Natural Herbicides by Phytopathogenic Fungi–Strategic Approaches for Discovering Fungal Phytotoxins to Control Weeds

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Abstract — Weeds are one of the most serious plant pests that farmers are forced to combat since the development of agriculture using different methods including mechanic and agronomy strategies. Weeds have generated significant losses of agriculture production, constituting a serious impediment for agricultural activities in reforestation practices and in important infrastructures. All these serious problems have induced the expansive and massive use of synthetic herbicides, which represents one of the main causes of environmental pollution, as well as serious risks for human and animal health. An alternative environmentally friendly control method could be the use of bioherbicides based on suitably bio formulated natural products, of which the main ones are fungal phytotoxins. This review paper represents the work that concerns fungal phytotoxins with potential herbicidal activity in order to obtain their efficacy as mycoherbicides for practical application in agriculture.

Keywords: Phytotoxins; Fungal Metabolites; Natural Herbicides; Plant Pathogens; Weed Management

I. INTRODUCTION

Weeds are among the most dangerous biotic stresses that attack crop, forest and ornamental plants. They cause crops marked losses in crop production (Gladbach et al 2022). In addition, the rapid spread of weeds worldwide reduces the areas available for grazing, and these plants also are poisonous and harmful to grazing animals (Mayo et al 2022) and the forest and park heritage (Goldwasser et al 2012, Cannizzo & Bellezza, 2018, Wheeler et al 2018). Another severe consequence due to weed diffusion in the forest landscape is the drastic reduction in precious wood production (Evidente et al 1992, Gazoulis et al 2021).

The main control method used in the last five to six decades has been the massive and extensive use of synthetic herbicides with heavy effects on crop safety, risk for human and animal health and the increasing of environmental pollution, which noteworthily contributes to climate changes. These negative effects have increased with the rise of parallel weed resistance and the consequent increase in treatment repetitions (Evidente & Abouzeid 2006; Joel et al 2007; Evidente et al 2011)]. These problems prompt the finding of alternative and ecofriendly strategies to control weeds, in particular those based on the use of natural compounds, which are biodegradable and not toxic. The fungal phytotoxins alone or in integrated strategy have been extensively studied as one of the more efficacious methods to combat weeds (Rimando & Duke 2006; Loddo et al 2021; Koivunen et al 2013).

Fungal phytotoxins are secondary metabolites that play an important role in the induction of disease symptoms in agrarian and forest plants and weeds, and belong to different classes of naturally occurring compounds (Ballio & Graniti 1991; Garcia & Collado 2003; Strange 2007; Berestetskiy 2008; Mobius & Hertweck 2009; Varejao et al 2013; Schueffler & Anke 2014; Cimmino et al 2015).

This review is focused on fungal phytotoxins with potential herbicidal activity on several weeds so as to obtain their efficacy as bioherbicides for recent development for purification and identification of natural herbicidal compound and future perspectives are also discussed.

II. PHYTOTOXIC FUNGAL METABOLITES AS HERBICIDES

Fungi are well investigated to herbicidal production for weedy management (Singh & Pandey, 2019). Phytopathogenic molds generate metabolites that play a great role in the improvement of weed control. Fungal phytotoxins are natural secondary metabolites produced by plant pathogenic fungi during host-pathogen interactions. They have received considerable particular attention for elucidating disease etiology, and consequently to design strategies for disease control. Due to wide differences in their chemical structures, these toxic metabolites have different ecological and environmental roles and mechanisms of action. They can represent an ecofriendly alternative to manage weeds. Indeed, the phytotoxins produced by weed pathogenic fungi are an efficient tool to design natural, safe mycoherbicides. Broth cultures of several fungi showed considerable herbicidal activity in both crude and purified forms against various weeds (Singh & Pandey, 2024). In addition, in vitro cultivation of the isolated phytopathogenic fungi in the laboratory was done to obtain filtrates containing biologically active metabolites with herbicidal action and evaluate their herbicidal effects against some weeds. Mycoherbicides are ecofriendly materials and usually have shorter half-life than synthetic herbicides (Singh & Pandey, 2020).

The list of the fungal metabolites with herbicidal activity, their source, the chemical name and the biological activity were briefly described for the biocontrol of weeds summarized in Table1.

