



**HAL**  
open science

## Radical intermediates and monoalkoxyphenols: anti-and prooxidant activities

Yannick Port-Lougarre, Bertrand Vilen, Elena Gimenez-Arnau

► **To cite this version:**

Yannick Port-Lougarre, Bertrand Vilen, Elena Gimenez-Arnau. Radical intermediates and monoalkoxyphenols: anti-and prooxidant activities. Journées Scientifiques de l'ARPE (Association Française de Résonance Paramagnétique Électronique), Mar 2022, Paris, France. hal-03607735

**HAL Id: hal-03607735**

**<https://hal.science/hal-03607735v1>**

Submitted on 14 Mar 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

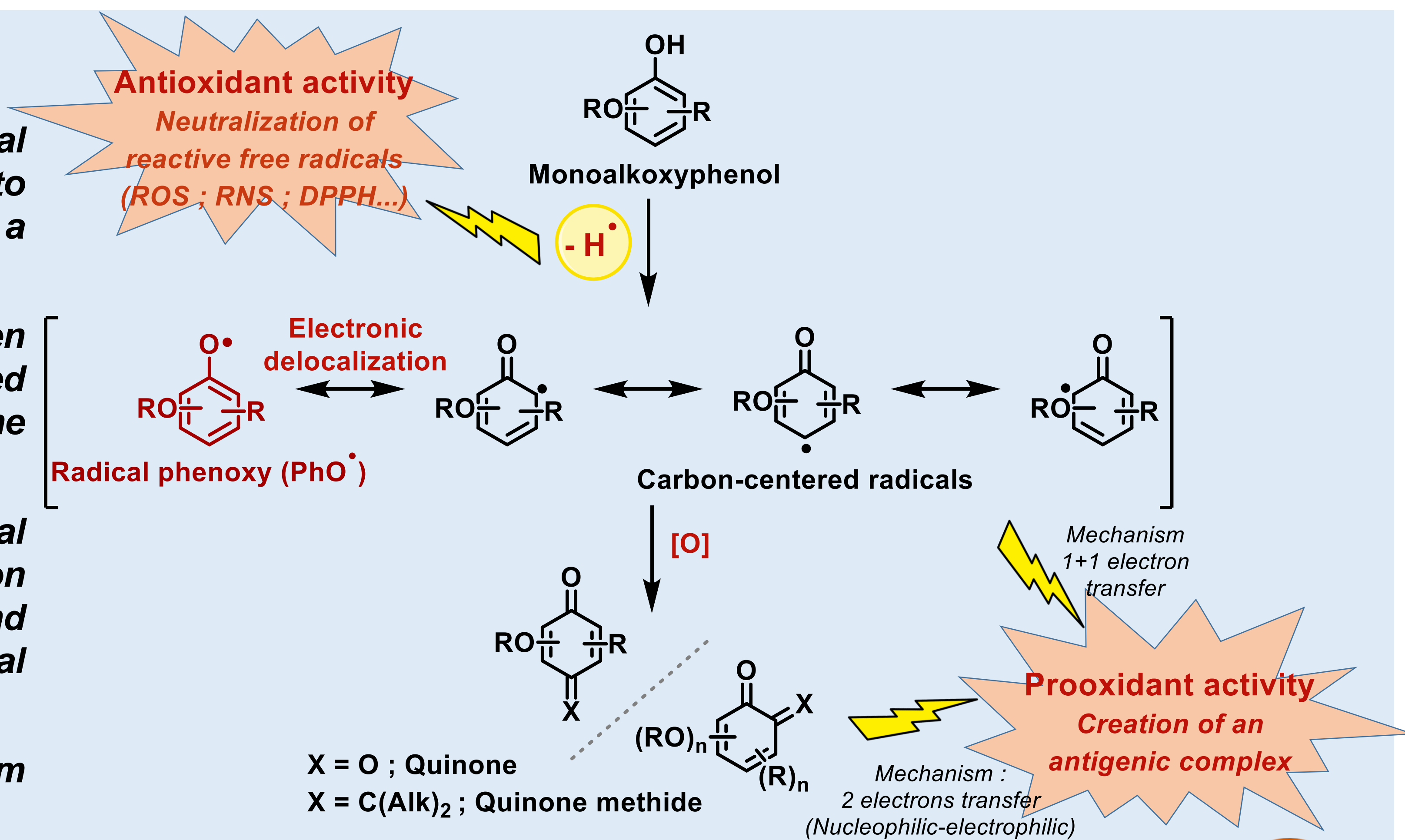
## BACKGROUND

Monoalkoxyphenols are well-known for having an antioxidant potential by releasing an hydrogen ( $H^{\bullet}$ ). This property allows these molecules to quench reactive free-radicals, such as ROS, RNS or DPPH (used as a reference to measure the antioxidant activity).<sup>1,2</sup>

Despite of these cytoprotective benefits, those compounds often possess a cytotoxic activity (e.g. allergic contact dermatitis<sup>3</sup>) suspected for many years to result from sensitization to the electrophilic quinone derivatives.<sup>4</sup>

However, due to the aromatic core, the unpaired electron of the initial phenoxy radical formed is delocalized giving many different free carbon centered radicals.<sup>3</sup> Moreover, today, radical mechanisms are more and more assumed to be involved in the skin sensitization process to several allergens.<sup>5</sup>

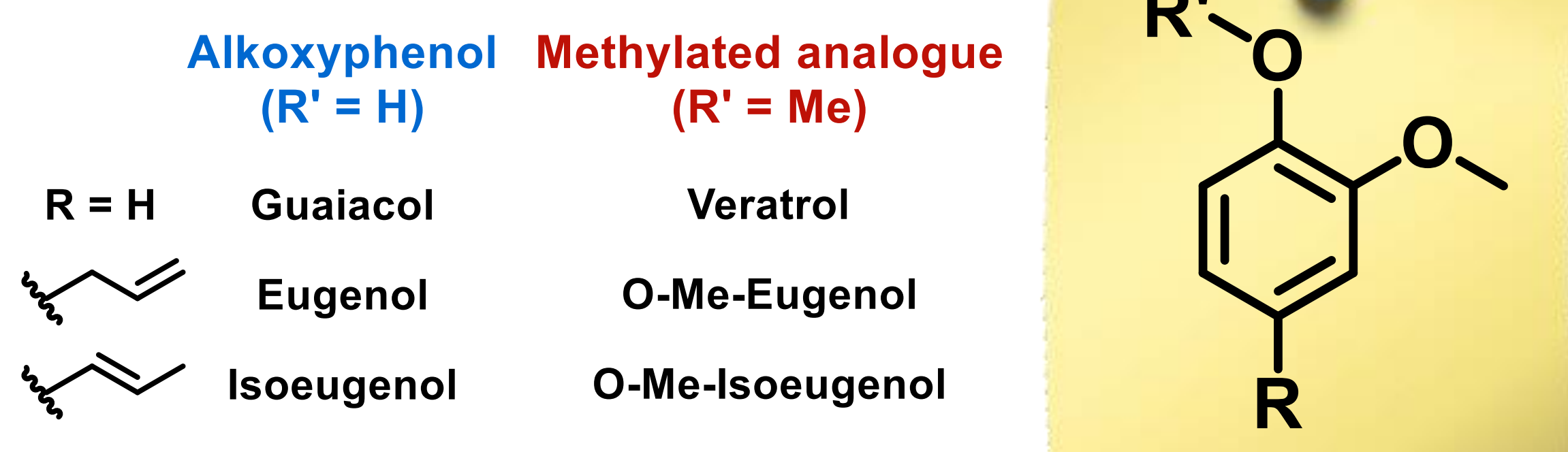
Nevertheless, the link between free radicals formed and their mechanism of action leading to the cytotoxic response is far from being unraveled.



