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Phytotoxic metabolites produced by *Diaporthe eres* involved in cane blight of grapevine in Italy

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ABSTRACT

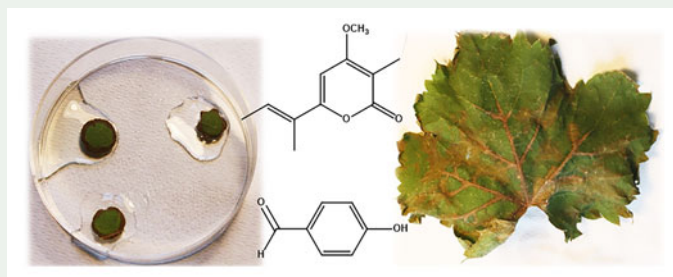
Grapevine trunk diseases (GTDs) are one of the most serious biotic stresses affecting this important crop. Among them a range of diseases were identified and associated to a plethora of phytopathogenic fungi, including species of *Diaporthe*. *Diaporthe eres* was recently identified as one of the species involved in cane blight of grapevine. The ability of a strain of this fungus isolated from infected grapevine plant in Italy to produce *in vitro* phytotoxic metabolites was investigated. Five phytotoxic metabolites were identified by their physical and spectroscopic properties as 4-hydroxybenzaldehyde, 4-hydroxybenzoic acid, nectriapyrone, *p*-cresol and tyrosol. When tested on grapevine leaf disks and by leaf absorption, 4-hydroxybenzoic acid induced symptoms on both disks and leaves, 4-hydroxybenzaldehyde and *p*-cresol showed, respectively, phytotoxicity on leaf disks and on the leaf absorption bioassay.

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1. Introduction

Grapevine (*Vitis vinifera* L.) can be affected by many different biotic stresses, including pathogenic fungi that induce severe disease symptoms on different plant organs. The diseases affecting the woody tissues, i.e. trunk and cordons, grapevine trunk diseases

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(GTDs), are among the major threats in grapevine cultivation reducing vineyard longevity and productivity in all the areas where grapevine is cultivated. GTDs are caused by various pathogenic fungi which are able to produce a wide range of toxic metabolites belonging to different classes of naturally occurring compounds (Masi et al. 2018). Species of *Diaporthe* have also been recently reported as GTDs agents in different regions as in China (Dissanayake et al. 2015), Croatia (Kaliterna et al. 2012), California (Úrbez-Torres et al. 2013), South America (Sessa et al. 2017) and Europe (Guarnaccia et al. 2018; Guerin-Dubrana et al. 2019). *D. eres* was one of the most commonly detected species, isolated for the first time in Italy from infected grapevines in Tuscany (Cinelli et al. 2016) showing discoloration of the canes, often surrounded by irregular dark spots and dead sprouts. *D. eres*, was also associated, together to other *Diaporthe* spp., with wood cankers of fruit and nut crops in northern California (Lawrence et al. 2015).

Fungi belonging to the genus *Diaporthe* are well known as plant pathogens and as producers of phytotoxins as *D. foeniculi* (Evidente et al. 1994) and *D. gulyae*, (Andolfi et al. 2015; Cimmino et al. 2015). *D. eres*, recently isolated from infected leaves of *Hedera helix*, also produced 3,4-dihydro-8-hydroxy-3,5-dimethylisocoumarin and tyrosol which together with some isocoumarin analogs were proposed as potential herbicides (Meepagala et al. 2018).

This manuscript reports the isolation and the chemical and biological characterization of the phytotoxic metabolites produced by a strain of *D. eres* isolated in Italy from grapevines showing cane bleach symptoms.

2. Results and discussion

The organic extract of the culture filtrates of *D. eres* was purified, by combination of column and TLC as detailed described in the Experimental section, to yield five homogeneous compounds. These latter were identified by TLC analysis carried out in different conditions, in comparison with the corresponding standard and also by co-chromatography. Furthermore, their spectroscopic properties (essentially ^1H NMR and MS) were very similar to those previously reported for **1** (Avent et al. 1992), for **2** (Venkatasubbaiah et al. 1991; Zhang et al. 2012), for **3** (Kasthuraiah et al. 2004; Passmore et al. 2018) for **4** (Kimura and Tamura 1973; Venkatasubbaiah et al. 1991; Capasso et al. 1992) for **5** (Zhang et al. 2012; Cimmino et al. 2017). For **1** we carried out a complete ^1H and ^{13}C NMR study for the first time using 1D and 2D NMR experiments (COSY, HSCQ and HMBC) (Figures S1–S5, Supplementary materials) that allowed to unambiguously assign the chemical shifts to all the carbons and the corresponding protons as reported in Table S1 of Supplementary materials, in respect to the data previously reported using only 1D NMR (Avent et al. 1992).

Nectriapyrone (**1**), a pentaketide monoterpenoid, was isolated from a Bulgarian strain of *Phomopsis foeniculi* together with some already known anthracenones. Assayed by tomato leaf-puncture **1** showed only slightly activity, inducing small watery lesions around the inoculated point of the same leaves (Evidente et al. 2011). The phytotoxic activity of **1** was also assayed on some other non host plants (*Cirsium arvense* L., Scop., *Sonchus oleraceus* L. and *Chenopodium album* L.) in comparison to its

dihydro derivative and pestalopyrone. The latter is the main phytotoxic metabolite isolated from the culture filtrates of *Pestalotiopsis guepinii*, the fungus causing twig blight of hazelnut (Türkkan et al. 2011).

4-Hydroxybenzaldehyde (**2**) was first reported as phytotoxin produced by *Phaeomoniella chlamydospora* involved in the esca complex disease of grapevine (Tabacchi et al. 2000) and later from *Spencermartinsia viticola*, one of the causal agents of grapevine Botryosphaeria dieback in Australia (Reveglia et al. 2018). *p*-Cresol (**3**), which has been recently isolated from the culture of *Clostridium difficile*, a Gram-positive spore-forming anaerobe and a major cause of antibiotic-associated diarrhoea. It had bacteriostatic activity against microorganisms including *Escherichia coli*, *Klebsiella oxytoca* and *Bacteroides thetaiotaomicron* (Passmore et al. 2018). However, this is the first time that *p*-cresol was detected as a secondary phytotoxic metabolite from a fungus pathogenic for grapevine.

Tyrosol (**4**), is a toxic compound extracted both from plants (Capasso et al. 1992) and fungi (Masi et al. 2018) including the grapevine pathogenic fungi *Lasiodiplodia euphorbicola* and *Lasiodiplodia hormozganensis* (Cimmino et al. 2017), *Neofusicoccum australe*, associated with grapevine cordon and branch dieback (Andolfi et al. 2012) and *N. parvum* (Evidente et al. 2010). It was also produced, together with some melleins and *p*-hydrobenzaldehyde (**2**) by *Diplodia seriata* (syn. *Botryosphaeria obtusa*), which causes black rot of apple fruit and frog-eye leaf spots (Venkatasubbaiah et al. 1991). Tyrosol (**4**) is toxic to tomato and is a quorum sensing molecule in *Candida albicans*, controlling growth, morphogenesis, and biofilm formation (Albuquerque and Casadevall 2012).

4-Hydroxybenzoic acid (**5**) is present in the root exudate of grapevine and other plants (Einhellig and Rasmussen 1978; Guo et al. 2010; Yu and Matsui 1994) and has more recently been reported as one of the metabolites produced by *D. gulyae*, a fungal species that has been proposed as a mycoherbicide to control the annual weed *Carthamus lanatus* (Andolfi et al. 2015). 4-Hydroxybenzoic acid (**5**) is toxic to lettuce seedlings (Yu et al. 1994) and inhibits radish and grain sorghum germination and growth (Einhellig and Rasmussen 1978).

Metabolites **1-5** were assayed on grapevine (*Vitis vinifera*) by the leaf disk bioassay and by the leaf absorption bioassay as fully described in the Experimental part. The observed symptoms included marginal darkening and necrosis of the disk and wilting, reddening of the leaf veins and lamina distortion on the leaves (Figures 2 and 3). In general, for all the compounds in both bioassays, phytotoxicity increased with concentration (range 0.1–1 mg/mL). 4-Hydroxybenzoic acid induced the greatest symptoms on both leaf disks and leaves, while 4-hydroxybenzaldehyde and *p*-cresol showed, respectively, phytotoxicity on leaf disks and leaf absorption bioassay (Table 1).