Phytopathogenic Fungi	Host Weed	Phytotoxin Produced	Activity against	References
Alternaria alternata	Johnsongrass (Sorghum halepense) L.	Tenuazonic acid	Phytotoxic activity on tobacco leaves	Iwasaki et al 1972
Alternaria eichorniae	Water hyacinth (Eichhornia crassipes)	Altheichin	Phytotoxic activity on the host plant water hyacinth (Eichhornia	Robeson et al 1984

Alternaria alternata			crassipes) and non-host plant Pigment	Okuno et al 1983
Alternaria alternata	Knapweed, (Centaurea maculosa)	Cyclo(-L-Pro-L-Tyr-)	Phytotoxic activity against the host knapweed	Stierle et al 1988
Alternaria alternata	Knapweed (Centaurea maculosa)	Alterlosin I	Phytotoxic on knapweed	Stierle et al 1989
Alternaria alternata	Jimsonweed (Datura stramonium)	AAL-toxin	Phytotoxic activity on jimsonweed	Abbas et al 1993
Alternaria euphorbiicola	wild poinsettia (Euphorbia heterophylla)	Anhydromevalonolactone	Phytotoxicity on host plant and other weed	Varejao et al 2013
Alternaria zinniae	Xanthium occidentale.	Brefeldin	Phytotoxicity against the host plant and other weeds	Vurro et al 1998
Alternaria sonchi	Canada Thisle (S. arvensis)	8-Hydroxy-3-methyl-4-chloro-9-oxo-9H-xanthene-1-carboxylate	Phytotoxicity on S. arvensis and E. repens	Dalinova et al 2020;
Ascochyta araujiae	White blade flower (Araujia hortorum)	Araufuranone	Phytotoxicity on different weeds	Masi et al 2022
Ascochyta cypericola	Purple nutsedge (Cyperus rotundus L.)	Cyperine	Phytotoxic activity on Cyperus spp.	Stierle et al 1991
Ascochyta hyalospora	Lambsquarters or ft hen (Chenopodium album L.)	Ascochytine	Phytotoxic activity on the host lambs quarters and 8 other weeds	Venkatasubaiah & Chilton 1992
Ascochyta pisi	Pea and bean (Pisum sativum and Phaseolus vulgaris)	Ascosalitoxin	Phytotoxic activity on the host plants	Evidente et al 1993
A. sonchi	Sowthistle (Socnhus arvensis)	Chloromonilicin	No toxicity	Gladbach et al 2022
Ascochyta sonchi	Sowthistle (Socnhus arvensis)	Ascosonchine	Phytotoxicity on several weed and cultivated plants	Evidente et al 2004;
Ascochyta agropyrina var. nana	Quack grass (Elytrigia repens)	Papyracillic acid	Phytotoxicity against different weeds	Evidente et al 2009
Bipolaris cynodontis	Bermuda grass (Cynodon dactylon L.)	Bipolaroxin	Specific activity against the two host plants Bermuda grass and Johnson grass	Sugawara et al 1985;
Coniolariella sp.	No infected weed	Mevalocidin	Phytotoxicity against broadleaf and grass species	Sica et al 2016; Gerwick et al 2013
Cochliobolus australiensis	buffelgrass (Pennisetum ciliare or Cenchrus ciliaris)	Cochliotoxin	Phytotoxic activity on the host plant and other two native weeds	Masi et al 2017d
Colletotrichum higginsianum	Brassica sp.	Colletochlorin E	Phytotoxicity on weeds, parasitic and cultivated plants	Masi et al 2017a
Colletotrichum gloeosporioides	Ragweed (Ambrosia artemisiifolia)	Colletochlorin A	Phytotoxicity on the host weed	Masi et al 2017b
C. higginsianum	Rape (Brassica sp.)	Colletopyrandione	Phytotoxicity on S. arvensis and Helianthus annuus	Masi et al 2017a
C. gloeosporioides	Ragweed (A. artemisiifolia)	Orcinol	Phytotoxicity on the host weed	Masi et al 2018

Colletotrichum gloeosporioides	blackberry (Rubus spp.)	Ferrocinin	Phytotoxic activity on some weeds	Ohra et al 1995
Dendryphiella sp.	Kuroguwai (Eleocharis kuroguwai)	Dendryol A	Phytotoxic activity against barnyardgrass	Tanaka et al 1995
Drechslera gigantea	Several grasses as weed cabgrass (Digitaria spp.), quackgrass (Agropyron repens) and Bermuda grass (Cynodon dactylon)	Gigantenone	Phytotoxic activity on monocot species	Kenfield et al 1989;
Drechslera siccans	Ryegrass (Lolium perenne)	Drazepinone	Phytotoxicity on several weeds	Evidente et al 2005;
Dydimella pinodes	Pisum sativum L.	Pinolidoxin	Phytotoxic activity on some weed and crop plants	Evidente et al 1993
Guanomyces polythrix	No infected weed	4-Hydroxybenzoic acid methyl ester	Phytotoxic activity against Amaranthus hypochondriacus and Echinochloa crusgalli	Venkatasubbaiah et al 1992
Nimbya scirpicola	Kuroguwai (Eleocharis kuroguwai)	Depudecin	Phytotoxic activity on host weed and some crops	Tanaka et al 1994;
Phoma sorghina	Pockeweed (Phytolacca americana L.)	6-Methylsalicylic acid	Phytotoxic activity on the host pokeweed and 8 other weeds	Venkatasubaiah 1992
Phomopsis convolvulus	Bindweed (Corzvolvulus arvensis)	Convolvulanic acid A	Phytotoxic activity against bindweed (Corzvolvulus arvensis)	Tsantrizos et al 1992
Phoma putaminum	Annual flaebane (Erigeron annuus)	Putaminoxin	Phytotoxic activity on the host annual fleabane, some other weeds and cultivated plants	Evidente et al 1995
Phoma herbarum	Prine's father (Amaranthus hypochondriacus)	Herbarumin I	Phytotoxic activity against Amaranthus hypochondriacus	Rivero et al 2000
Pyrenophora semeniperda	Annual grasses (Bromus spp.)	Cytochalasin Z1	Phytotoxicity on wheat and tomato	Medd 1992
Phoma exigua var. heromorpha	Oleander nerium L.	Cytochalasin A	Not tested on weed	Cimmino et al 2008
Pyrenophora semeniperda	Cheatgrass (Bromus tectorum)	Spirostaphylotrichin A	Phytotoxicity on cheatgrass and non-host plants	Masi et al 2014
Phoma macrostoma	Canada thistle (Cirsium arvense)	Macrocidins A	Phytotoxicity on different weeds	Graupner 2003;
Phyllosticta cirsii	Canada thistle Cirsium arvense	Phyllostoxin	Phytotoxicity on host plant	Evidente et al 2008
Phomopsis sp.	Saffron twistle (C. arvense)	Phomentrioloxin	Phytotoxicity on several weeds and some cultivated plants	Cimmino et al 2012
Perycularia grisea	buffelgrass (Pennisetum ciliare or Cenchrus ciliaris)	Peryculin A	Phytotoxicity on the host weed	Masi et al 2017c
Paraphoma sp.	Saffron thisle (C. arvense)	Curvulin	No toxicity	Poluektova et al 2018
Rutstroemia capillus-albis	Cheatgrass (Bromus tectorum)	9-O-Methylfusarubin	Phytotoxicity on the host plant	Masi et al 2018b;

Scytalidium uredinicola	Pine-pine gall rust (Endocronartium harknessii)	Scytolide	Inhibition of inhibition of germination of E. harknessii spores	Ayer et al 1993
Stagonospora cirsii	Cirsium arvense (Canada thisle)	Stagonolide A	Phytotoxic activity against the host plant C. arvense, and several other weeds and cultivated plants	Yuzikhin et al 2007
Sporormiella australis	No infected weed	Australifungin	Phytotoxicity against duckweed (Lemna pausicostata)	Abbas et al 1998;
Stagonospora apocyni	hemp dogbane (Apocynum cannabinum L.).	Citrinin	Toxicity on several weeds	Evidente et al 2002