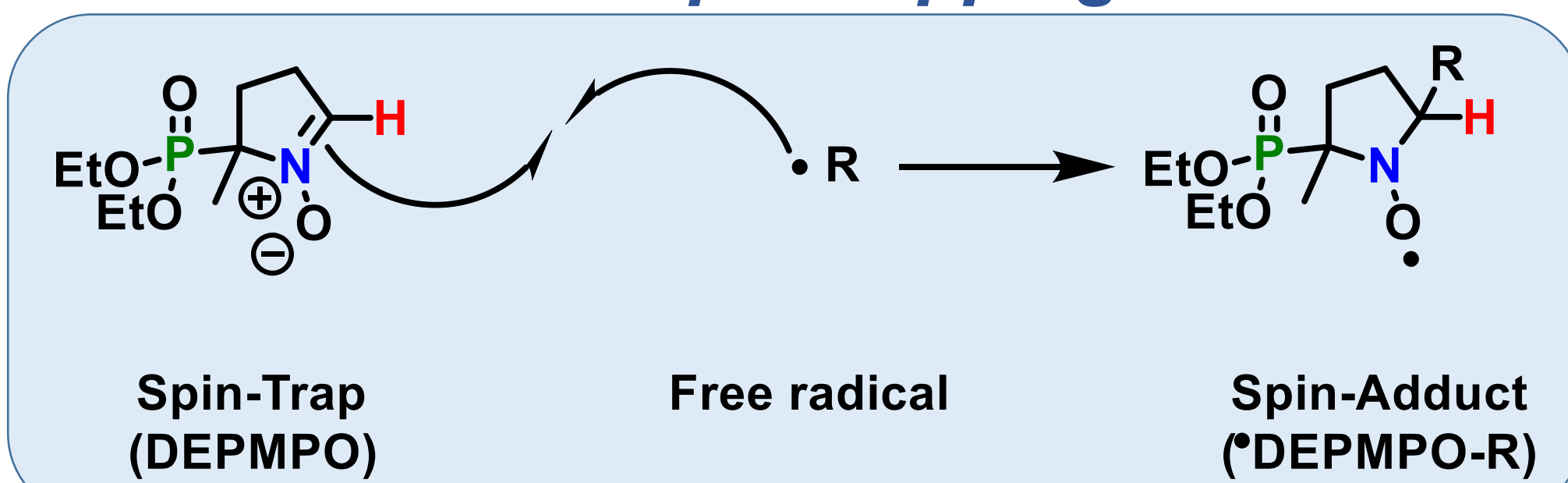
## OBJECTIVES

Get insights on the involvement of free radical intermediates issued from monoalkoxyphenol derivatives to elucidate the duality between their antioxidant-cytoprotective and their prooxidant-cytotoxic activities in the skin

