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Radical intermediates and monoalkoxyphenols: anti-and prooxidant activities

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► To cite this version:

Yannick Port-Lougarre, Bertrand Vileno, 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

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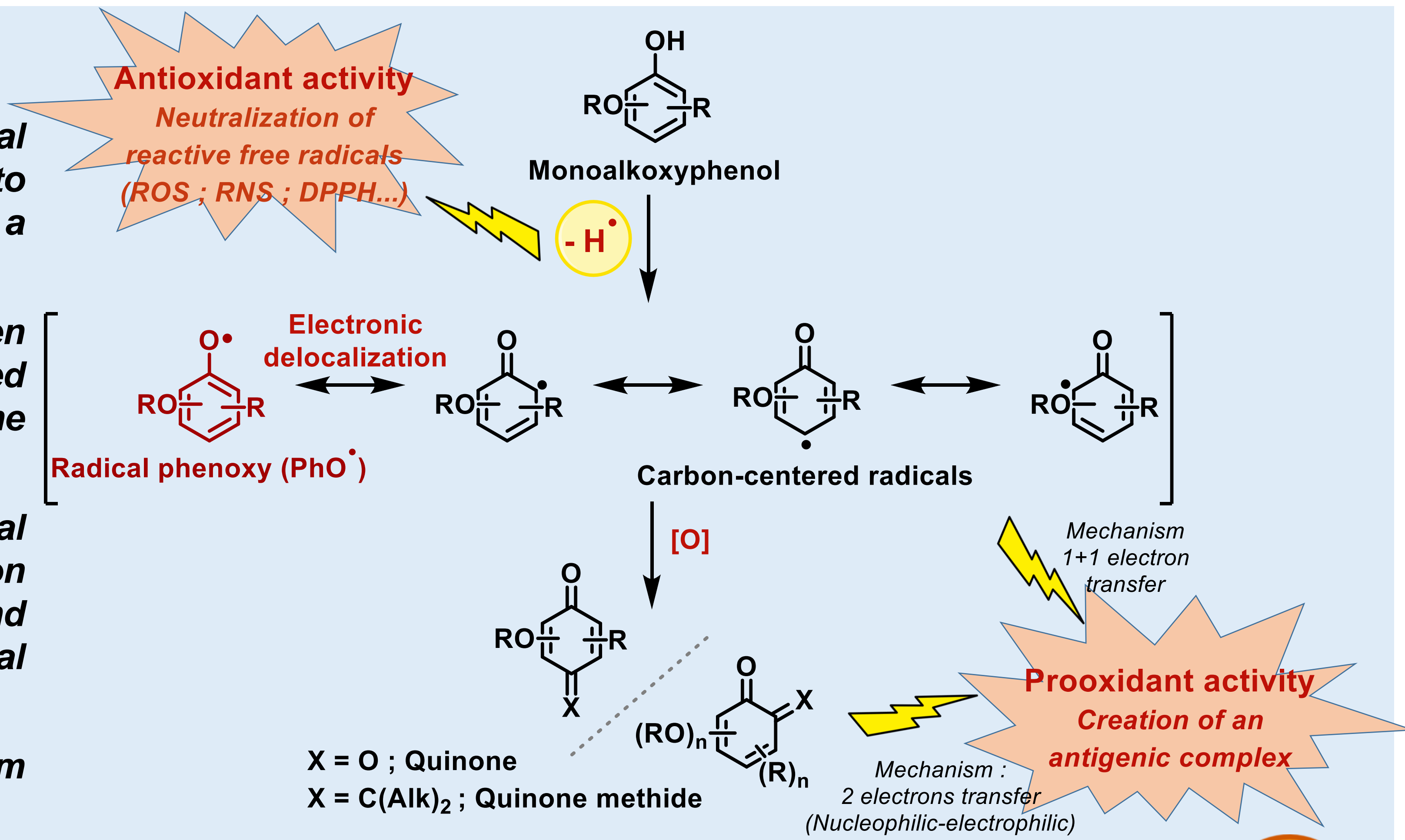
BACKGROUND

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).^{1,2}

Despite of these cytoprotective benefits, those compounds often possess a cytotoxic activity (e.g. allergic contact dermatitis³) suspected for many years to result from sensitization to the electrophilic quinone derivatives.⁴

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

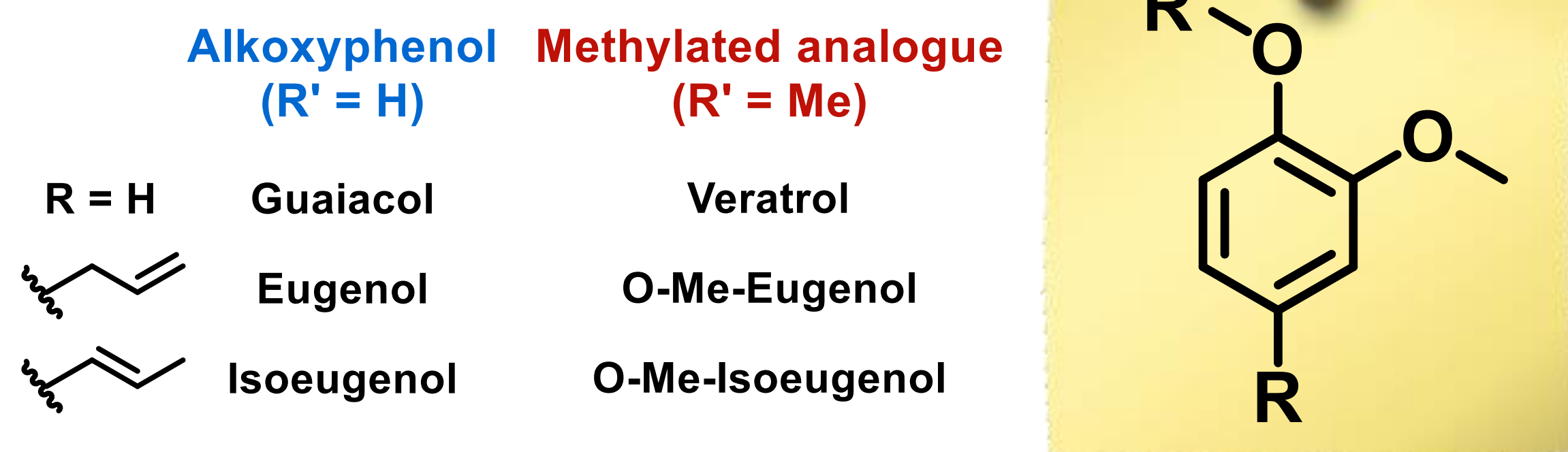
Nevertheless, the link between free radicals formed and their mechanism of action leading to the cytotoxic response is far from being unraveled.



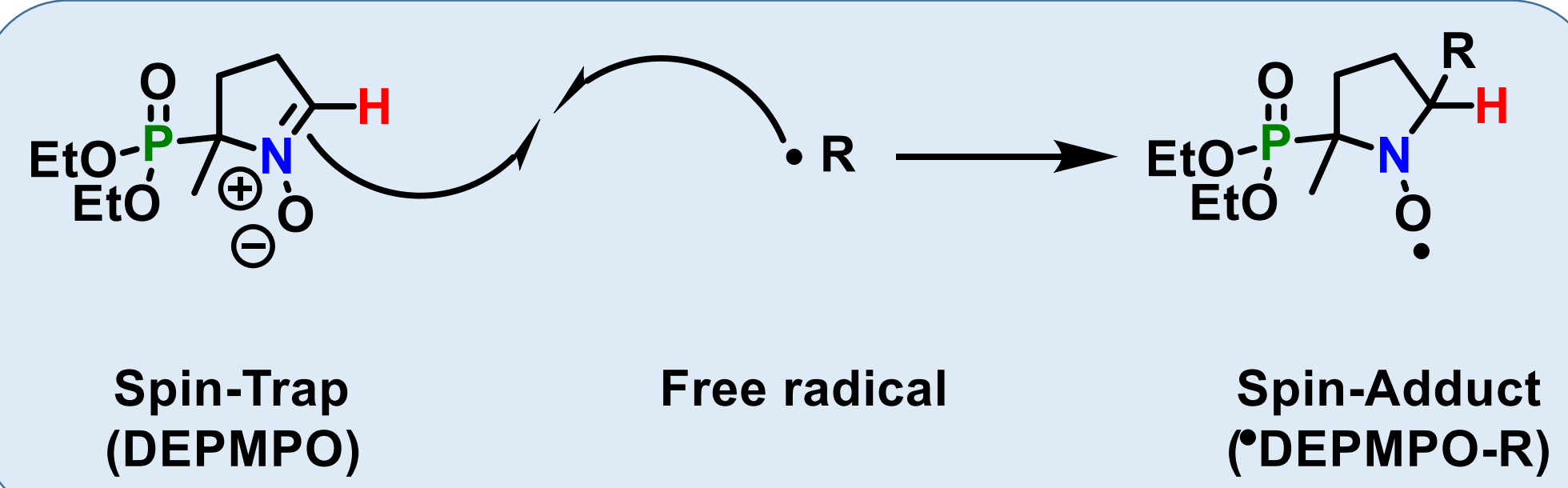
OBJECTIVES

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

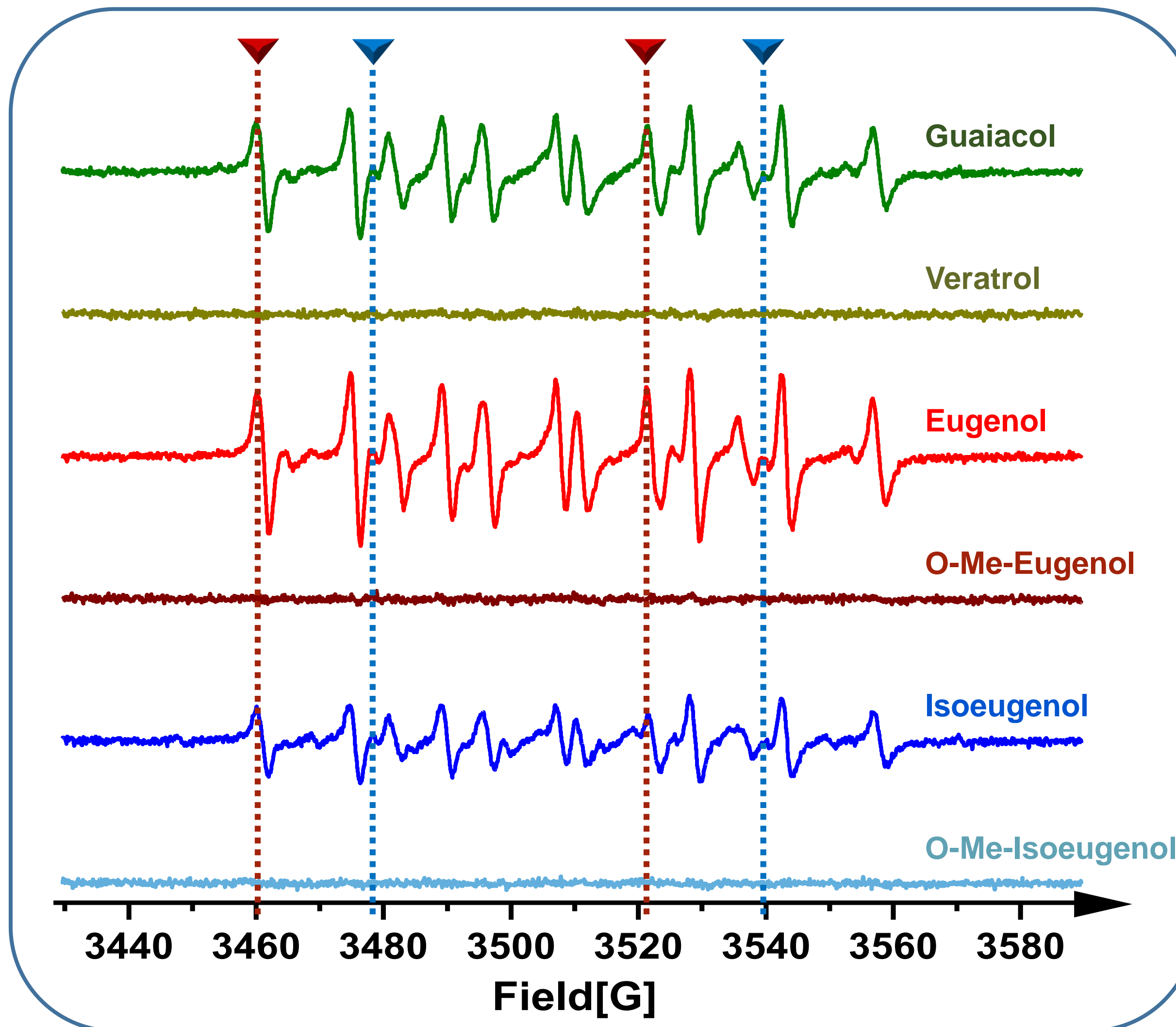
SPIN-TRAPPING IN SOLUTION



EPR spin trapping



Experiment done by creating an oxidative media:
Spin-Trap: 50 mM
Target compound: 20 mM
HRP/H₂O₂: 5 U.mL⁻¹ / 32 mM
Solvent: HEPES Buffer pH 6.8 : Acetone (85:15)



Monoalkoxyphenols tested present 2 similar systems:

- **System 1:**
 $g = 2.0053$
 $a_H = 21.0$ G
 $a_N = 14.5$ G
 $a_P = 46.7$ G
- **System 2:**
 $g = 2.0054$
 $a_H = 17.7$ G
 $a_N = 13.2$ G
 $a_P = 42.3$ 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)

Natural compounds in essential oils
 Cloves, Ylang-ylang

Many industrial fields and daily life use:
 ✓ Cosmetics
 ✓ Food preservatives
 ✓ Aromatherapy
 ✓ Dental care
 ✓ ...

SOLUTION HRP/H₂O₂ or solar irradiation

RHE

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:

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3. Y. Chang et al., *Journal of Endodontics*, 2000, 26, 440–443.
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Acknowledgements:

