushmaro, A.; Loya, Y. Toxicopathological Effects of the Sunscreen UV Filter, Oxybenzone (Benzophenone-3), on Coral Planulae and Cultured Primary Cells and Its Environmental Contamination in Hawaii and the U.S. Virgin Islands. *Arch Environ Contam Toxicol* **2016**, *70* (2), 265–288. <https://doi.org/10.1007/s00244-015-0227-7>.
- (10) Mojsiewicz-Pieńkowska, K.; Krenczkowska, D. Evolution of Consciousness of Exposure to Siloxanes—Review of Publications. *Chemosphere* **2018**, *191*, 204–217. <https://doi.org/10.1016/j.chemosphere.2017.10.045>.
- (11) Lempereur, I.; Rouau, X.; Abecassis, J. Genetic and Agronomic Variation in Arabinoxylan and Ferulic Acid Contents of Durum Wheat (*Triticum durum*L.) Grain and Its Milling Fractions. *Journal of Cereal Science* **1997**, *25* (2), 103–110. <https://doi.org/10.1006/jcrs.1996.0090>.
- (12) Kroon, P. A.; Faulds, C. B.; Ryden, P.; Robertson, J. A.; Williamson, G. Release of Covalently Bound Ferulic Acid from Fiber in the Human Colon. *J. Agric. Food Chem.* **1997**, *45* (3), 661–667. <https://doi.org/10.1021/jf9604403>.
- (13) Buranov, A. U.; Mazza, G. Extraction and Purification of Ferulic Acid from Flax Shives, Wheat and Corn Bran by Alkaline Hydrolysis and Pressurised Solvents. *Food Chemistry* **2009**, *115* (4), 1542–1548. <https://doi.org/10.1016/j.foodchem.2009.01.059>.
- (14) Ou, S.; Kwok, K.-C. Ferulic Acid: Pharmaceutical Functions, Preparation and Applications in Foods. *Journal of the Science of Food and Agriculture* **2004**, *84* (11), 1261–1269. <https://doi.org/10.1002/jsfa.1873>.
- (15) Mancuso, C.; Santangelo, R. Ferulic Acid: Pharmacological and Toxicological Aspects. *Food and Chemical Toxicology* **2014**, *65*, 185–195. <https://doi.org/10.1016/j.fct.2013.12.024>.



- (16) Barber, M. S.; McConnell, V. S.; DeCaux, B. S. Antimicrobial Intermediates of the General Phenylpropanoid and Lignin Specific Pathways. *Phytochemistry* **2000**, *54* (1), 53–56. [https://doi.org/10.1016/S0031-9422\(00\)00038-8](https://doi.org/10.1016/S0031-9422(00)00038-8).
- (17) Park, E.-S.; Moon, W.-S.; Song, M.-J.; Kim, M.-N.; Chung, K.-H.; Yoon, J.-S. Antimicrobial Activity of Phenol and Benzoic Acid Derivatives. *International Biodeterioration & Biodegradation* **2001**, *47* (4), 209–214. [https://doi.org/10.1016/S0964-8305\(01\)00058-0](https://doi.org/10.1016/S0964-8305(01)00058-0).
- (18) Cho, J.-Y.; Moon, J.-H.; Seong, K.-Y.; Park, K.-H. Antimicrobial Activity of 4-Hydroxybenzoic Acid and Trans 4-Hydroxycinnamic Acid Isolated and Identified from Rice Hull. *Bioscience, Biotechnology, and Biochemistry* **1998**, *62* (11), 2273–2276. <https://doi.org/10.1271/bbb.62.2273>.
- (19) Stojković, D.; Petrović, J.; Soković, M.; Glamočlija, J.; Kukić-Marković, J.; Petrović, S. In Situ Antioxidant and Antimicrobial Activities of Naturally Occurring Caffeic Acid, p-Coumaric Acid and Rutin, Using Food Systems. *Journal of the Science of Food and Agriculture* **2013**, *93* (13), 3205–3208. <https://doi.org/10.1002/jsfa.6156>.
