3rd European Conference on
Xylella fastidiosa and XF-ACTORS final meeting

Fungal metabolites for the biocontrol of *Xylella fastidiosa*

Cimmino A. (presenter)[1], Masi M.[1], Marsico, G.[2], Scafato P.[2], Superchi, S.[2], Evidente A.[1],

[1]Department of Chemical Sciences University of Naples Federico II, Naples, Italy

[2]Department of Sciences, University of Basilicata, Potenza, Italy

THE DISEASE INDUCED ON OLIVE TREE

Xylella fastidiosa **is a Gram-negative bacterium causing devastating diseases of many plants, including important crops as grapevine, peach, citrus, almond, coffee and pear. In the last decade, *X. fastidiosa* has devastated olive heritage in Apulia region (Southern Italy) inducing a severe disease called "Olive Quick Decline Syndrome" (OQDS).[1] The disease also infected millennial olive plants. The bacterium was introduced in this region from abroad and rapidly spread causing heavy economical losses and cultural and social damages.**

1)Jlilat, A. Et al. *Sci. Rep.*, 2021, *11*, 1-11.

Old diseased olive orchade in Salento Italy on 2015

The so called «Gingante di Calliste» in a small village near to Lecce, Salento, Italy, infeceted by *X. fastidiosa*

Symptoms induced by *X. fastidia* on olive tree (left) and its diseased leaves (above)

XYLELLA FASTIDIOSA CONTROL METHOD

The eradication of infected plants in the restricted area at beginning of infection could be an efficient approach to eliminate the bacterium. Unfortunately, this method was too late and partially applied. Studies carried out successively demonstrated that a zinc-copper-citric acid biocomplex allows a consistent reduction of the infection on olive trees.[2] The use of synthetic bacteriocides was discouraged as their use could cause resistance in the host plants and a long term impact of residues in agricultural products with a risk to human and animal health.[3]

Infected olive plants eradicated

2) Scortichini, M. et al. *Agronomy,* 2020, *10*, 1445.

3) Cimmino, A. Et al. Nat. Prod. Rep., 2015, 32, 1629-165.

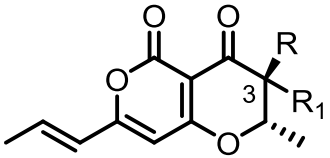
ALTERNATIVE METHOD TO CONTROL *X. FASTIDIOSA* BASED ON THE USE OF NATURAL COMPOUNDS

Some year ago radicinin, a dihydropyranopyran-4,5-dione, was proposed as natural pesticide to control the infection of *X. fastidiosa* causing grapevines (*Vitis vinifera* L.) Pierce's disease.[4] More recently, radicinin, together with some analogues were isolated from *Cochliobolus australiensis*, a fungus proposed as mycoherbicide to control buffelgrass (*Centrus ciliaris*) an invasive weed in North America.[5]

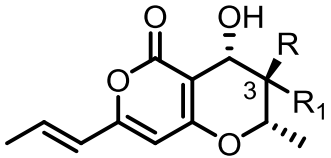
Cenchrus ciliaris

4) Aldrich, T.J. et al. *Phytochemistry*, 2015, 116, 130-137.

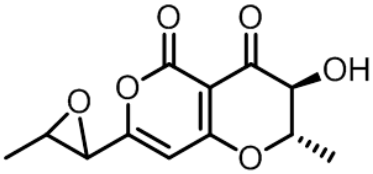
5) Masi et al. *J. Nat. Prod.*, 2017, *80*, 1241-1247



Radicinin R=OH, R_1=H
3-*epi*-Radicinin R=H, R_1=OH



Radicinol R=OH, R_1=H
3-*epi*-Radicinol R=H, R_1=OH



Cochliotoxin

Metabolites produced by *Cochliobolus australiensis*

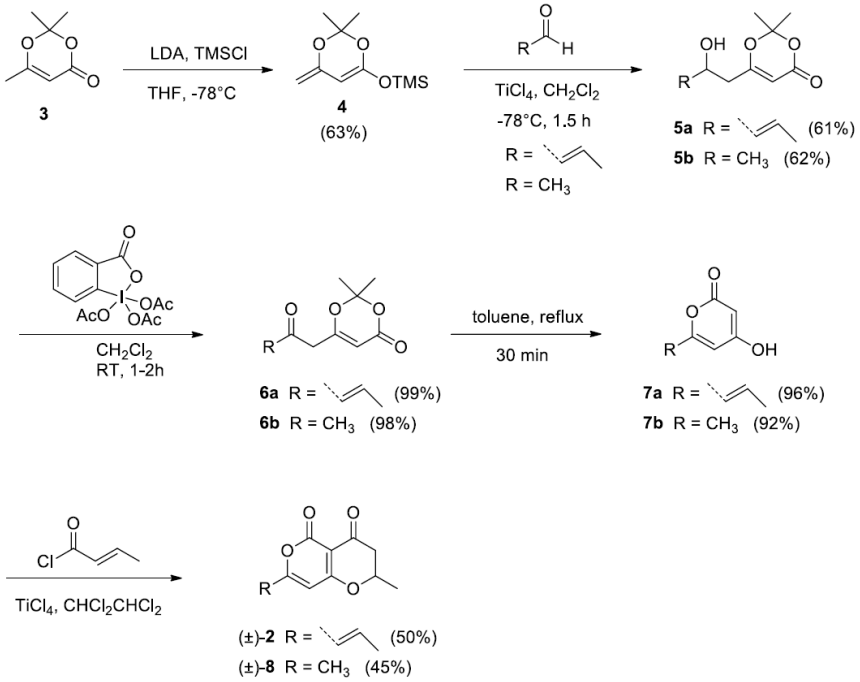
SYNTHESIS OF (±)-3-DEOXYRADICININ

The fungal production of radicinin was however very low yielding and this prompted the development of an efficient total synthesis that afforded in good yield (±)-3-deoxyradicinin (2), the synthetic and biochemical precursor of radicinin.[6]

This synthetic methodology (Scheme 1) is significantly more efficient than those previously reported in the literature and also shows higher versatility towards the introduction of different side-chains at both C-7 and C-2.

(±)-3-Deoxyradicinin ((±)-2) displays phytotoxic activity against buffelgrass[6] and antibacterial activity against *X. fastidiosa*[7] comparable with those of radicinin.

Therefore, (±)-2 can constitute a more practical synthetic alternative as bioherbicide for buffelgrass control and antibacterial against *X. fastidiosa*.[6]



Scheme 1. Synthesis of (±)-3-deoxyradicinin (**2**) and analogue (±)-**8**.

Conclusions

These results allow us to propose these compounds as potential natural pesticides, which conveniently bioformulated, could be used to control of *X. fastidiosa*.

6) Marsico et al. Molecules 2019, 24, 2793

7) Brandenburg, C. A. J. Nat. Prod. 2020, 83, 1810.