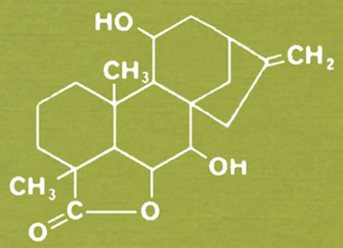
Topics in Secondary Metabolism 2

Fusarium
Mycotoxins, Taxonomy and Pathogenicity



Edited by

J. Chełkowski

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Topics in Secondary Metabolism - Volume 2

Fusarium: Mycotoxins, Taxonomy and Pathogenicity

Topics in Secondary Metabolism

Titles in this series

Volume 1 ***Bacillus subtilis*: Molecular Biology and Industrial Application**
edited by B. Maruo and H. Yoshikawa

Volume 2 ***Fusarium*: Mycotoxins, Taxonomy and Pathogenicity**
edited by J. Chełkowski

Topics in Secondary Metabolism - Volume 2

Fusarium
Mycotoxins, Taxonomy and Pathogenicity

Editor

J. Chełkowski

Department of Plant Pathology, Agricultural University, Nowoursynowska 166, 02 766 Warsaw, Poland

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LIST OF CONTRIBUTORS

J. BAUER Institut für Med. Mikrobiologie, Infektions- und Seuchenmedizin, Ludwig-Maximilians-Universität, Tierärztliche Fakultät, Veterinärstrasse 13, D-8000 München 22, F.R.G.

A. BOTTALICO Consiglio Nazionale della Ricerche, Istituto Tossine e Micotossine da Parassiti Vegetali, via G. Amendola 197/F, 70 126 Bari, Italy

J. CHELKOWSKI Department of Plant Pathology, Agricultural University, Nowoursynowska 166, 02 766 Warsaw, Poland

B.M. CUNFER Department of Plant Pathology, University of Georgia, Experiment Stations, Georgia Station, Griffin, GA 30223-1797, U.S.A.

C. ENDERS Institut für Med. Mikrobiologie, Infektions- und Seuchenmedizin, Ludwig-Maximilians-Universität, Tierärztliche Fakultät, Veterinärstrasse 13, D-8000 München 22, F.R.G.

J.M. FARBER Bureau of Microbial Hazards, Food Directorate, Health Protection Branch, Health and Welfare Canada, Ottawa, Ontario K1A 0L2, Canada

W. GAMS Centraalbureau voor Schimmelcultures, P.O. Box 273, 3742 AG Baarn, The Netherlands

M. GAREIS Institut für Med. Mikrobiologie, Infektions- und Seuchenmedizin, Ludwig-Maximilians-Universität, Tierärztliche Fakultät, Veterinärstrasse 13, D-8000 München 22, F.R.G.

B. GEDEK Institut für Med. Mikrobiologie, Infektions- und Seuchenmedizin, Ludwig-Maximilians-Universität, Tierärztliche Fakultät, Veterinärstrasse 13, D-8000 München 22, F.R.G.

J. GILBERT Ministry of Agriculture, Fisheries and Food, Food Science Laboratory, Haldin House, Queen Street, Norwich NR2 4SX, U.K.

P. GOLINSKI Department of Chemistry, The Agricultural University of Poznan, ul. Wojska Polskiego 75, 60 625 Poznan, Poland

E.-L. HINTIKKA National Veterinary Institute, P.O. Box 368, 00 101 Helsinki, Finland

W. KRÜGER Biologische Bundesanstalt für Land- und Forstwirtschaft, Institut für Pflanzenschutz in Ackerbau und Grünland, Messeweg 11/12, D-3300 Braunschweig, F.R.G.

B. LACICOWA Department of Plant Pathology, Agricultural University, Akademicka 15, 20 935 Lublin, Poland

A. LOGRIECO Consiglio Nazionale delle Ricerche, Istituto Tossine e Micotossine da Parassiti Vegetali, via G. Amendola 197/F, 70 126 Bari, Italy

M. MANKA Department of Plant Pathology, Agricultural University, Dabrowskiego 159, 60 354 Poznan, Poland

A. MESTERHAZY Cereal Research Institute, P.O. Box 391, H-6701 Szeged, Hungary

M. MICHNIEWICZ University of Mikolaj Kopernik, Institute of Biology, Gagarina 9, 87 100 Torun, Poland

H.I. NIRENBERG Biologische Bundesanstalt für Land- und Forstwirtschaft, Institut für Mikrobiologie, Königin-Luise-Strasse 19, D-1000 Berlin 33 Dahlem, F.R.G.