- (20) Rioux, B.; Mention, M. M.; Alarcán, J.; Abiola, T. T.; Peyrot, C.; Brunissen, F.; Braeuning, A.; Stavros, V. G.; Allais, F. Sustainable Synthesis, in Silico Evaluation of Potential Toxicity and Environmental Fate, Antioxidant and UV-Filtering/Photostability Activity of Phenolic-Based Thiobarbituric Derivatives. *Green Chemistry Letters and Reviews* **2022**, *15* (1), 116–127. <https://doi.org/10.1080/17518253.2021.2022219>.
- (21) Mouterde, L. M. M.; Peru, A. A. M.; Mention, M. M.; Brunissen, F.; Allais, F. Sustainable Straightforward Synthesis and Evaluation of the Antioxidant and Antimicrobial Activity of Sinapine and Analogues. *J. Agric. Food Chem.* **2020**, *68* (26), 6998–7004. <https://doi.org/10.1021/acs.jafc.0c02183>.
- (22) Rioux, B.; Peyrot, C.; Mention, M. M.; Brunissen, F.; Allais, F. Sustainable Synthesis of p-Hydroxycinnamic Diacids through Proline-Mediated Knoevenagel Condensation in Ethanol: An Access to Potent Phenolic UV Filters and Radical Scavengers. *Antioxidants* **2020**, *9* (4), 331. <https://doi.org/10.3390/antiox9040331>.
- (23) Rioux, B.; Combes, J.; Woolley, J. M.; Rodrigues, N. d. N.; Mention, M. M.; Stavros, V. G.; Allais, F. From Biomass-Derived p-Hydroxycinnamic Acids to Novel Sustainable and Non-Toxic Phenolics-Based UV-Filters: A Multidisciplinary Journey. *Frontiers in Chemistry* **2022**, *10*. <https://doi.org/10.3389/fchem.2022.886367>.
- (24) Nadal, J.; Pedrosa, F. de B.; Minozzo, B. R.; Brito, P. S. de; Farago, P. V.; Velloso, J. C. R.; Miyoshi, E. A Simple and High-Yield Synthesis of Hexadecyl Ferulate and Its *In Vitro* Antioxidant Potential. *Braz. arch. biol. technol.* **2018**, *61*, e18170809. <https://doi.org/10.1590/1678-4324-2018170809>.
- (25) Valkute, T. R.; Aratikatla, E. K.; Bhattacharya, A. K. Efficient Synthesis of Functionalized Olefins by Wittig Reaction Using Amberlite Resin as a Mild Base. *Synthetic Communications* **2017**, *47* (6), 581–589. <https://doi.org/10.1080/00397911.2016.1276191>.
- (26) Mention, M. M.; Flourat, A. L.; Peyrot, C.; Allais, F. Biomimetic Regioselective and High-Yielding Cu(I)-Catalyzed Dimerization of Sinapate Esters in Green Solvent Cyrene<sup>TM</sup>: Towards Sustainable Antioxidant and Anti-UV Ingredients. *Green Chem.* **2020**, *22* (6), 2077–2085. <https://doi.org/10.1039/D0GC00122H>.
- (27) Abiola, T. T.; Rodrigues, N. d. N.; Ho, C.; Coxon, D. J. L.; Horbury, M. D.; Toldo, J. M.; do Casal, M. T.; Rioux, B.; Peyrot, C.; Mention, M. M.; Balaguer, P.; Barbatti, M.; Allais, F.; Stavros, V. G. New Generation UV-A Filters: Understanding Their Photodynamics on a

- Human Skin Mimic. *J. Phys. Chem. Lett.* **2021**, *12* (1), 337–344. <https://doi.org/10.1021/acs.jpcllett.0c03004>.
- (28) Bhattacharya, S.; Sherje, A. P. Development of Resveratrol and Green Tea Sunscreen Formulation for Combined Photoprotective and Antioxidant Properties. *Journal of Drug Delivery Science and Technology* **2020**, *60*, 102000. <https://doi.org/10.1016/j.jddst.2020.102000>.
- (29) Piccinino, D.; Capecchi, E.; Tomaino, E.; Gabellone, S.; Gigli, V.; Avitabile, D.; Saladino, R. Nano-Structured Lignin as Green Antioxidant and UV Shielding Ingredient for Sunscreen Applications. *Antioxidants* **2021**, *10* (2), 274. <https://doi.org/10.3390/antiox10020274>.
- (30) Peyrot, C.; Mention, M. M.; Brunissen, F.; Allais, F. Sinapic Acid Esters: Octinoxate Substitutes Combining Suitable UV Protection and Antioxidant Activity. *Antioxidants* **2020**, *9* (9), 782. <https://doi.org/10.3390/antiox9090782>.
- (31) Hinneburg, I.; Kempe, S.; Rüttinger, H.-H.; Neubert, R. H. H. Antioxidant and Photoprotective Properties of an Extract from Buckwheat Herb (*Fagopyrum Esculentum* MOENCH). *Die Pharmazie - An International Journal of Pharmaceutical Sciences* **2006**, *61* (3), 237–240.
- (32) Willig, G.; Brunissen, F.; Brunois, F.; Godon, B.; Magro, C.; Monteux, C.; Peyrot, C.; Ioannou, I. Phenolic Compounds Extracted from Cherry Tree (*Prunus Avium*) Branches: Impact of the Process on Cosmetic Properties. *Antioxidants* **2022**, *11* (5), 813. <https://doi.org/10.3390/antiox11050813>.
- (33) Mention, M. M.; Peyrot, C.; Godon, B.; Alarcán, J.; Brunissen, F.; Grimaldi, M.; Balaguer, P.; Braeuning, A.; Allais, F. Straightforward Sustainable Synthesis of Novel Non-Endocrine Disruptive Bio-Based Organic UV-B Filters with Antimicrobial Activity. *Green Chemistry Letters and Reviews* **2023**, *16* (1), 2188125. <https://doi.org/10.1080/17518253.2023.2188125>.
- (34) Minsat, L.; Peyrot, C.; Brunissen, F.; Renault, J.-H.; Allais, F. Synthesis of Biobased Phloretin Analogues: An Access to Antioxidant and Anti-Tyrosinase Compounds for Cosmetic Applications. *Antioxidants* **2021**, *10* (4), 512. <https://doi.org/10.3390/antiox10040512>.
- (35) Chen, J.; Ran, M.; Wang, M.; Liu, X.; Liu, S.; Ruan, Z.; Jin, N. Evaluation of Antityrosinase Activity and Mechanism, Antioxidation, and UV Filter Properties of Theaflavin. *Biotechnology and Applied Biochemistry* **2022**, *69* (3), 951–962. <https://doi.org/10.1002/bab.2166>.
- (36) Goussard, V.; Aubry, J.-M.; Nardello-Rataj, V. Bio-Based Alternatives to Volatile Silicones: Relationships between Chemical Structure, Physicochemical Properties and Functional Performances. *Advances in Colloid and Interface Science* **2022**, *304*, 102679. <https://doi.org/10.1016/j.cis.2022.102679>.
- (37) Rawlings, A. V.; Lombard, K. J. A Review on the Extensive Skin Benefits of Mineral Oil. *International Journal of Cosmetic Science* **2012**, *34* (6), 511–518. <https://doi.org/10.1111/j.1468-2494.2012.00752.x>.
- (38) Divijak, J. M. Jr. Production of Technical White Mineral Oil. US3629096A, 1971. <https://patents.google.com/patent/US3629096A/en> (accessed 2023-05-05).
- (39) Littich, R.; Ilseman, A.; Hategan, G.; Liang, Y.; Koers, K.; Morie-Bebel, M. Bio-Based Alternatives for Silicone and Petrochemical Emollients from Natural Oil Metathesis. *H&PC Today* **2014**, *9*, 18–20.

- (40) McPhee, D.; Pin, A.; Kizer, L.; Perelman, L. Deriving Renewable Squalane from Sugarcane. *Cosmetics & Toiletries* **2014**, *129* (6), 20–26.
- (41) Thomas, A.; Matthäus, B.; Fiebig, H.-J. Fats and Fatty Oils. In *Ullmann's Encyclopedia of Industrial Chemistry*; John Wiley & Sons, Ltd, 2015; pp 1–84. [https://doi.org/10.1002/14356007.a10\\_173.pub2](https://doi.org/10.1002/14356007.a10_173.pub2).
- (42) Montiel, M. C.; Máximo, F.; Serrano-Arnaldos, M.; Ortega-Requena, S.; Murcia, M. D.; Bastida, J. Biocatalytic Solutions to Cyclomethicones Problem in Cosmetics. *Engineering in Life Sciences* **2019**, *19* (5), 370–388. <https://doi.org/10.1002/elsc.201800194>.
- (43) Douguet, M.; Picard, C.; Savary, G.; Merlaud, F.; Loubat-bouleuc, N.; Grisel, M. Spreading Properties of Cosmetic Emollients: Use of Synthetic Skin Surface to Elucidate Structural Effect. *Colloids and Surfaces B: Biointerfaces* **2017**, *154*, 307–314. <https://doi.org/10.1016/j.colsurfb.2017.03.028>.
- (44) Chao, C.; Génot, C.; Rodriguez, C.; Magniez, H.; Lacourt, S.; Fievez, A.; Len, C.; Pezron, I.; Luart, D.; van Hecke, E. Emollients for Cosmetic Formulations: Towards Relationships between Physico-Chemical Properties and Sensory Perceptions. *Colloids and Surfaces A: Physicochemical and Engineering Aspects* **2018**, *536*, 156–164. <https://doi.org/10.1016/j.colsurfa.2017.07.025>.
- (45) Van Aken, K.; Streckowski, L.; Patiny, L. EcoScale, a Semi-Quantitative Tool to Select an Organic Preparation Based on Economical and Ecological Parameters. *Beilstein J. Org. Chem.* **2006**, *2* (1), 3. <https://doi.org/10.1186/1860-5397-2-3>.
- (46) Curzons, A. D.; Constable, D. J. C.; Mortimer, D. N.; Cunningham, V. L. So You Think Your Process Is Green, How Do You Know?—Using Principles of Sustainability to Determine What Is Green—a Corporate Perspective. *Green Chem.* **2001**, *3* (1), 1–6. <https://doi.org/10.1039/B007871I>.
- (47) Pion, F. F.; Armando, F. A. F. R.; Ducrot, P. H. P. H.; Allais, F. F. Chemo-Enzymatic Preparation of New Bio-Based Bis-and Trisphenols: New Versatile Building Blocks for Polymer Chemistry. *RSC Advances* **2013**, *3* (23), 8988. <https://doi.org/10.1039/c3ra41247d>.
- (48) Reano, A. F.; Chérubin, J.; Peru, A. M. M.; Wang, Q.; Clément, T.; Domenek, S.; Allais, F. Structure–Activity Relationships and Structural Design Optimization of a Series of *p* - Hydroxycinnamic Acids-Based Bis- and Trisphenols as Novel Sustainable Antiradical/Antioxidant Additives. *ACS Sustainable Chem. Eng.* **2015**, *3* (12), 3486–3496. <https://doi.org/10.1021/acssuschemeng.5b01281>.
- (49) Hollande, L.; Domenek, S.; Allais, F. Chemo-Enzymatic Synthesis of Renewable Sterically-Hindered Phenolic Antioxidants with Tunable Polarity from Lignocellulose and Vegetal Oil Components. *IJMS* **2018**, *19* (11), 3358. <https://doi.org/10.3390/ijms19113358>.
- (50) Reano, A. F.; Domenek, S.; Pernes, M.; Beaugrand, J.; Allais, F. Ferulic Acid-Based Bis/Trisphenols as Renewable Antioxidants for Polypropylene and Poly(Butylene Succinate). *ACS Sustainable Chem. Eng.* **2016**, *4* (12), 6562–6571. <https://doi.org/10.1021/acssuschemeng.6b01429>.
- (51) Constable, D. J. C.; Curzons, A. D.; Cunningham, V. L. Metrics to ‘Green’ Chemistry—Which Are the Best? *Green Chem.* **2002**, *4* (6), 521–527. <https://doi.org/10.1039/B206169B>.
- (52) Dean, J. C.; Kusaka, R.; Walsh, P. S.; Allais, F.; Zwier, T. S. Plant Sunscreens in the UV-B: Ultraviolet Spectroscopy of Jet-Cooled Sinapoyl Malate, Sinapic Acid, and Sinapate Ester Derivatives. *J. Am. Chem. Soc.* **2014**, *136* (42), 14780–14795. <https://doi.org/10.1021/ja5059026>.

- (53) Mishra, K.; Ojha, H.; Chaudhury, N. K. Estimation of Antiradical Properties of Antioxidants Using DPPH Assay: A Critical Review and Results. *Food Chemistry* **2012**, *130* (4), 1036–1043. <https://doi.org/10.1016/j.foodchem.2011.07.127>.
- (54) Savary, G.; Grisel, M.; Picard, C. Impact of Emollients on the Spreading Properties of Cosmetic Products: A Combined Sensory and Instrumental Characterization. *Colloids and Surfaces B: Biointerfaces* **2013**, *102*, 371–378. <https://doi.org/10.1016/j.colsurfb.2012.07.028>.
- (55) Warra, A., A. Castor Seed Oil and Its Potential Cosmetic Application. *EQUIJOST* **2013**, *1* (1), 104–109.
- (56) Pakkang, N.; Uraki, Y.; Koda, K.; Nithitanakul, M.; Charoensaeng, A. Preparation of Water-in-Oil Microemulsion from the Mixtures of Castor Oil and Sunflower Oil as Makeup Remover. *Journal of Surfactants and Detergents* **2018**, *21* (6), 809–816. <https://doi.org/10.1002/jsde.12189>.
- (57) Loubat-Bouleuc, N. Les esters en cosmétologie : généralités et fonctionnalités. *OCL* **2004**, *11* (6), 454–456. <https://doi.org/10.1051/ocl.2004.0454>.
- (58) Fauchoux, E.; Picard, C.; Grisel, M.; Savary, G. Residual Film Formation after Emulsion Application: Understanding the Role and Fate of Excipients on Skin Surface. *International Journal of Pharmaceutics* **2020**, *585*, 119453. <https://doi.org/10.1016/j.ijpharm.2020.119453>.
- (59) Parente, M. E.; Ga' Mbaro, A.; Solana, G. Study of Sensory Properties of Emollients Used in Cosmetics and Their Correlation with Physicochemical Properties. *International Journal of Cosmetic Science* **2005**, *27* (6), 354–354. [https://doi.org/10.1111/j.1467-2494.2005.00289\\_3.x](https://doi.org/10.1111/j.1467-2494.2005.00289_3.x).
- (60) *VITRO-SKIN®*. IMS. <https://ims-usa.com/vitro-skin-substrates/vitro-skin/> (accessed 2023-07-10).

## SYNOPSIS

Ferulic acid was functionalized into bio-based multifunctional emollients, reducing the reliance on petroleum-based ingredients and promoting sustainability in the cosmetic industry.

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