NEW ANTIFUNGAL AND ANTIBACTERIAL COMPOUNDS: 1,3-OXAZOLINE- AND 1,3-OXAZOLIDINE-2-THIONES

F.V.M. Silva,[a,b,c] J. Justino,[b] S. Silva,[a,d] A. Tatibouët,[d] P. Rollin,[d] A.P. Rauter[a]*

[a]Grupo de Química dos Glúcidos do Centro de Química e Bioquímica / Departamento de Química e Bioquímica, Faculdade de Ciências da Universidade de Lisboa, Portugal; *Email: aprauter@fc.ul.pt

[b]Escola Superior Agrária, Instituto Politécnico de Santarém, Portugal

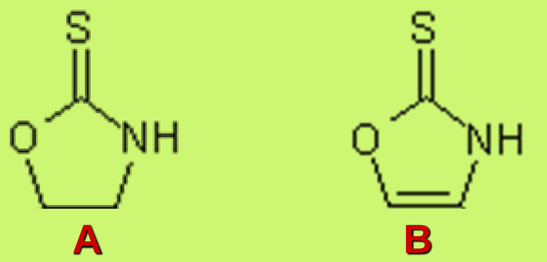
[c]Instituto Nacional dos Recursos Biológicos (INRB-INIA), Fonte Boa, Vale de Santarém, Portugal

[d]Institut de Chimie Organique et Analytique - UMR 6005, Université d'Orléans, France

Objectives

- To produce new compounds which possess the structural moiety 1,3-oxazoline-2-thione (compounds containing **A**) or 1,3-oxazolidine-2-thione (compounds containing **B**)[1,2].

Oxazoline **Oxazolidine**



A **B**

- To investigate antibacterial and antifungal activity of twenty four compounds over a panel of pathogenic and phytopathogenic microorganisms.

Method for microbial susceptibility testing

- The antimicrobial activity of 300 µg of each compound was assessed by the paper disk diffusion method in agar[3-5], being the diameter of inhibition, Ø, expressed in mm.
- Chloramphenicol and actidione were used as controls for bacteria and fungi, respectively.
- Microorganisms used in the susceptibility tests belonged to ATTC (USA) and CBS (The Netherlands) cultures, and others were local isolates kept in our lab:

Moulds and Yeast

Alternaria alternata (CBS 108.41)
Biscogniauxia mediterranea (CBS 101016)
Byssochlamys fulva (CBS 146.48)
Colletotrichum coffeanum (CBS 396.67)
Fusarium culmorum (CBS 129.73)
Pyricularia oryzae (CBS 433.70)
Stachybotrys chartarum (CBS 414.95)
Botrytis spp. *Rhizopus* spp.
Yeast: Candida albicans (ATCC 10231)

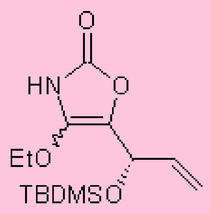
Bacteria

Bacillus cereus (ATCC 11778)
Bacillus subtilis (ATCC 6633)
Enterococcus faecalis (ATCC 29212)
Escherichia coli (ATCC 8739)
Listeria monocytogenes (ATCC 7644)
Pseudomonas aeruginosa (ATCC 27853)
Salmonella enteritidis (ATCC 13076)
Staphylococcus aureus (ATCC 25923)

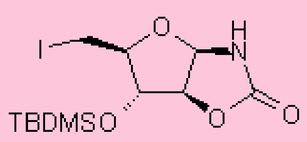
Results of most bioactive compounds (inhibition diameter, ∅ ≥ 12 mm)

Antifungal and antibacterial

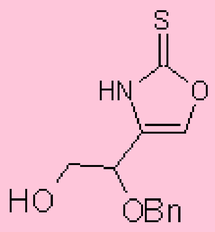
B. mediterranea ∅=12 mm
Botrytis spp. ∅=15 mm
B. fulva ∅=19 mm
C. albicans ∅=20 mm
C. coffeanum ∅=15 mm
P. oryzae ∅=18 mm
Rhizopus spp. ∅=15 mm
B. cereus ∅=19 mm
B. subtilis ∅=28 mm
E. faecalis ∅=16 mm
S. aureus ∅=21 mm



C. albicans ∅=14 mm
B. cereus ∅=13 mm
B. subtilis ∅=17 mm

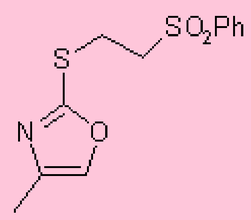


C. albicans ∅=12 mm
B. cereus ∅=19 mm
B. subtilis ∅=20 mm
E. faecalis ∅=14 mm
S. aureus ∅=14 mm

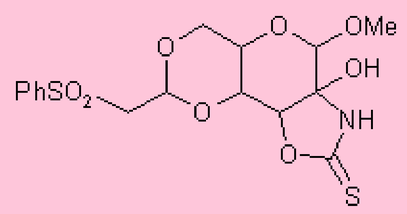


C. albicans ∅=12 mm
C. coffeanum ∅=12 mm
B. cereus ∅=12 mm

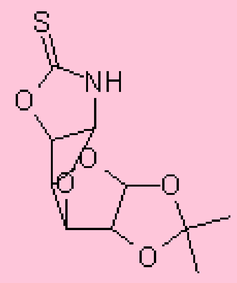
Antibacterial



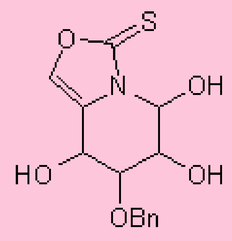
B. cereus ∅=13 mm
B. subtilis ∅=20 mm



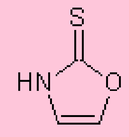
B. subtilis ∅=16 mm



B. subtilis ∅=14 mm
S. aureus ∅=12 mm

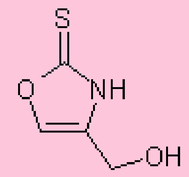


B. subtilis ∅=16 mm



B. cereus ∅=12 mm
B. subtilis ∅=12 mm
S. aureus ∅=12 mm

Antifungal



Botrytis spp. ∅=15 mm

Control actidione

Microorganism	Ø (mm) 300 µg
B. mediterranea	70
Botrytis spp.	20
B. fulva	45
C. coffeanum	24
P. oryzae	70
Rhizopus spp.	19

Control chloramphenicol

Microorganism	Ø (mm) 300 µg
B. cereus	45
B. subtilis	46
E. faecalis	43
S. aureus	41
C. albicans	15

Conclusions

- The results revealed strong antifungal and antibacterial activities of various compounds.
- Eleven compounds were antifungal, fourteen were antibacterial and eight compounds were active against both fungi and bacteria microbes.
- The most potent antifungal and antibacterial compound was an oxazoline derivative which caused a potent inhibition of six fungi (inhibition diameter ∅ between 15 to 20 mm) and four bacteria (∅ between 16 to 28 mm).

Acknowledgements

Research grants of Filipa V.M. Silva and Sandrina Silva from Fundação para a Ciência e Tecnologia (FCT), Portugal.

References

1. Silva S., Simão A.C., Tatibouët A., Rollin P., Rauter A.P. *Tetrahedron Letters* 2008a, 49, 682-686.
2. Silva S., Tardy S., Routier S., Suzenet F., Tatibouët A., Rauter A.P., Rollin P. *Tetrahedron Letters* 2008b, 49, 5583-5586.
3. Bauer A.W., Kirby W.M., Sherris J.C., Turck M. *The Amer. J. Clinical Pathology* 1966, 45, 493-496.
4. NCCLS. *Performance standards for antimicrobial disk susceptibility tests: approved standard*. 1993, 4th ed., National Committee for Clinical Laboratory Standards document M2-A4.
5. Silva F.V.M., Goulart M., Justino J., Neves A., Santos F., Caio J., Lucas S., Newton A., Sacoto D., Barbosa E., Santos M.S., Rauter A.P. *Bioorg. Med. Chem.* 2008, 16, 4083-4092.