## SPIN-TRAPPING IN SOLUTION

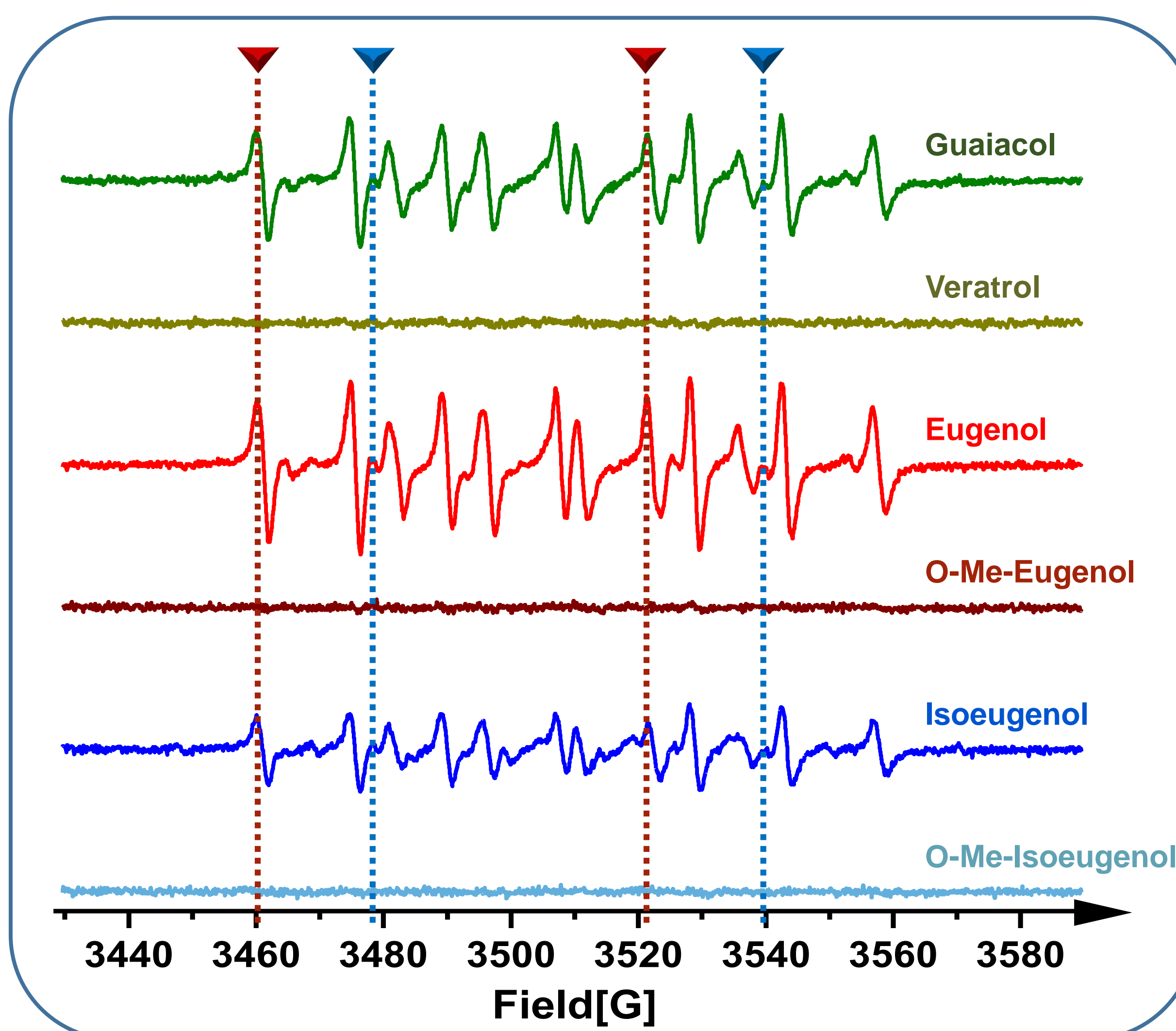


### EPR spin trapping



Experiment done by creating an oxidative media:

Spin-Trap: 50 mM  
Target compound: 20 mM  
HRP/H<sub>2</sub>O<sub>2</sub>: 5 U.mL<sup>-1</sup> / 32 mM  
Solvent: HEPES Buffer pH 6.8 : Acetone (85:15)



Monoalkoxyphenols tested present 2 similar systems:

- System 1:  
g = 2.0053  
a<sub>H</sub> = 21.0 G  
a<sub>N</sub> = 14.5 G  
a<sub>P</sub> = 46.7 G
- System 2:  
g = 2.0054  
a<sub>H</sub> = 17.7 G  
a<sub>N</sub> = 13.2 G  
a<sub>P</sub> = 42.3 G

Phenol-methylated analogues present no EPR signature

System 1 points out to C-radicals trapped, thus delocalization of the radical on the aromatic core.

## Focus on eugenol & isoeugenol: comparing with in situ radicals formed in reconstructed human epidermis (RHE)

Many industrial fields and daily life use:

- ✓ Cosmetics
- ✓ Food preservatives
- ✓ Aromatherapy
- ✓ Dental care
- ✓ ...

Natural compounds in essential oils

Topical application spin-trap (20 μmol.cm<sup>-2</sup>) → Incubation (15 min, 37 °C, 5% CO<sub>2</sub>) → Topical application target compound (3.6 μmol.cm<sup>-2</sup>) → Irradiation (5 min) → EPR acquisition

SOLUTION HRP/H<sub>2</sub>O<sub>2</sub> or solar irradiation

RHE

Photo from Episkin.com

Same radicals obtained in solution and in RHE (Episkin®, Lyon, France) under sunlight exposure.

## Outputs:

- ✓ First results show that monoalkoxyphenols require to be free at the phenolic position to induce reactive carbon radicals when acting as antioxidants
- ✓ Comparing eugenol and isoeugenol with guaiacol suggests that carbon-centered radicals are probably located in the aromatic core
- ✓ Interestingly, irradiation affords the same radical's signature than oxidative media in solution
- ✓ This has been corroborated by irradiation of RHE exposed topically to eugenol and isoeugenol

## References:

1. C. Marteau et al., *Flavour Fragr. J.*, 2013, 28, 30–38
2. L.-L. Zhang et al., *Food & Nutrition Research*, 2017, 61, 1353356
3. Y. Chang et al., *Journal of Endodontics*, 2000, 26, 440–443.
4. R. Bortolomeazzi et al., *Food Chem.*, 2010, 118, 256-265
5. B. Vilen et al., *Contact Dermatitis*, 2022

## Acknowledgements:

