BIOTECH ATTRACTION 2026 | FRUIT ATTRACTION

From Microbial Biodiversity to Innovative Solutions for Sustainable Crop Protection



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MEDINA: Microbial Natural Products Discovery

Reference Center in Natural Products Discovery

Multidisciplinary team
of scientists

2300 m²
fully equipped facilities

One of the **largest microbial collections** (190K strains) and **libraries** (200K samples) for natural products drug discovery

High capacity center for high throughput screening

eu-openscreen
MIRRI MICROBIAL RESEARCH INFRASTRUCTURE ERIC

Partner site of European Infrastructures

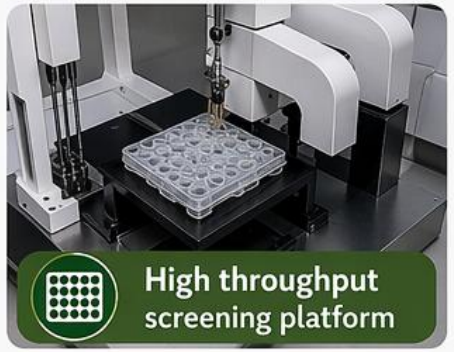
Drug discovery research programs in human health **infectious diseases, cancer** and **neurodegeneration**

Collaborations and contract research in **Pharma, Agroveg, Cosmetics and Microbial Biotechnology**









Infectious diseases

Cancer

Neurodegeneration

Natural products for human health

Pharma
New therapeutics

Agroveg
Biocontrol and plant health

Cosmetics
Natural ingredients and actives

Microbial Biotechnology
Bioprocesses and bioactive compounds

Largest Microbial Collection Worldwide

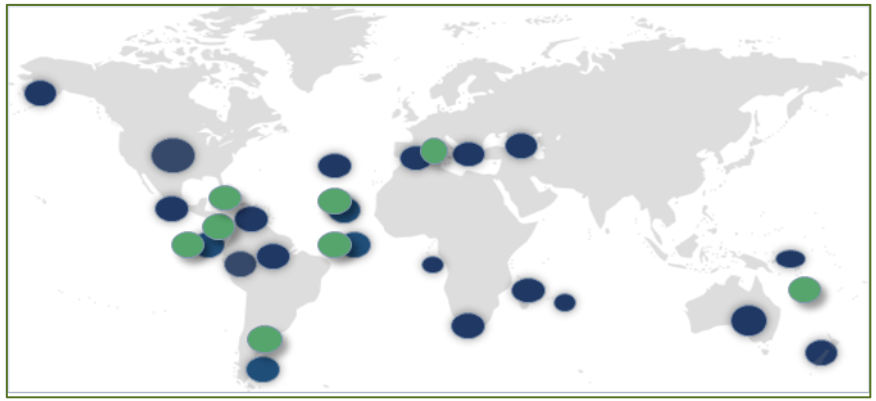
190.000 strains

Compliant with CBD and Nagoya Protocol





Worldwide sources in collection



Sources:

- Terrestrial
- Marine

Forests | Grasslands | Arid & Deserts | Marine Environments | Cultivated Plants | Rhizosphere Soils | Many more niches

Fungi:
Fungal plant endophytes
(32%)

Bacteria:
Marine actinomycetes
(<10%)

Soil & plant rhizosphere actinomycetes
(86%)

- Global biodiversity coverage
- Legally compliant access & benefit sharing
- Secure long-term preservation (-80 °C / lyophilized)
- High-quality characterization and metadata
- Powering discovery of novel natural products and bioactivities

Approaches for the discovery of new **Biopesticides** from microbial natural products

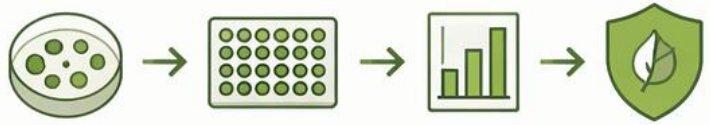


Surveying culturable microbial diversity from unexplored ecosystems (arid areas, marine resources, endemic xerophytic plants and lichens).





HTS *in vitro* Platform to identify metabolites with biocontrol properties.





Microbial Extracts as source of bioactive secondary metabolites.



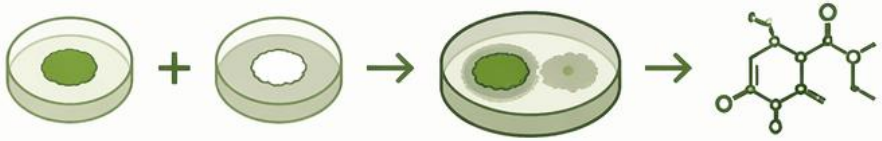


Metabolomics: UV and mass spectrometry imaging (MSI) for deconvolution of microbial interactions.





Coculturing as model to induce new antifungal agents.



Exploring microbial diversity in Andalucía



One of the most biodiverse regions in Europe:

- About **30%** land area in **natural reserves**: Alpine, desert, and marine habitats, complex geology
- **553 endemic plant species** in the southern Iberian Peninsula
- Focus on **fungi and bacteria isolation** including novel culturing approaches

DIVERSE ECOSYSTEMS
Sampling across unique habitats

→

SAMPLE COLLECTION
Soil, water, plants, lichens, sediments, etc.

→

MICROBIAL ISOLATION
Fungi and bacteria cultivation

→

NOVEL CULTURING APPROACHES
To access the uncultured majority

→

BIODISCOVERY
New strains and metabolites with biocontrol potential

Isolation of Endophytes and Lichen Associated Fungi from endemic plants and lichens collected in arid areas in Granada and Almeria

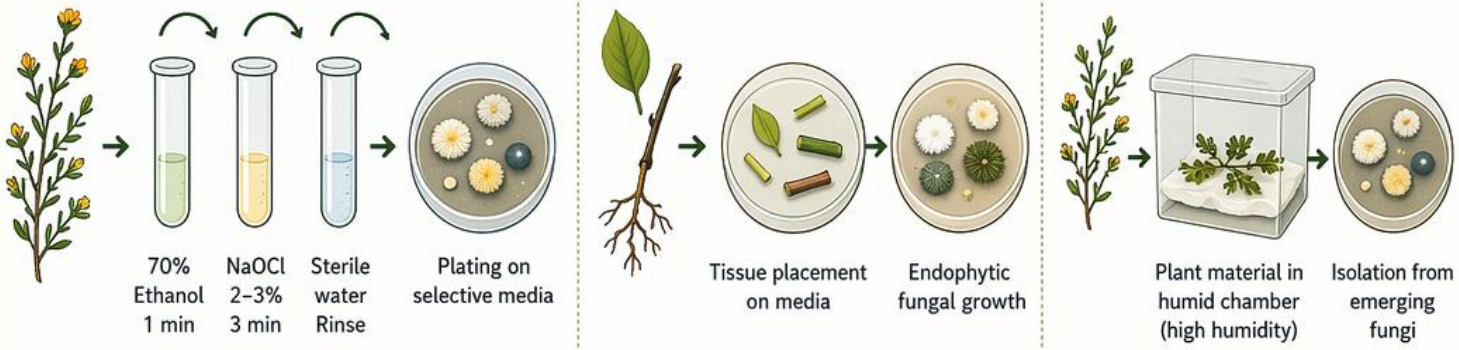


One of the most biodiverse regions in Europe:
About 30% land area in natural reserves: Alpine, desert, and marine habitats, complex geology

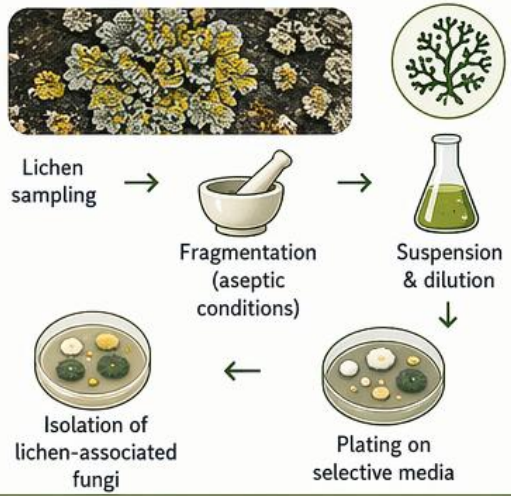
553 endemic plant species in the southern Iberian Peninsula

Focus on fungi and bacteria isolation including novel culturing approaches

MICROBIAL ISOLATION FROM ENDEMIC PLANTS



MICROBIAL ISOLATION FROM LICHENS (Lichen associated fungi)



A potential source for isolation of novel symbionts and host-specific endophytes not described yet.