Table 1: Fungal phytotoxins for biocontrol of weeds

III. Separation, Purification and Identification of Natural Compounds- Recent Progress

Development of innovative technologies have played an important role in the chemistry of natural compounds. The compound purification from a complex/crude fungal mixture, HPLC (high-performance liquid chromatography) has assumed a crucial role in addition to the traditional chromatographic methods by column and TLC (Thin layer chromatography). HPLC is routinely used in the separation of natural compounds and the development of its hyphenated techniques, as LC/UV-photodiode array (LC/UV-DAD), LC/Mass Spectrometry (LC/MS) and LC/Nuclear Magnetic Resonance (LC/NMR) provide very efficacious tools to reach the fundamental goal of having a pure natural compound to submit to its identification. Biological samples managing the preparation of the sample to apply to the columns is a very important step. In fact, the sample may contain complex macromolecules and contaminants which could damage the column and are frequently expensive. Thus, these contaminants should be preliminary removed (Hostettmann et al 1998). The chemical composition of a given mixture of natural compounds is generally analyzed conjointly by a gas chromatography-flame ionization detector (CG-FID) and GC-mass spectrometry (MS) techniques for quantitative and qualitative purposes. The identification of compounds is performed by comparison of the experimental results with those reported in the electron ionization mass spectrometry (EI-MS) spectra library. However, in many cases (i.e., less than 90% of agreement), the identification is not unambiguous and further investigation are necessary. To have the confirmation of the structure of the compound analysed, the NMR methodologies (1D ^{1}H, ^{13}C and/or two-dimensional (2D) NMR) must be used. NMR is the most powerful tool for the structural determination of organic compounds which frequently are completely novel and often possess unusual or unprecedent reported structural features. However, when two or more compounds with similar structure are present in the same sample, NMR spectra could contain signal systems which are difficult to assign (e.g., low signal intensity and/or significant chemical shift overlapping). In this context, the joint use of electrospray ionization mass spectrometry (ESI–MS) could be an efficient alternative method. In fact, ESI does not induce the molecular structure changing, and the spectra recorded are substantially devoid of fragment ions. However, significant structural data could only be provided by tandem mass spectrometry experiments (MS/MS), which permit the post-ionization process into a collision cell, and allow controlled ion dissociation (Tringali 2000; Spano et al 2022).

In addition, in the last decade, ion mobility mass spectrometry (IM-MS) has been developed that more easily allow the unambiguous identification of an organic compound. In IM-MS experiments, using a buffer gas and applying a weak electric field, two ions that have the same mass-to-ratio pass through the drift cell and are differentially decelerated according to their active surface. This process is called Collision Cross Section (CCS). Thus, the IM-MS method could be very suitable to analysing isomer mixtures (Wilkins & Trimpin 2010).

IV. Future perspectives

Future prospects envisage different strategies for improving the efficacy of bioherbicides. The biological processes involve the identification of new targets, new agents, the multiple use of different pathogens and the simultaneous application of phytotoxins and pathogens as well as that of insects and pathogens. The technological strategies include the production methods, the increasing virulence of pathogens and precision agriculture. Integrated pest management involves the use of chemical products and the weed defense suppressants. Genetic methods involve the reduction in pesticide resistance, the development of biomarkers and the assessment of the environmental risks.

V. Conclusions

Weeds plants represent one of the most serious constraints in agrarian and pasture production, in reforestation practices in wood-producing countries, and in protection of forest and ornamental heritage as well as historic garden, archeological ruins and monuments. These infestations determine heavy economic losses and require the use of efficacy methods to combat weeds and parasitic plants diffusion. In the past, agronomic and agrarian methods were used, but because of their low efficacy, these traditional methods were overcome in recent decades by the massive and extensive use of synthetic herbicides, which have generated the large problem of environmental pollution with a consequent contribution to climate changes, and due also to the repetition of treatment and the subsequent resistance developed by weedy plants. Severe risks for human and animal health were frequently recognized as being due to their transmission along the food chain. Thus, peoples and politicians inquire as to the development of alternative methods based on natural substance with herbicidal efficacy, selectivity, and ecofriendly properties. This paper review overview of the several fungal metabolites with herbicidal activity, reporting in details their source, the chemical name and biological activity were presented. All the results shown for the biocontrol of weeds are summarized in Table 1. However, for the most promising compounds found in the research, work should evaluate the eco- and human toxicological profile and develop their large production at an industrial level by fermentation or a total convenient and ecofriendly synthesis.

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