3. Experimental

3.1. General experimental procedures

¹H and ¹³C NMR spectra were recorded at 400 or 500 and 100 or 125 MHz in CDCl₃ or otherwise noted, on Bruker (Karlsruhe, Germany) and Varian (Palo Alto, CA, USA) instruments. The same solvent was also used as an internal standard. DEPT, COSY-45,

HSQC, HMBC and experiments (Berger and Braun 2004) were performed using Bruker or Varian microprograms. ESI MS and LC/MS analyses were performed using the LC/MS TOF system AGILENT (Agilent Technologies, Milan, Italy) 6230B, HPLC 1260 Infinity. Analytical and preparative TLCs were carried out on silica gel (Kieselgel 60, F_{254r}, 0.25 and 0.5 mm respectively) or on reverse phase (RP-18 F_{254r}, 0.25 mm) plates (Merck, Darmstadt, Germany). The spots were visualized by exposure to UV radiation, or by spraying first with 10% H₂SO₄ in MeOH, and then with 5% phosphomolybdic acid in EtOH, followed by heating at 110 °C for 10 min. Column chromatography was performed using silica gel (Kieselgel 60, 0.063-0.200 mm) (Merck). The standard samples of tyrosol, *p*-hydroxybenzaldehyde, *p*-hydroxybenzoic acid and *p*-cresol were purchased from Sigma (Milan, Italy). A standard sample of nectriapyrone was obtained from purification of culture filtrates of a Bulgarian strain of *Phomopsis foeniculi* (syn *Diaporthe angelicae*) (Evidente et al. 2011).

3.2. Fungal isolates and culture conditions

The strain of *D. eres* (CPC 28423) used in this study was obtained from infected grapevine wood of a vineyard in Tuscany and stored in the Culture collection of P.W. Crous, housed at Westerdijk Fungal Biodiversity Institute (CPC), Utrecht, The Netherlands. For phytotoxin production it was inoculated and grown in stationary culture of modified Difco Czapek Dox medium (Benton, MD, USA) with 0.5% yeast and 0.5% malt extract (both from Difco, Pittsburgh, PA, USA), for 21 days at 25 °C in the dark. The mycelium was removed and the liquid cultures were lyophilized prior to the extraction procedure.

3.3. Extraction and purification *D. eres* CPC 28423 metabolites

The culture filtrates (10 L) of *D. eres* CPC 28423 were reduced under vacuum until they reached 500 mL. The solution was extracted with EtOAc (3 × 400 mL). The organic extracts were combined, dried (Na₂SO₄), and evaporated under reduced pressure. The corresponding residue (494 mg) was purified by silica gel column chromatography, eluted with CHCl₃-*i*-PrOH (95:5), yielding seven homogeneous fraction groups. The residue of fraction one (10 mg) was purified by TLC eluted with CHCl₃-*i*-PrOH (98:2), resulting in one amorphous solid recognized as nectriapyrone (**1**, Figure 1, R_f 0.8, 2.2 mg). The residue of fraction two (11.4 mg) was purified on silica TLC, eluted with CHCl₃-EtOAc (6:4), yielding a brown amorphous solid characterized, 4-hydroxybenzaldehyde (**2**, Figure 1, R_f 0.4, 0.4 mg). The residue of fraction four (25.2 mg) was further purified by preparative TLC on silica gel, using CHCl₃-*i*-PrOH (98:5) as an eluent, affording a viscous yellow oil identified as *p*-cresol (**3**, Figure 1, R_f 0.8, 1.7 mg) and a white amorphous solid identified as tyrosol (**4**, Figure 1, R_f 0.7, 5.7 mg). Finally, from the purification of fraction five (7.6 mg) by reverse phase using MeOH-H₂O (1:1) yielded 4-hydroxybenzoic acid (**5**, Figure 1, R_f 0.6, 1.5 mg).