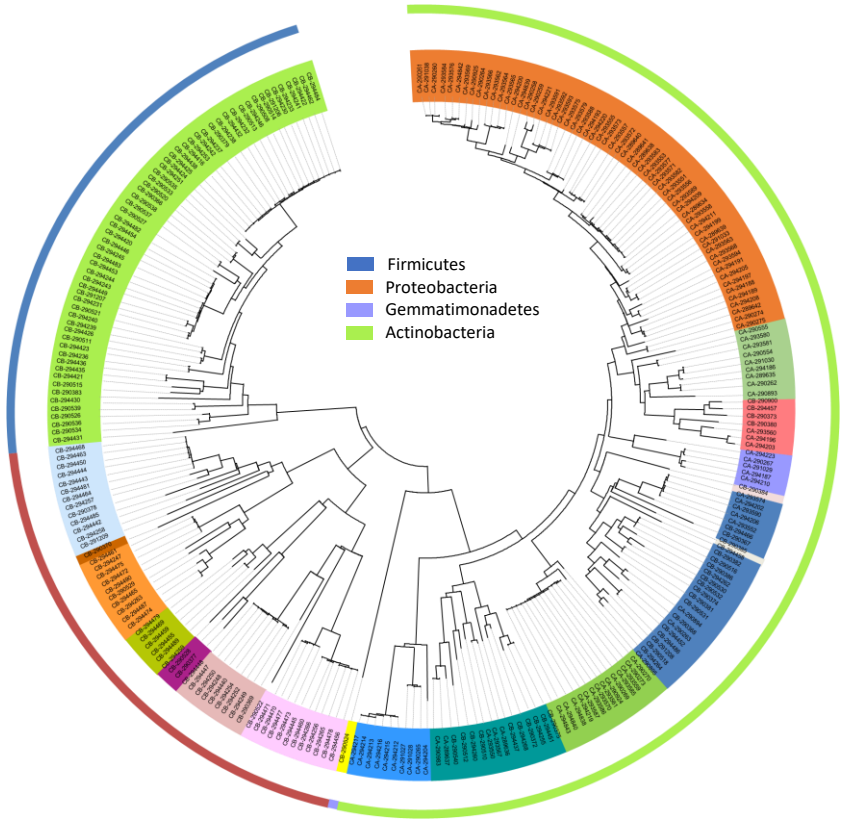


MICROBIAL ENDOPHYTES CHARACTERIZATION

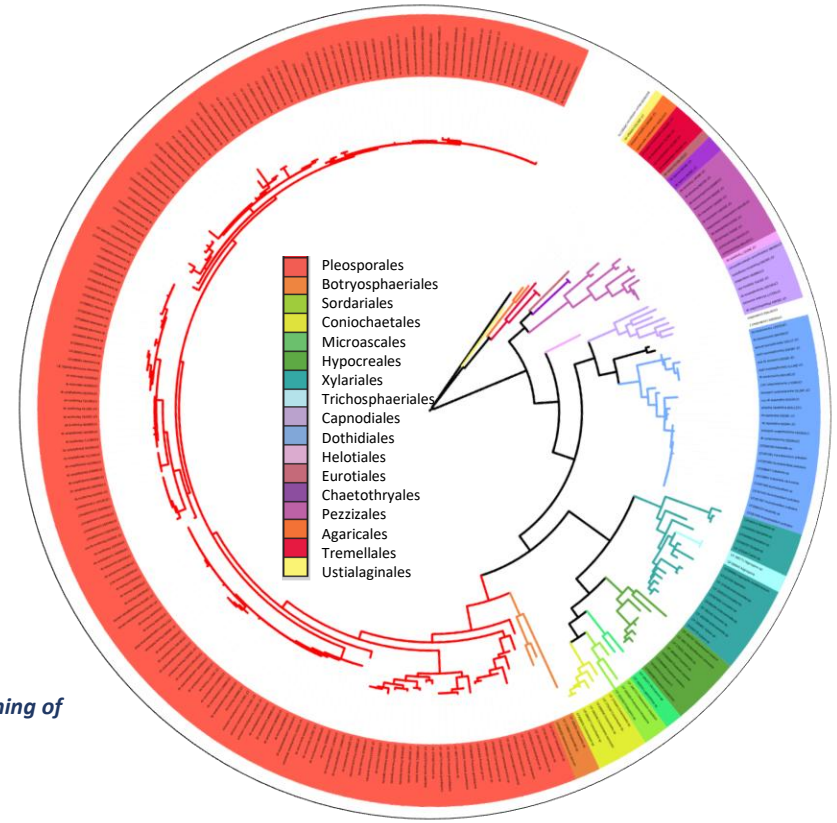
From **54** Xerophytic plant species



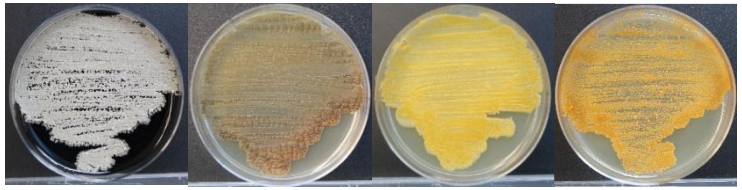
MEDINA
Medicamentos Innovadores Andaluza



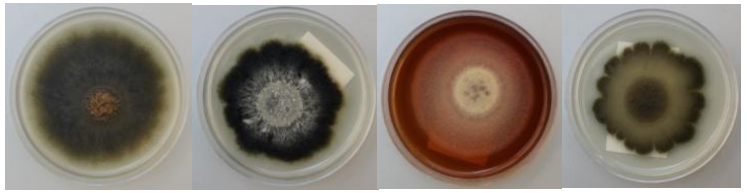
Neighbor Joining of rDNA



280 BACTERIA STRAINS



349 FUNGAL STRAINS



Exploring hidden diversity in extreme environments

Host-specific adaptations

Discovery of novel microbial taxa

Promising candidates for sustainable agriculture

Isolation of Plant microbiome associated to crops from a Traditional Agricuitural Land

Plants and Rhizosphere
Barley, Ray Grass and Wheat





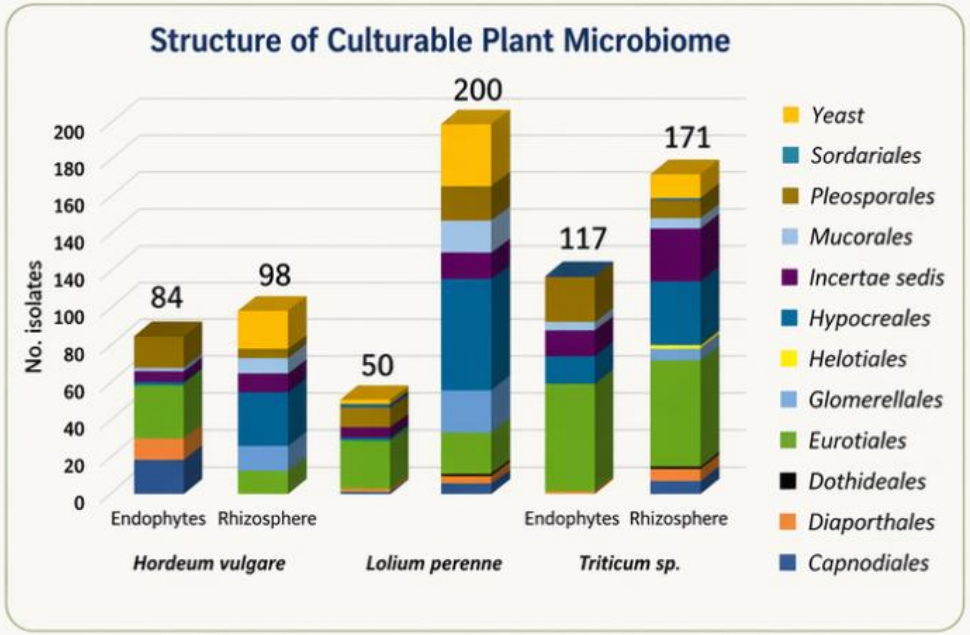


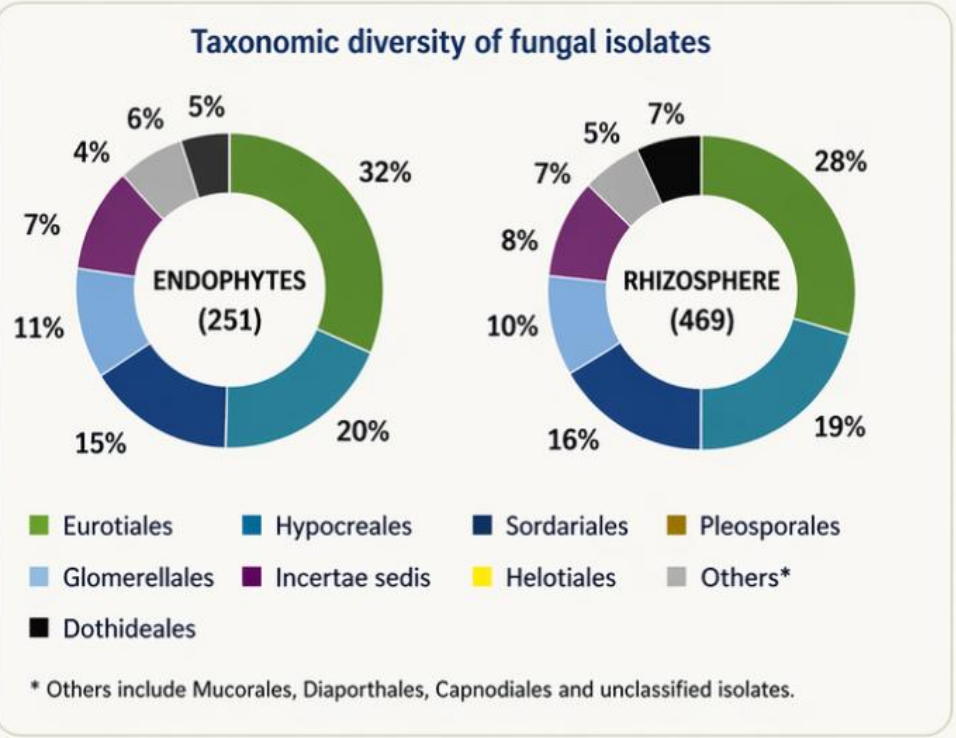
720 Fungal strains isolated

251 Endophyte

469 Rhizosphere

A rich source of novel microorganisms with potential for biocontrol and biopesticide discovery





GENERATION OF MICROBIAL EXTRACT COLLECTION

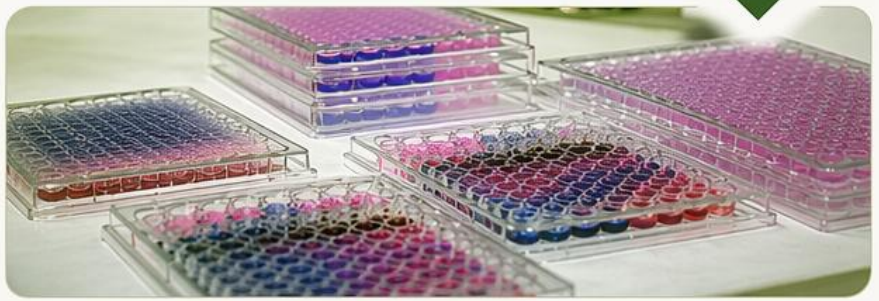
MEDINA



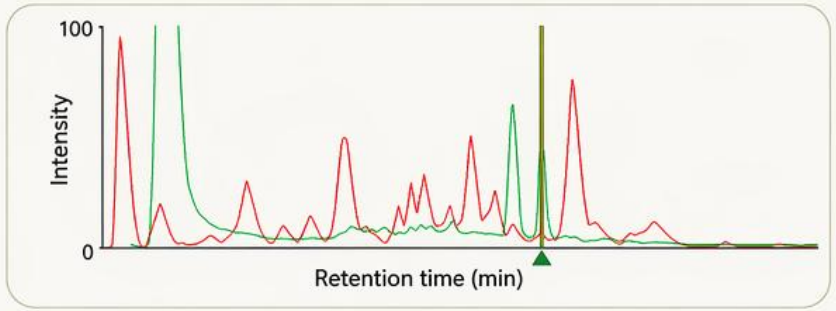
1 **Microbial strains** were fermented in different culture conditions (OSMAC approach)



2 **Automated extraction:** generation of **fungal extracts** transferred to 96-well microplates



3 Antifungal activity against **important plant pathogens** (HTS)



4 **LC-MS Dereplication** of active extracts and identification of known compounds (NPs libraries)

From microbial diversity to bioactive extracts: a pipeline for the discovery of new biopesticides

- Diverse microbial resources
- Automated and scalable workflow
- High-throughput bioactivity screening
- Advanced chemical analysis