M. OLSEN Toxicology Laboratory, The Swedish National Food Administration, Box 622, S-75126 Uppsala, Sweden

A.L. PATEY Ministry of Agriculture, Fisheries and Food, Food Science Laboratory, Haldin House, Queen Street, Norwich NR2 4SX, U.K.

R. SCHMIDT HWS Mycotoxin Research Laboratory, P.O. Box 3628, D-6500 Mainz, F.R.G.

P.M. SCOTT Bureau of Chemical Safety, Food Directorate, Health Protection Branch, Health and Welfare Canada, Ottawa, Ontario K1A 0L2, Canada

E. SEPPÄNEN Agricultural Research Centre, Department of Plant Pathology, SF-31600 Jokioinen, Finland

A.H. TEICH Agriculture Canada Research Station, Harrow, Ontario N0R 1G0, Canada

U. THRANE Department of Biotechnology, Building 221, Technical University of Denmark, DK-2800 Lyngby, Denmark

H. URBANEK Institute of Plant Physiology and Cytology, The University of Lodz, Banacha 12, 90 237 Lodz, Poland

R.F. VESONDER USDA/ARS, Northern Regional Research Center, 1815 North University Street, Peoria, IL 61604, U.S.A.

A. VISCONTI Consiglio Nazionale delle Ricerche, Istituto Tossine e Micotossine da Parassiti Vegetali, via Amendola 197/F, 70 126 Bari, Italy

W. WAKULINSKI Department of Plant Pathology, The Agricultural University, Nowoursynowska 166, 02 766 Warsaw, Poland

PREFACE

The idea of this book was born at the Seminar "Fusarium - Mycotoxins, Taxonomy, Pathogenicity", held at the Agricultural University of Warsaw, Poland, on September 8-10, 1987. This book is the result of the effort and cooperation of 30 contributors from many disciplines. It contains actual basic and applied knowledge on *Fusarium* species, on their metabolites and taxonomy, in connection with pathogenicity to cereal plants and potato tubers.

Veterinarians observe mycotoxicoses of livestock (like an estrogenic syndrome or emesis and refusal in swine) and, together with mycologists and chemists, try to elucidate which fungal metabolites are hazardous to animals, when present in feed. On the other hand, plant pathologists realize research on epidemics of diseases of plants, like *Fusarium* corn ear rot ("scab") and wheat head fusariosis ("head blight"), causing not only a serious reduction in grain yield, but also an accumulation of toxic metabolites in plant tissues.

For several decades, but particularly during the last, maize, wheat, triticale and rye breeders have tried to create cultivars immune to infection by *Fusaria*. They all have one aim, to avoid infection of cereals with *Fusaria*, causing plant diseases, leading to contamination of grain with *Fusaria* metabolites, which may be toxic to animal and human.

For scientists working on mycotoxicoses direct contact with farmers is very important, advising them on agricultural practice, the cultivars least susceptible to infection and other factors which may affect yield and seed quality. Many details concerning *Fusaria*, and presented at this seminar, have recently been published in a special issue of the journal "Mycotoxin Research".

There are many groups working on *Fusarium* in different parts of the world. Their activity is reflected in the international newsletter "Fusarium Notes", published each year by the *Fusarium* Subcommittee of the International Society for Plant Pathology (ISPP). The Editor's intention was to give in this book information about as many scientific centers working on *Fusarium*, as possible, but particularly European scientists are represented (because the seminar was held in Europe).

Over the last few years several books on *Fusaria* have been published and the intention of the Editor and Contributors was not to repeat problems presented in previous books, but to describe new aspects of research.

The book is not divided into three individual parts, as its title may suggest, because many chapters deal with several problems and could be placed in different sections. So the chapters are ordered according to the main problems presented. At the beginning are chapters on mycotoxins (and other metabolites), on their toxicity and metabolism in animals followed by papers dealing with taxonomic aspects and then problems of pathogenicity and breeding of resistant genotypes. Chapters on hyperparasitism of *Fusaria* on ergot fungi and on potato tubers are placed at the end of the book.

The following are some short remarks by the Editor on particular groups of chapters.

MYCOTOXINS

The meaning of the name "mycotoxin" is still not unequivocal. Mycotoxins are not toxic to fungi, as one might suspect by analogy with names such as zootoxin and phytotoxin, if using the same linguistic convention. In phytopathology the name mycotoxin encompasses metabolites of fungi with phytotoxic, zootoxic and antibiotic activity. However, in animal sciences, in veterinary and in human medicine the word mycotoxin is used for fungal metabolites toxic to human and animal organisms. Bennet [*Mycopathologia*, **100** (1987) 3-5] recently suggested the following working definition: "Mycotoxins are natural products produced by fungi that evoke a toxic response when introduced in low concentration to higher vertebrates and other animals by a natural route. Some mycotoxins have multiple effects and may cause phytotoxic and antimicrobial syndromes in addition to animal toxicity". An example of this is T-2 toxin, exhibiting strong zootoxicity, phytotoxicity to many plants, particularly to seedlings, as well as antibacterial activity. The name fungal metabolite seems to be less confusing in interdisciplinary papers and discussions.

A comprehensive list of *Fusarium* metabolites and their properties has been prepared by R.F. Vesonder and P. Golinski in Chapter 1. Everybody using it should take into consideration that the actual name of the *Fusarium* species may be different from that used in the original paper, where data on isolation of a given compound for the first time are given. In many cases it is not possible to know the correct name of the species, because the original culture is no longer available.

Data on zootoxicity of *Fusarium* metabolites are available in other books on mycotoxins and mycotoxicoses. In this book E.-L. Hintikka presents her observations on fish poisoning with trichothecene mycotoxins. On the other hand J. Bauer and M. Olsen wrote very useful reviews on the metabolism of the most important *Fusarium* mycotoxins in domestic animals.

TAXONOMY

We found the problem of *Fusarium* taxonomy is still not resolved satisfactorily, which has caused a lot of misunderstanding in the past. Classical examples are the names nivalenol and neosolaniol, formed from the names of species which really are not able to produce those metabolites. It is true that the definition of *Fusarium* genus as well as some *Fusarium* species was not precise enough, but it is also really a kind of art and needs long experience.

The situation in *Fusarium* species taxonomy and nomenclature is still not clear. H.I. Nirenberg prepared a chapter on taxonomy taking into consideration the fact that the contributors used in their chapters three taxonomic systems, namely those of Booth (1971), Gerlach and Nirenberg (1982) and Nelson, Toussoun and Marasas (1983). She presents comparison of existing works and some new findings as well as synoptic keys to the sections and to the species, listed on wheat, maize and potato. Information on how to culture and isolate *Fusarium* strains to avoid their degeneration, stimulated particularly by rich media, are also included.

Since 1984 *Fusarium nivale* (and later other members of the section *Arachnites*) was excluded from the genus *Fusarium* and placed in *Microdochium*, as described in a separate chapter by W. Gams.

"It is likely that the direction of taxonomy in the future will be towards fewer species than nine", suggested W.C. Snyder in the introduction to the book "Fusarium: Diseases, Biology and Taxonomy". The existing schoolsof *Fusarium* taxonomy will not agree with this statement. There is essential agreement between the three above-mentioned systems of taxonomy. The differences concern several species names as well as the existence of several rarely occurring, and not sufficiently documented, species. Numerous *Fusarium* species develop perfect stages of *Gibberella* and *Nectria* genera within *Ascomycetes* and some authors list such species using names according to perfect stages, others use only names of anamorphs.

More research and discussions are still necessary to elaborate a unified system of *Fusarium* nomenclature and taxonomy, to reduce synonyms like *F. Moniliforme* and *F. vertcillioides* and elucidate true teleomorph-anamorph relationships. The chapter of H.I. Nirenberg is one step in this direction. The Technical University of Denmark and other laboratories started research on the taxonomy and metabolite profile relationship in *Fusarium* and the new research offers promising results to solve some taxonomic questions, as discussed in a special chapter by U. Thrane.

PATHOGENICITY

Fusaria are pathogens of cereal plants at all stages of their development, from the first hours of kernel germination, to harvest time, including post-harvest decay of grains. This has been presented in several chapters on *Fusarium* species pathogenicity. In various regions of the world various species are prevalent as cereal pathogens. Contamination of cereal grains and other tissues with mycotoxins is related to ear diseases. In some regions with humid and warm climates, it is important to select or to create genotypes resistant to infection by *Fusarium* and accumulation of mycotoxins, mostly vomitoxin, in kernels of infected spikelets. This was found to be very difficult. However, progress during the last decade is reviewed by A. Mesterhazy, of the Hungarian center for breeding research in cereals. Particularly interesting are results concerning the relationship between resistance (or susceptibility) of flowering heads and resistance of seedlings of the same wheat genotype. As long as resistant varieties are not available on large scale, it is advisable to use agricultural practice to reduce infection rate; this is reviewed by A.H. Teich from the experience of Canadian Agriculture scientists.

Are *Fusaria* in some cases profitable in agricultural practice? It is possible to find the answer in fusarial hyperparasitism on ergot fungi, discussed by B.M. Cunfer. In some countries producing large amounts of potatoes the dry rot of potato tubers, caused by some *Fusarium* species, is economically important. The pathogens involved and the risk of infected tuber toxicity has been reviewed using results of research realized in Finland (E. Seppänen) and in Poland (J. Chelkowski).

At the end of the book a Glossary with short definitions and explanations of names used in individual chapters may help the reader to understand all questions of this interdisciplinary book.

We hope that the book, covering as many aspects of *Fusarium* genus and fusarial diseases of cereals and potato tubers as possible, will be helpful to persons studying and teaching various disciplines, in which *Fusaria* and their metabolites play an important role.

J. Chelkowski
Editor

Chapter 1

METABOLITES OF FUSARIUM

Ronald F. Vesonder and Piotr Goliński

Fusarium, a genus containing many common soil saprophytes as well as plant pathogens, is frequently found in cereal grains. Many species of Fusarium produce a number of secondary metabolites, which elicit physiological and pharmacological responses in plants and animals. Recognized responses are: Mycotoxicoses (hemorrhagic diseases, alimentary toxic aleukia, estrogenism, and emesis-refusal response) in animals and humans on ingestion of grains infected with Fusarium; phytotoxicoses of plants; and initiation of the sexual stage in some fungi.

Mycotoxins attained high research priority because of the effects of aflatoxins in turkey poults and their extreme carcinogenicity. The most prevalent mycotoxins produced by the Fusaria are the 12,13-epoxy-Δ9-trichothecenes. Fusarium spp. elaborate about 45 trichothecenes. These metabolites are also produced by species of Trichoderma, Trichothecium, and Stachybotrys.

Only the trichothecenes T-2 toxin, vomitoxin (deoxynivalenol), diacetoxyscirpenol, nivalenol, fusarenon-X, and their derivatives have been isolated from grains molded by Fusarium. However, many papers in the literature describe the toxic effects of trichothecenes in laboratory animals, and extrapolate these biological effects to man and farm animals. T-2 toxin is associated with lethal toxicoses to dairy cattle, and vomitoxin produces a refusal-vomiting phenomenon in swine. An estrogenic toxin, zearalenone, is also commonly found in corn infected with Fusarium spp.

This chapter will list, in addition to the trichothecenes, specific groups of metabolites from Fusarium, based on biological activity. These groups are: Pigments, mycotoxins, antibiotics, phytotoxins, and derivatives of zearalenone. A miscellaneous group will include derivatives of di- and tri-terpenoids, along with various other ring-structured compounds whose biological activities have not been investigated. The following microbial products are excluded: Alicyclic compounds (steroids and gibberellins), aliphatic and related compounds (carboxylic acids, carotenoids), enzymes, simple nitrogen compounds.

The compounds listed in each biological category are alphabetized and will include structure, physicochemical data, the reference source of structure, and biological activity. When a compound possesses various biological activities, the compound will be cross-indexed.

There is extensive literature on Fusarium metabolites, but we will list only key references, with several reviews and books. Our literature search included Chemical Abstracts and books on fungal metabolites (Turner, 1971; Turner and Aldridge, 1983; Miller, 1961; Shibata, Natori, and Udagawa, 1964; and Korszybski, Kowszyk-Gindifer, and Kurylowicz, 1967). Besides Fusarium, literature inquiry encompassed the perfect state names for Fusarium, including Calonectria, Gibberella, Nectria, and Hypomyces.

Our search indicated that some compounds were listed under more than one name; these are also reported. We were greatly aided by use of the Dictionary of the Fungi (Ainsworth 1971). As one would expect, a number of toxins were reported for which structure has not yet been determined.

GENERAL REFERENCES

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2 Brian, P. W. 1951. Antibiotics produced by fungi. Bot. Rev. 17: 357-430.

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4 Korzybski, T., Z. Kowszyk-Gindifer, and W. Kurylowicz. 1967. Antibiotics, origin, nature, and properties. Vol. II, p. 1310-1325, 1402. Pergamon Press, London.

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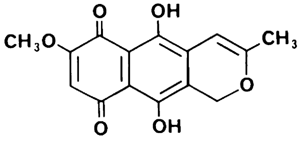
8 Shibata, S., S. Natori and S. Udagawa. 1964. List of fungal products. Charles C. Thomas, Springfield, Illinois. 170 p.

9 Turner, W. B. 1971. Fungal metabolites. Academic Press. New York. 446 p.

10 Turner, W. B. and D. C. Aldridge. 1983. Fungal metabolites II. Academic Press, New York. 631 p.

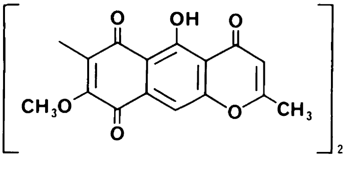
PIGMENTS (1-30)

1. ANHYDROFUSARUBIN. $C_{15}H_{12}O_6$ MW 288 m.p. 195-198 C. λ_{max} 295, ~460, 500, 535, ~585 nm. Insecticidal activity against Calliphora erythrocephala.



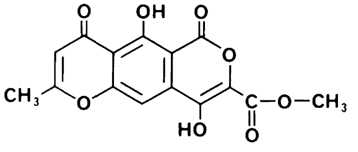
Source: Fusarium solani strain #47. Reference: [1]

2. AUROFUSARIN. $C_{30}H_{18}O_{12}$ MW 570 Yellow prisms, m.p. >320 C d. $\lambda_{max}^{dioxane}$ 243, 267, 372 nm.



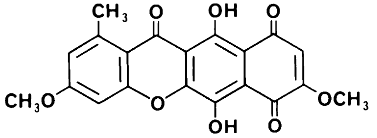
Source: Fusarium culmorum, F. graminearum CMI 89367. References: [2-5]

3. AVENACEIN Y (Antibiotic Y, Lateropyrone). $C_{15}H_{10}O_8$ MW 318 m.p. 281-282 C. UV λ_{max}^{CH3OH} 242, 265, 278, 347, 365 nm ($\varepsilon_{mol.}$ 4.23, 4.13, 4.09, 3.98, 4.02, respectively). Antibiotic properties for *Staphylococcus aureus* 209 P (MIC 0.37 and 5.45 µg/ml at pH 6.2 and 7.4, respectively). Dose levels of 0.5 to 200 µg of Avenacein Y per egg was nontoxic to chicken embryo; 3T3 mouse cells were not affected at a level of 5 µg/ml.



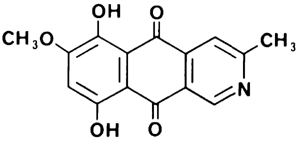
Source: *Fusarium avenaceum* (Fries) Sacc.
References: [6, 7]

4. BIKAVERIN, LYCOPERSIN, PASSIFLORIN, MYCOGONIN (10H-Benzo[b]xanthene-7,10,12-trione-6,11-dihydroxy-3,8-dimethoxy-1-methyl). $C_{20}H_{14}O_8$ MW 382 Red crystals, m.p. 322-324 C d. $\lambda_{max}^{CHCl_3}$ 254, 278, 518 nm. Vacuolation factor, aging factor; active against *Leishmania brasiliensis*, 0.15 µg/ml.



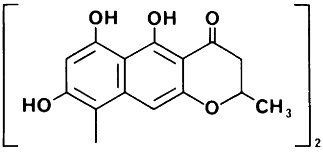
Source: *Gibberella fujikuroi* NRRL 2633, Brian 917, and *Fusarium oxysporum*.
References: [8-11]

5. BOSTRYCOIDIN. $C_{15}H_{11}NO_5$ MW 285 Red plates, m.p. 243-244 C. λ_{max}^{EtOH} 251, 320, 475, 497, 525 nm. LD_{50} mice, i.p., s.c., or per os >250 mg/kg for 2-21 days. Inhibits acid-fast, gram-positive, and gram-negative organisms.



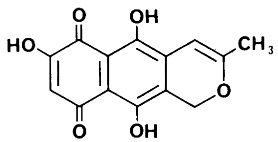
Source: *Fusarium oxysporum* (*F. bostrycoides*), *F. solani*.
References: [12-14]

6. CEPHALOCHROMIN. $C_{28}H_{22}O_{10}$ MW 518 Orange crystals, m.p. >300 C d. λ_{max} 232, 270, 295, 330, 415 nm. $[\alpha]_D$ + 523° ($CHCl_3$). Active against *Staphylococcus aureus* at a concentration of 1 ppm.



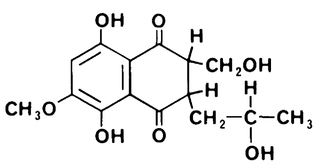
Source: *Nectria flavo-virides* (*Fusarium melanochlorum*).
Reference: [15]

7. O-DEMETHYLANHYDROFUSARUBIN. $C_{14}H_{10}O_6$ MW 274 Purple needles, m.p. 202-204 C. λ_{max}^{EtOH} 237, 285, 353, 492 sh, 546 nm.



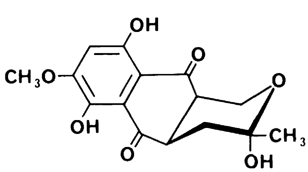
Source: Gibberella fujikuroi ACC 917. Reference: [16]

8. 2,3-DIHYDRO-5,8-DIHYDROXY-6-METHOXY-2-HYDROXYMETHOXY-3(2'-HYDROXYPROPYL)-1,4-NAPHTHALENEDIONE. $C_{15}H_{18}O_7$ MW 310
Light red crystals, m.p. 135 C.
λ_{max}^{EtOH} 213, 244, 277, 303 sh, 391, 400 sh nm ($\varepsilon_{mol.}$ 3.98, 4.21, 3.83, 3.64, 3.88, 3.83, respectively).



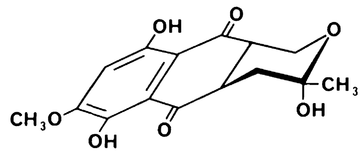
Source: Fusarium solani.
Reference: [17]

9. 4a,10a-DIHYDROFUSARUBINS [rel-(3R,4aR,10aS)-5,10-dioxo-3,4,4a,5,10,10a-hexahydro-7-methoxy-3-methyl-3,6,9-trihydroxy-1H-naphtho {2,3-c} pyran].
$C_{15}H_{16}O_7$ MW 308 m.p. 117-118 C. $[\alpha]_D^{20}$ + 23.3^o (acetone)
λ_{max}^{EtOH} 213, 243, 273, 300, 391 nm ($\varepsilon_{mol.}$ 4.15, 3.89, 3.70, 3.96, respectively).



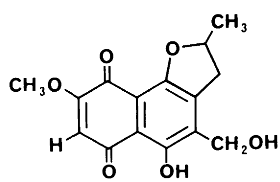
Source: Fusarium solani.
Reference: [18]

10. 4a,10a-DIHYDROFUSARUBINS [rel-(3R,4aR,10aR)-5,10-dioxo-3,4,4a,5,10,10a-hexahydro-7-methoxy-3-methyl-3,6,9-trihydroxy-1H-naphtho {2,3-c} pyran].
$C_{15}H_{16}O_7$ MW 308 m.p. 153-154 C. $[\alpha]_D^{20}$ + 145.4^o (acetone)
λ_{max}^{EtOH} 213, 243, 273, 300, 391 nm ($\varepsilon_{mol.}$ 4.17, 4.30, 3.87, 3.71, 3.94, respectively).