Nectriapyrone (**1**): ¹H and ¹³C NMR spectra were similar to those previously reported (Avent et al. 1992), 1D and 2D ¹H and ¹³C NMR spectra are reported in the

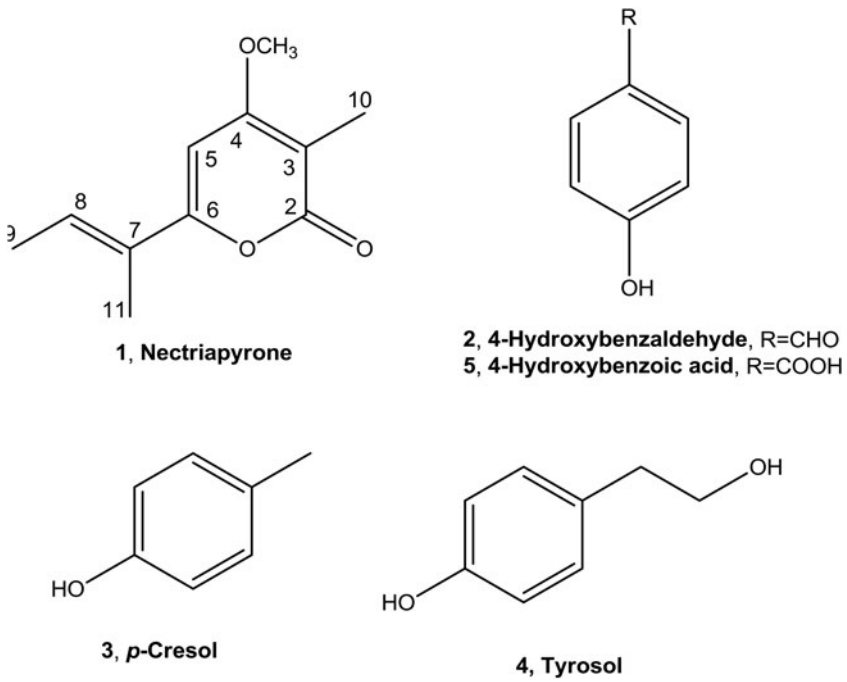


Figure 1. Structure of nectriapyrone, 4-hydroxybenzaldehyde, *p*-cresol, tyrosol and 4-hydroxybenzoic acid (1–5).

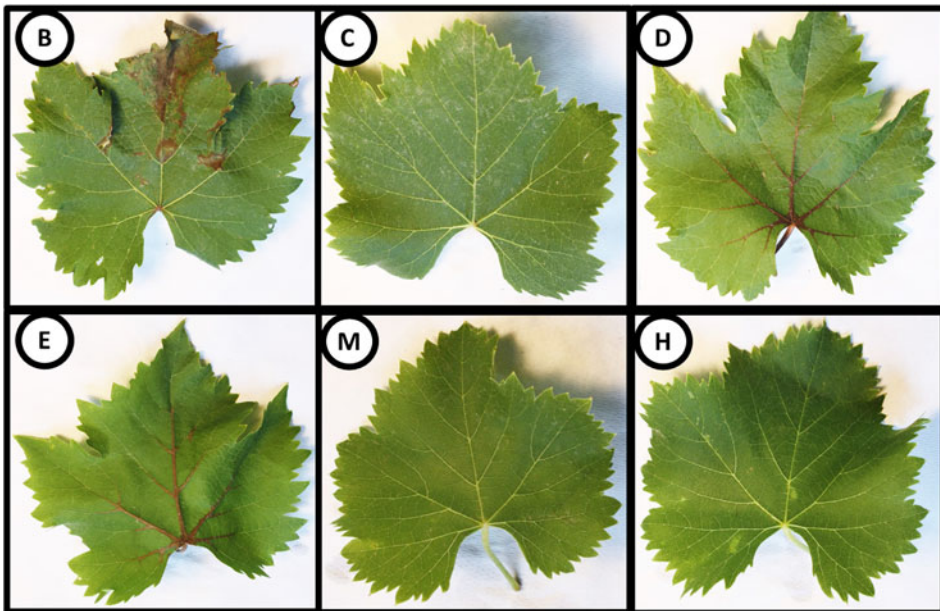


Figure 2. Symptoms caused by compounds 1–5 on leaves of *Vitis vinifera* *in vitro* at concentration of 1 mg/ml after 48 h; (B) 4-hydroxybenzaldehyde (2); (C) *p*-cresol (3); (D) tyrosol; (E) 4-hydroxybenzoic acid (5); (H) distilled H₂O; (M) 10% methanol in distilled H₂O.

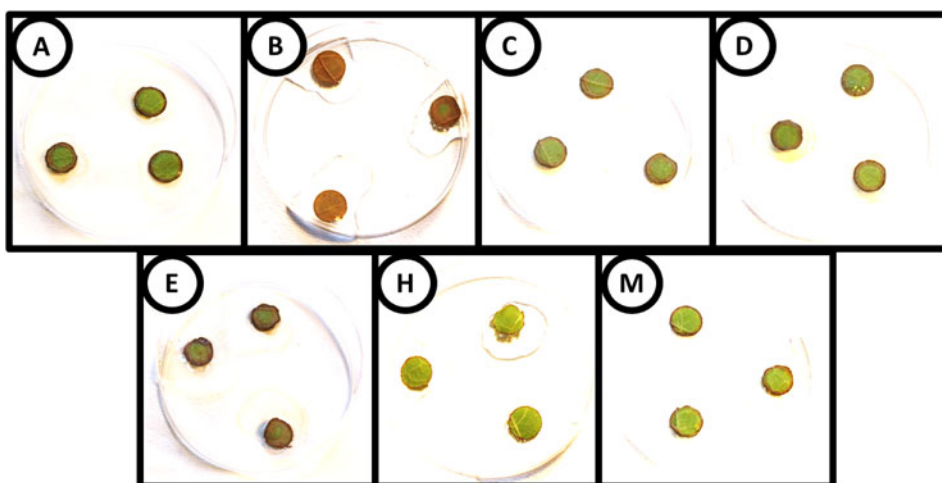


Figure 3. Symptoms caused by compounds 1–5 on disks of *Vitis vinifera* *in vitro* at concentration of 1 mg/mL after 48 h; (A) nectriapyrone (1); (B) 4-hydroxybenzaldehyde (2); (C) *p*-cresol (3) (D) tyrosol (4); (E) 4-hydroxybenzoic acid (5); (H) distilled H₂O; (M) 10% methanol in distilled H₂O.

Table 1. Phytotoxic effect of *Diaporthe eres* metabolites (1–5) on grapevine leaf disks and leaf absorption assayed at 1 mg/mL^a at 48 h from inoculation.

Compound	Disk	Leaf
Nectriapyrone (1)	2.7	na
4-hydroxybenzaldehyde (2)	5	2.7
<i>p</i> -Cresol (3)	3.3	4.3
Tyrosol (4)	2	0
4-hydroxybenzoic acid (5)	4.3	4.3
Control (10% MeOH in H ₂ O)	1	0.3
Distilled H ₂ O	1.3	0.7

^aIntensity of wilting, reddening of the veins and lamina deformation by a visual scale from 0 to 4 (0 = no effect; 4 = severe symptoms).
na = Not assayed.

Supplementary materials (Table S1 and Figures S1–S5); ESI-MS (+) m/z : 605 [3M + Na]⁺, 411 [2M + Na]⁺, 389 [2M + H]⁺, 233 [M + K]⁺, 217 [M + Na]⁺, 195 [M + H]⁺.

4-Hydroxybenzaldehyde (2): ¹H NMR (CD₃OD), δ : 9.78 (s, HCO), 7.88 (d, J = 8.0 Hz, H-2 and H-6), 6.92, (d, J = 8.0 Hz, H-3 and H-5); ESI/MS, m/z : 123 [M + H]⁺. These data are in agreement with the data previously reported (Venkatasubbaiah et al. 1991; Zhang et al. 2012). *p*-Cresol (3): ¹H NMR, δ : 7.04 (d, J = 8.0 Hz, H-3 and H-5), 6.74 (d, J = 8.0 Hz, H-2 and H-6), 4.83 (br s, OH), 2.28 s, Me) ESI/MS (+), m/z : 109 [M + H]⁺. These data are in agreement with the data previously reported (Kasthuraiah et al. 2004; Passmore et al. 2018).

Tyrosol (4): ¹H NMR, δ : 7.20 (d, J = 8.0 Hz, H-2 and H-6), 6.80 (d, J = 8.0 Hz, H-3 and H-5), 4.90 (s, OH), 3.80 (t, J = 6.4 Hz, H₂-8), 2.80 (t, J = 6.4 Hz, H₂-7). ESI/MS (+), m/z : 299 [2 M + Na]⁺, 139 [M + Na]⁺. These data are in agreement with those previously reported (Kimura et al. 1973; Venkatasubbaiah et al. 1991; Capasso et al. 1992; Cimmino et al. 2017).

4-Hydroxybenzoic acid (**5**): ^1H NMR (CD_3OD), δ : 7.9 (d, $J=8.0$ Hz, H-2 and H-6), 6.8 (d, $J=8.0$ Hz, H-3 and H-5). ESI/MS (+), m/z : 139 $[\text{M} + \text{H}]^+$. These data are in agreement with the data previously reported (Zhang et al. 2012; Cimmino et al. 2017).

3.4. Phytotoxic bioassays

3.4.1. Leaf absorption bioassay

Grapevine leaves were cut and the petiole placed in a tube containing 1 mL of compound solution. The compounds **1-5** were dissolved in 10% of MeOH in sterile distilled water (SDW) and tested at three different concentrations: 0.1, 0.5 and 1 mg/mL. After 12 h or when the toxic solution was completely absorbed the leaf was moved to another tube containing SDW. The symptoms were visually assessed after 48 h using a 0 to four scale, where 0 = no symptoms 4 = severe symptom. SDW and 10% MeOH SDW were used as negative control. The experiment was carried out in triplicate.

3.4.2. Leaf disk bioassay

10 mm (diameter) disks of the lamina of grapevine leaves were obtained using a sharp corkborer. The leaf disks were immersed in 0.5 mL of compound solution. The compounds **1-5** were dissolved in 10% of MeOH in sterile distilled water (SDW) and tested at three different concentrations: 0.1, 0.5 and 1 mg/mL. After 12 h or when the solution was completely absorbed the disks were moved to SDW. The symptoms were visually assessed after 6 h, using a 0 to four scale, where 0 = no symptoms 4 = severe symptoms. SDW and 10% MeOH SDW were used as negative control. The experiment was carried out in triplicate.

4. Conclusion

Five metabolites were isolated from the culture filtrates of *D. eres*, a fungus isolated from symptomatic grapevine plants in a vineyard in Tuscany, and for the first time detected in Italy on grapevine. They were identified as 4-hydroxybenzaldehyde (**2**), 4-hydroxybenzoic acid (**5**), nectriapyrone (**1**), *p*-cresol (**3**) and tyrosol (**4**) by comparing their physico and spectroscopic data with those of standard samples and those previously reported in literature. All, except **3**, are already reported as phytotoxic metabolites produced by phytopathogenic fungi, while tyrosol and 4-hydroxybenzaldehyde are already known metabolites produced by other fungi involved in GTDs. *p*-Cresol is isolated for the first time as fungal phytotoxic microbial metabolites.

The role of these phytotoxic metabolites in the disease is not clear. In other GTDs phytotoxic metabolites are proved to contribute to symptom development in the crown, as in *Eutypa lata*, but we can also hypothesize that they have a role in fungal colonization of the tissue. Anyway, they are putative virulence factors available for the pathogenic fungi and deserve further investigation on plant tissue.

Disclosure statement

The authors declare that there are no conflict of interest.

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References

- Albuquerque P, Casadevall A. 2012. Quorum sensing in fungi—a review. *Med Mycol.* 50(4): 337–345.
- Andolfi A, Boari A, Evidente M, Cimmino A, Vurro M, Ash G, Evidente A. 2015. Gulyprones A and B and phomentrioloxins B and C produced by *Diaporthe gulyae*, a potential mycoherbicide for saffron thistle (*Carthamus lanatus*). *J Nat Prod.* 78(4):623–629.
- Andolfi A, Maddau L, Cimmino A, Linaldeddu BT, Franceschini A, Serra S, Basso S, Melck D, Evidente A. 2012. Cyclobotryoxide, a phytotoxic metabolite produced by the plurivorous pathogen *Neofusicoccum australe*. *J Nat Prod.* 75(10):1785–1791.
- Avent AG, Hanson JR, Truneh A. 1992. The biosynthesis of nectriapyrone and vermopyrone. *Phytochemistry.* 31(10):3447–3449.
- Berger S, Braun S. 2004. 200 and more basic NMR experiments: A practical course. 1st ed. Weinheim: Wiley-VCH.
- Capasso R, Cristinzio G, Evidente A, Scognamiglio F. 1992. Isolation, spectroscopy and selective phytotoxic effects of polyphenols from vegetable waste waters. *Phytochemistry.* 31(12): 4125–4128.
- Cimmino A, Cinelli T, Masi M, Reveglia P, da Silva MA, Mugnai L, Michereff SJ, Surico G, Evidente A. 2017. Phytotoxic lipophilic metabolites produced by grapevine strains of *Lasiodiplodia* species in Brazil. *J Agric Food Chem.* 65(6):1102–1107.
- Cimmino A, Masi M, Evidente M, Superchi S, Evidente A. 2015. Fungal phytotoxins with potential herbicidal activity: chemical and biological characterization. *Nat Prod Rep.* 32(12):1629–1653.
- Cinelli T, Mondello V, Marchi G, Burruano S, Alves A, Mugnai L. 2016. First report of *diaporthe* eres associated with cane blight of grapevine (*Vitis vinifera*) in Italy. *Plant Dis.* 100(2):532–532.
- Dissanayake AJ, Liu M, Zhang W, Chen Z, Udayanga D, Chukeatirote E, Li XH, Yan JY, Hyde KD. 2015. Morphological and molecular characterisation of *Diaporthe* species associated with grapevine trunk disease in China. *Fungal Biol.* 119(5):283–294.
- Evidente A, Lanzetta R, Abouzeid MA, Corsaro MM, Mugnai L, Surico G. 1994. Foeniculoxin, a new phytotoxic geranylhydroquinone from *Phomopsis foeniculi*. *Tetrahedron.* 50(34): 10371–10378.
- Evidente A, Punzo B, Andolfi A, Cimmino A, Melck D, Luque J. 2010. Lipophilic phytotoxins produced by *Neofusicoccum parvum*, a grapevine canker agent. *Phytopathol Mediterr.* 49:74–79.
- Evidente A, Rodeva R, Andolfi A, Stoyanova Z, Perrone C, Motta A. 2011. Phytotoxic polyketides produced by *Phomopsis foeniculi*, a strain isolated from diseased Bulgarian fennel. *Eur J Plant Pathol.* 130(2):173–182.
- Einhellig FA, Rasmussen JA. 1978. Synergistic inhibitory effects of vanillic and *p*-hydroxybenzoic acids on radish and grain sorghum. *J Chem Ecol.* 4(4):425–436.

- Guarnaccia V, Groenewald JZ, Woodhall J, Armengol J, Cinelli T, Eichmeier A, Ezra D, Fontaine F, Gramaje D, Gutierrez-Aguirregabiria A, et al. 2018. Diaporthe diversity and pathogenicity revealed from a broad survey of grapevine diseases in Europe. *Persoonia*. 40(1):135–153.
- Guerin-Dubrana L, Fontaine F, Mugnai L. 2019. Grapevine trunk disease in European and Mediterranean vineyards: occurrence, distribution and associated disease-affecting cultural factors. *Phytopathol Mediterr*. 58:49–71.
- Guo XW, Li K, Sun YN, Zhang LH, Hu XX, Xie HG. 2010. Allelopathic effects and identification of allelochemicals in grape root exudates. *Acta Horti Sinica*. 37:861–868.
- Kaliterna J, Miličević T, Cvjetković B. 2012. Grapevine trunk diseases associated with fungi from the Diaporthaceae family in Croatian vineyards. *Arch Ind Hyg Toxicol*. 63:471–479.
- Kasthuraiah M, Kumar KA, Reddy CS. 2004. Facile synthesis, spectral characterization and antimicrobial activity of 6-substituted-2, 4, 8, 10-tetra-*t*-butyl dibenzo [*d*, *g*][1, 3, 6, 2] dioxathia-phosphocin 6-oxides. *J Heterocycl Chem*. 41(3):413–417.
- Kimura Y, Tamura S. 1973. Isolation of *l*-β-phenyllactic acid and tyrosol as plant-growth regulators from *Gloeosporium laeticolor*. *Agric Biol Chem*. 37(12):2925–2925.
- Lawrence DP, Travadon R, Baumgartner K. 2015. Diversity of *Diaporthe* species associated with wood cankers of fruit and nut crops in northern California. *Mycologia*. 107(5):926–940.
- Masi M, Cimmino A, Reveglia P, Mugnai L, Surico G, Evidente A. 2018. Advances on fungal phytotoxins and their role in grapevine trunk diseases. *J Agric Food Chem*. 66(24):5948–5958.
- Meepagala KM, Briscoe WE, Techen N, Johnson RD, Clausen BM, Duke SO. 2018. Isolation of a phytotoxic isocoumarin from *Diaporthe eres*-infected *Hedera helix* (English ivy) and synthesis of its phytotoxic analogs. *Pest Manag Sci*. 74(1):37–45.
- Passmore IJ, Letertre MPM, Preston MD, Bianconi I, Harrison MA, Nasher F, Kaur H, Hong HA, Baines SD, Cutting SM, et al. 2018. Para-cresol production by *Clostridium difficile* affects microbial diversity and membrane integrity of Gram-negative bacteria. *PLoS Pathog*. 14(9): e1007191.
- Reveglia P, Savocchia S, Billones-Baaijens R, Masi M, Evidente A. 2018. Spencertoxin and spencer acid, new phytotoxic derivatives of diacrylic acid and dipyrindinbutan-1, 4-diol produced by *Spencermartinsia viticola*, a causal agent of grapevine Botryosphaeria dieback in Australia. *Arabian J Chem*. doi.org/10.1016/j.arabjc.2018.01.014.
- Sessa L, Abreo E, Bettucci L, Lupo S. 2017. Diversity and virulence of Diaporthe species associated with wood disease symptoms in deciduous fruit trees in Uruguay. *Phytopathol Mediterr*. 56:431–444.
- Tabacchi R, Fkyerat A, Poliard C, Dubin GM. 2000. Phytotoxins from fungi of esca of grapevine. *Phytopathol Mediterr*. 39:156–161.
- Türkkan M, Andolfi A, Zonno MC, Erper I, Perrone C, Cimmino A, Vurro M, Evidente A. 2011. Phytotoxins produced by *Pestalotiopsis guepinii*, the causal agent of hazelnut twig blight. *Phytopathol Mediterr*. 50:154–158.
- Úrbez-Torres JR, Peduto F, Smith RJ, Gubler WD. 2013. Phomopsis dieback: A grapevine trunk disease caused by *Phomopsis viticola* in California. *Plant Dis*. 97(12):1571–1579.
- Venkatasubbaiah P, Sutton TB, Chilton WS. 1991. Effect of phytotoxins produced by *Botryosphaeria obtusa*, the cause of black rot of apple fruit and frog-eye leaf spot. *Phytopathology*. 81(3):243–247.
- Yu JQ, Matsui Y. 1994. Phytotoxic substances in root exudates of cucumber (*Cucumis sativus* L.). *J Chem Ecol*. 20(1):21–31.
- Zhang H, Conte MM, Huang XC, Khalil Z, Capon RJ. 2012. A search for BACE inhibitors reveals new biosynthetically related pyrrolidones, furanones and pyrroles from a southern Australian marine sponge, *lanthella* sp. *Org Biomol Chem*. 10(13):2656–2663.