HTS PLATFORM USING PHYTOPATHOGENS

Whole cell *in vitro* liquid and agar-based assays

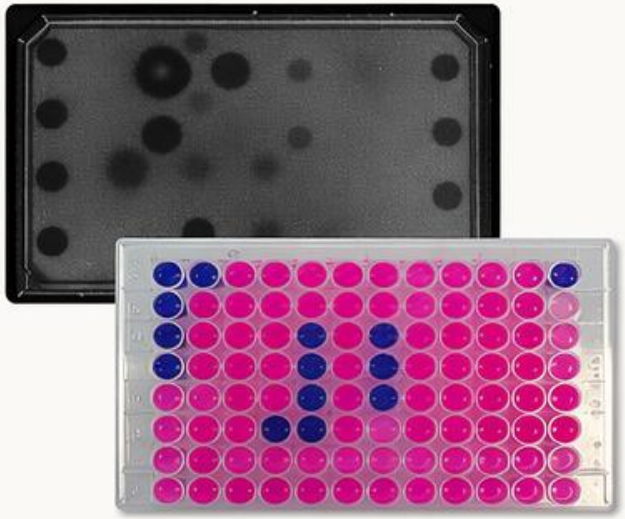
FUNGAL PHYTOPATHOGEN ASSAYS AVAILABLE

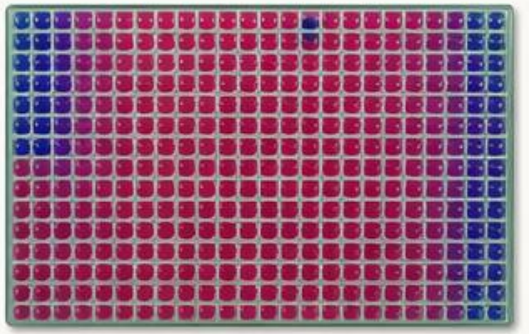
- ***Botrytis cinerea*** (Gray mold of vegetables, grape, strawbery crops)
- ***Colletotrichum acutatum*** (Anthracnose of citrus and olive crops)
- ***Fusarium cubense TR4 CBS*** (Wilt of banana)
- ***Fusarium culmorum*** (Common root rot and other cereals diseases)
- ***Fusarium graminearum*** (Devastating disease on wheat and barley)
- ***Fusarium raphani MF-4014*** (Wilt of radish)
- ***Fusarium proliferatum*** (Disease on asparagus, garlic, soybean crops)
- ***Magnaporthe grisea*** (Rice blast)
- ***Monilinia laxa*** (Brown rot of stone fruit crops)
- ***Phytophthora cinnamomi*** (Pathogens of dicot important crop species)
- ***Pythium ultimum*** (Damping off and root rot diseases of maize, soybean, potato, wheat.)
- ***Rhizoctonia solani*** (Stem and root plants and crops)
- ***Rosellinia necatrix*** (White root rot in several fruit crops)
- ***Verticillium dahliae*** (Verticillium wilt in olive, tomato, potato crops)
- ***Zymoseptoria tritici*** (Septoria leaf blotch on wheat crops)

BACTERIAL PHYTOPATHOGENS ASSAYS AVAILABLE

- ***Clavibacter michiganensis subsp. michiganensis*** (Maize diseases)
- ***Pectobacterium carotovorum subsp. carotovorum*** (Soft rot and stem rot diseases in several crops)
- ***Pseudomonas syringae*** (Tomato and cruciferous diseases)
- ***Xanthomonas ampelina*** (Vitis vinifera (=Xylophilus ampelinus)
- ***Xanthomonas axonopodis*** (Carpetgrass, Axonopus scoparius and Phaseolus vulgaris)
- ***Xanthomonas campestris*** (Black rot in cruciferous vegetables)
- ***Xylella fastidiosa*** (Wide host range)

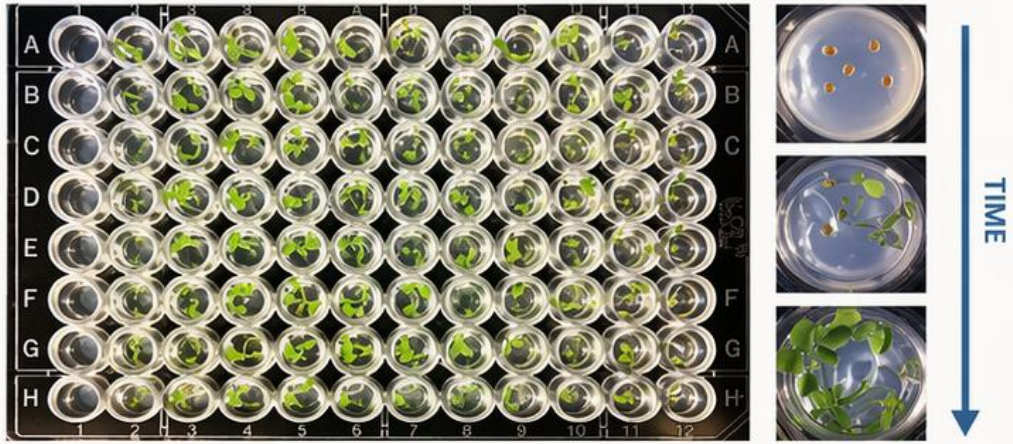






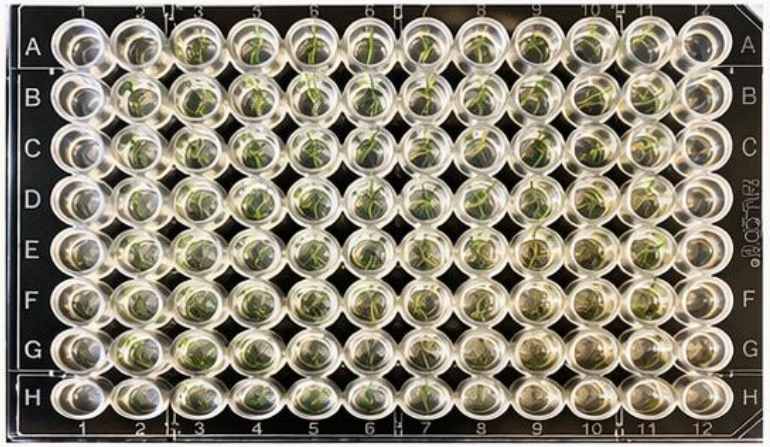
HERBICIDAL ASSAYS

HTS Screening
Arabidopsis thaliana as Model dicotyledon plant



TIME

HTS Screening
Agrostis capillaris as Model monocotyledon plant





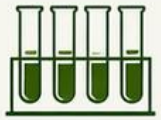
TIME

Controls and treatments at different times

Monitoring seed germination and seedling development in 96 well plates

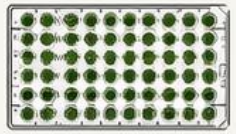
Identification of extracts that inhibit seed germination or cause plant growth retardation

1. COMPOUND LIBRARY



Microbial extracts and natural products

2. HTS ASSAY



Application in 96 well plates (dicots and monocots)

3. INCUBATION & MONITORING



Seed germination and seedling development monitored over time

4. DATA ANALYSIS



Quantification of growth inhibition / retardation

5. HIT SELECTION



Selection of active extracts for further validation

- Natural product discovery for herbicide leads
- High-throughput screening platform
- Robust and reproducible assays
- Dicot and monocot coverage
- Sustainable solutions for weed management and crop protection

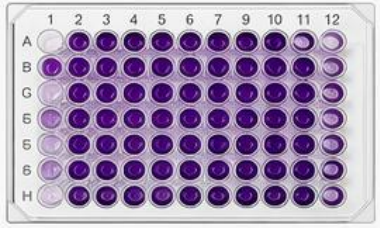
BIOINSECTICIDAL ASSAYS

HTS Cell line assay meant to prioritize candidates from a large set before assaying them on plants.

Natural products or **synthetic compounds** can be tested.

MTT Cell Proliferation Assay with insect cell lines:

- **SF9 ATCC CRL-1711 cell line:** derived from pupal ovarian tissue of the fall armyworm *Spodoptera frugiperda*
- **ATC-15 cell line** from larvae of the *Aedes albopictus* (Asian tiger mosquito)



MTT Assay measures the cell proliferation rate and conversely, when metabolic events lead to apoptosis or necrosis, the reduction in cell viability.



Target insect

Examples of target pests relevant to bioinsecticidal discovery



Crop protection

Bioinsecticidal solutions to protect crops from insect damage

1. COMPOUND LIBRARY
Natural products or synthetic compounds

2. MTT ASSAY
Application in 96 well plates (insect cell lines)

3. CELL RESPONSE
Cell proliferation measured by MTT reduction

4. DATA ANALYSIS
Quantification of viability and cytotoxic effects

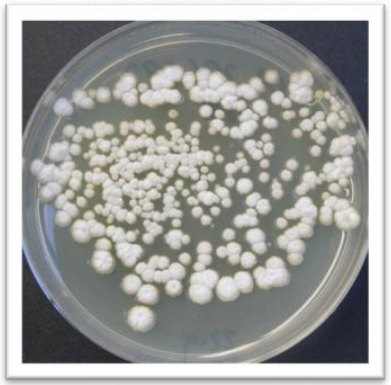
5. HIT SELECTION
Selection of active compounds for further validation

- Early-stage screening to prioritize potent bioinsecticidal leads
- High-throughput cell-based platform
- Reliable, reproducible and quantitative assays
- Supports discovery of selective and safe compounds
- Sustainable solutions for integrated pest management

New Secondary Metabolites (SMs) produced by Microbes

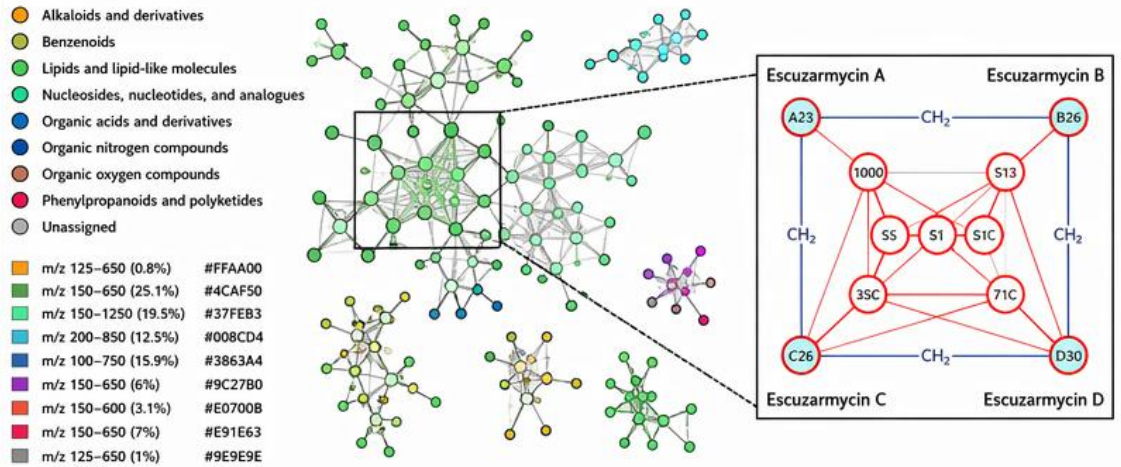
Purification of new antifungal compounds to control the causal agent of *Septoria tritici* blotch.

SOURCE MICROBE

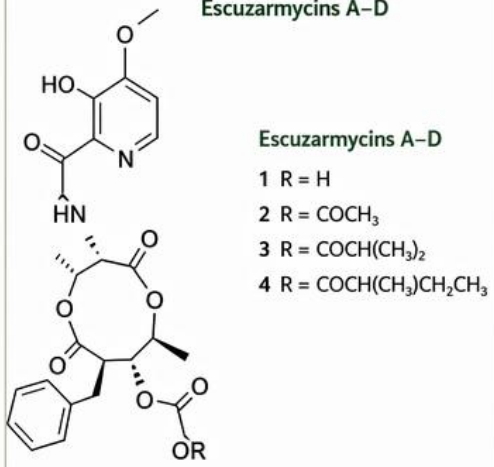


***Streptomyces* sp. CA-296093**
Isolated from gypsum outcrop in Escuzar (Granada)

MOLECULAR NETWORKING (GNPS)



STRUCTURE OF ESCUZARMYCINS

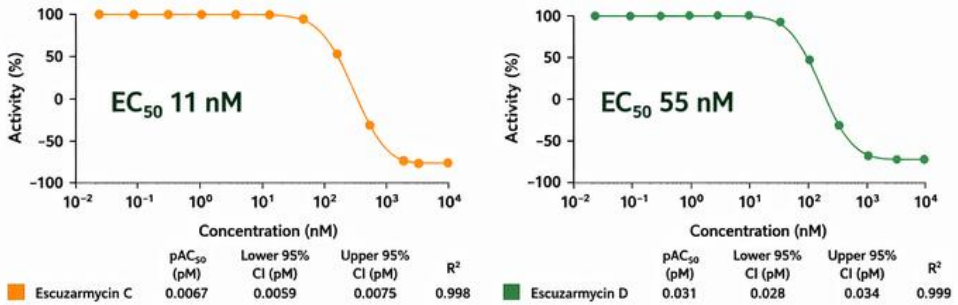


Escuzarmycins A–D

Escuzarmycins A–D

1 R = H
2 R = $COCH_3$
3 R = $COCH(CH_3)_2$
4 R = $COCH(CH_3)CH_2CH_3$

DOSE RESPONSE CURVES – *Z. tritici*



Compound	EC_{50} nM		
	B. cinerea	*C. acutatum*	*Z. tritici*
Escuzarmycin C	812	1200	11
Escuzarmycin D	81	55	55
Fenicoxamid	651	Inactive	2
Amphotericine B	292	1300	216

Four new secondary metabolites showed strong activity against the causal agent of *Septoria tritici* blotch (*Z. tritici*).

New secondary metabolites from endophytic *Streptomyces* represent a rich source of antifungal agents with high potential for development of next-generation biopesticides.

NATURAL SOURCE
Endophytic *Streptomyces* from extreme environments as a source of novelty

ADVANCED DEREPLICATION
GNPS molecular networking and HR-MS enabled rapid discovery

STRONG ANTIFUNGAL ACTIVITY
Escuzarmycin C and D showed the highest potency against *Z. tritici*

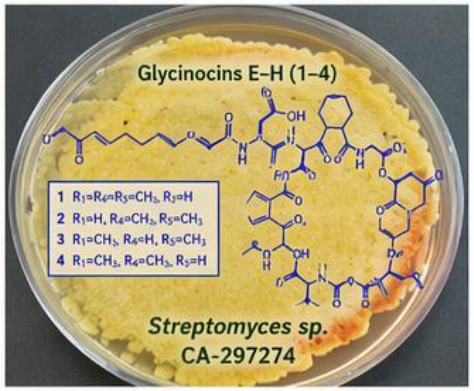
BIOPESTICIDE POTENTIAL
Promising lead compounds for sustainable crop protection

IMPACT
Supporting resilient agriculture and reducing dependence on chemical fungicides

New Secondary Metabolites (SMs) produced by Microbes

Glycinocins E–H, new lipopeptides to control *Septoria tritici* blotch.

SOURCE MICROB



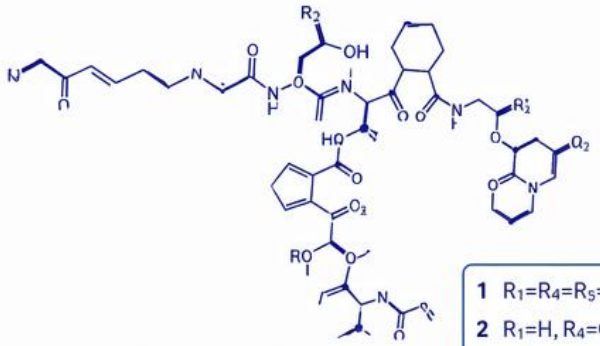
***Streptomyces* sp. CA-297274**
isolated from *Gyalolechia fulgida*
(Escuzar, Granada, Spain)

ANTIFUNGAL ACTIVITY AGAINST *Z. tritici*

EC_{50} values in µM and their corresponding 95% confidence limits in parenthesis for compounds 1–4 and Amphotericin B against *Z. tritici* based on absorbance and fluorescence ***in vitro*** assays.

Z. tritici IC_{50} values in µM (the corresponding 95% confidence limits)		
Compound	**Absorbance (growth inhibition)**	**Fluorescence (cell viability)**
1	49.8 (47–53)	25.9 (23–28)
2	47.9 (40–56)	30.8 (29–33)
3	23 (20–27)	11.4 (9–13)
4	**5.4 (5–6)**	**4.1 (3.8–4.5)**
Amphotericin B	0.2 (0.17–0.24)	0.2 (0.18–0.22)

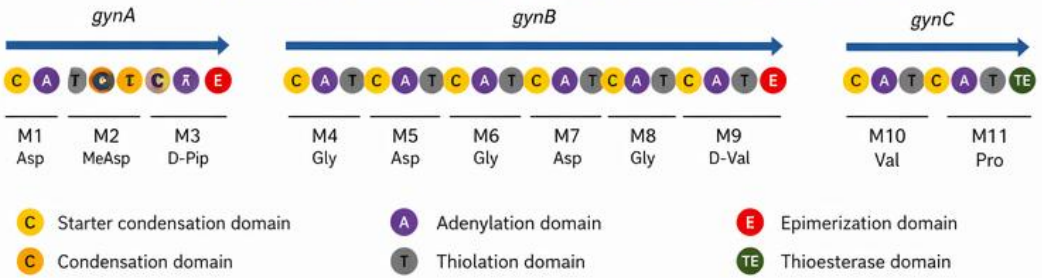
STRUCTURE OF GLYCINOCINS E–H



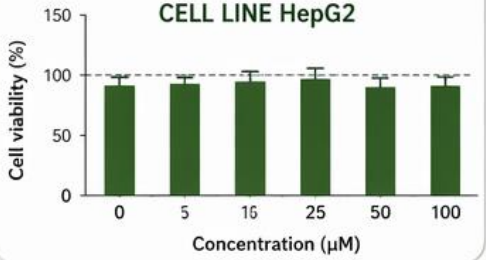
Glycinocins E–H (1–4)

1 $R_1=R_4=R_5=CH_3, R_2=H$
2 $R_1=H, R_4=CH_3, R_5=CH_3$
3 $R_1=CH_3, R_4=H, R_5=CH_3$
4 $R_1=CH_3, R_4=CH_3, R_5=H$

PROPOSED NRPS ASSEMBLY LINE FOR GLYCINOCIN BIOSYNTHESIS



NO CYTOTOXICITY AGAINST HUMAN LIVER CELL LINE HepG2



Glycinocins E–H are potent antifungal lipopeptides with low toxicity, representing promising lead compounds against the causal agent of *Septoria tritici* blotch (*Z. tritici*).

New lipopeptides from endophytic *Streptomyces* represent a rich source of antifungal agents with high potential for development of next-generation biopesticides.

NATURAL SOURCE
Endophytic *Streptomyces* from extreme environments as a source of novelty

ADVANCED DEREPLICATION
HR-MS and GNPS molecular networking enabled rapid discovery

STRONG ANTIFUNGAL ACTIVITY
Glycinocin 4 showed the highest potency against *Z. tritici*

LOW TOXICITY
No cytotoxicity against human liver cell line HepG2

BIOPESTICIDE POTENTIAL
Promising lead compounds for sustainable crop protection

New Secondary Metabolites (SMs) produced by Microbes

Libertamide, a new Fungicide to control *Zymoseptoria tritici*

a significant threat to wheat production in Europe due to its substantial impact on crop yields

SOURCE MICROBE



***Libertasomyces aloeticus* CF-168990**

Isolated from leaf litter

Coastal fynbos: *Diosma subulata*, Asteraceae

De Hoop Nature Reserve, Africa

CULTURE AND EXTRACTS



CF-168990



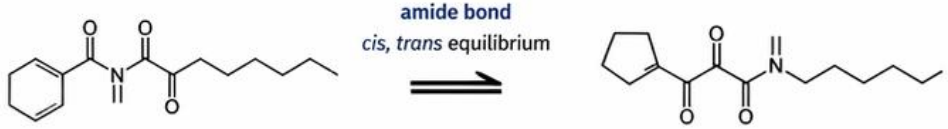
MCKX
liquid condition

Yield 188 mg/L

BRFT
solid condition

Yield 303 mg/L

DISCOVERY OF NEW ANTIFUNGAL LIBERTAMIDE



ANTIFUNGAL ACTIVITY AGAINST PHYTOPATHOGENS

Phytopathogen strain	IC_{50} (µg/mL)	
	Absorbance-based assay	Fluorescence-based assay
Zymoseptoria tritici CBS 115943	0.91 ± 0.12	1.30 ± 0.01
Botrytis cinerea B05.10	34.05 ± 4.06	49.74 ± 3.87
Verticillium dahliae CBS 717.96	31.83 ± 3.03	24.80 ± 3.18
Colletotrichum acutatum CF-137177	36.33 ± 1.09	41.08 ± 1.77
Fusarium oxysporum sbsp. *cubense* CBS 102025	61.80 ± 4.15	51.29 ± 7.20
Magnaporthe grisea CF-105765	67.81 ± 3.25	84.60 ± 0.80
Fusarium proliferatum CBS 115.97	120.43 ± 4.84	136.50 ± 7.55
Phytopthora cinnamomi CECT 20186	110.4 ± 8.4	125.4 ± 5.3
Pythium ultimum CECT 2365	91.8 ± 6.5	51.52 ± 3.1

CYTOTOXICITY EVALUATION	ED_{50} (µg/mL)
	MTT-based assay
HepG2 cell line	25.14 ± 2.45

Libertamide shows potent antifungal activity against key phytopathogens, including *Zymoseptoria tritici*, with low cytotoxicity, representing a promising lead compound for sustainable crop protection.

NATURAL SOURCE
Libertasomyces from coastal fynbos ecosystem as a source of novelty

NEW CHEMISTRY
Libertamide new compound with a unique amide bond *cis, trans* equilibrium

BROAD ANTIFUNGAL ACTIVITY
Potent activity against key phytopathogens including *Z. tritici*

LOW CYTOTOXICITY
Low toxicity towards human liver cell line HepG2

BIOPESTICIDE POTENTIAL
A promising lead compound for sustainable crop protection

FINAL COMMENTS



Microbial biodiversity

Microbial biodiversity remains one of the richest sources of **novel bioactive compounds** for sustainable crop protection.



Microbial collections

Large and well-characterized microbial collections enable **systematic access** to new microorganisms and natural products.



Extract library

Generation of diverse microbial extracts provides a valuable resource of **chemical diversity** for biological screening.



HTS screening

Integrated workflows combining isolation, fermentation, extract generation and HTS screening **accelerate the discovery** of biocontrol solutions.



Sustainable crop protection

Microbial-derived metabolites provide valuable opportunities for the development of **next-generation biofungicides, bioherbicides and bioinsecticides**.

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Thank you for your attention

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190,000 microbial strains

200,000 natural product extracts

HTS screening platforms

Discovering microbial solutions for **sustainable agriculture**

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Junta de Andalucía

UNIVERSIDAD DE GRANADA

MSD