Source: Fusarium solani.
Reference: [18]

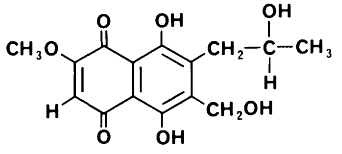
11. 2,3-DIHYDRO-5-HYDROXY-4-HYDROXY-METHYL-8-METOXYNAPHTHO [1,2-b] FURAN-6,9-DIONE. $C_{15}H_{14}O_6$
MW 290 Red crystals, m.p. 202-203 C. λ_{max}^{EtOH} 223, 297, 485, 502, 538 nm ($\varepsilon_{mol.}$ 4.06, 3.62, 3.50, 3.47, 3.17, respectively).



Source: Fusarium moniliforme.
Reference: [17]

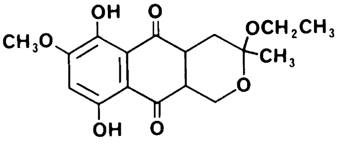
12. 5,8-DIHYDROXY-2-METHOXY-6-HYDROXYMETHYL-7-(2'-HYDROXYPROPYL)-1,4-NAPHTHALENEDIONE.
$C_{15}H_{16}O_7$ MW 308 Red crystals,

m.p. 206-212 C d. λ_{max}^{EtOH} 227, 306, 452 sh, 482, 509, 546 nm ($\varepsilon_{mol.}$ 4.38, 3.87, 3.56, 3.76, 3.80, 3.59, respectively).



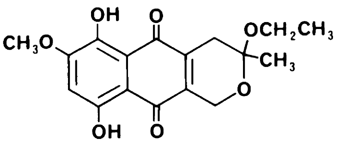
Source: Fusarium solani.
Reference: [17]

13. O-ETHYLDIHYDROFUSARUBIN. $C_{17}H_{20}O_7$ MW 336. This pigment may be a laboratory artifact.



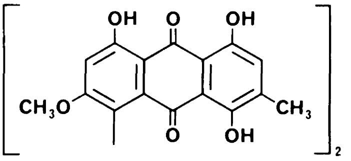
Source: Fusarium solani PP 96.
Reference: [19]

14. O-ETHYLFUSARUBIN. $C_{17}H_{18}O_7$ MW 334. This pigment may be a laboratory artifact.



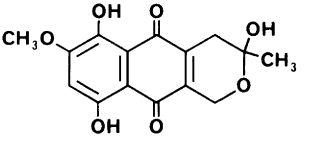
Source: Fusarium solani PP 90.
Reference: [20]

15. FUSAROSKYRIN (4,4',5,5',8,8'-Hexahydroxy-2,2'-dimethoxy-7,7'-dimethyl-1,1'-dianthraquinone). $C_{32}H_{22}O_{12}$ MW 598 Red crystals, m.p. >300 C. $\lambda_{max}^{CHCl_3}$ 256, 276, 305-310, 505 nm. Cause of "purple speck" disease of soybean.



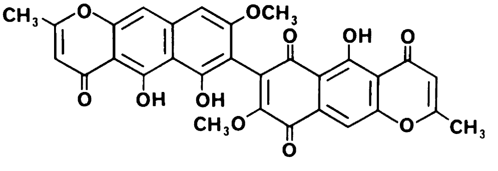
Source: Fusarium sp.
Reference: [21]

16. FUSARUBIN, OXYJAVANICIN. $C_{15}H_{14}O_7$ MW 306 Red prisms, m.p. 218 C d. $\lambda_{max}^{CHCl_3}$ 303, 505 nm. Inhibits Staphylococcus. Phytotoxic to tomato cuttings (40 µg/ml). LD_{50} Botrytis allii, 2 µg/ml. Inhibits anaerobic decarboxylation of pyruvate, 30 µg/ml; oxidative decarboxylation of α-ketoglutarate, 77 µg/ml.



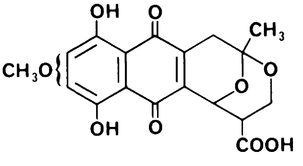
Source: Fusarium javanicum, F. solani.
References: [22, 23]

17. FUSCOFUSARIN. $C_{30}H_{20}O_{11}$ MW 556 Brown powder, m.p. >300 C. λ_{max}^{EtOH} 225, 281, 346, 405 nm.



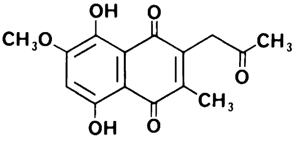
Source: *Fusarium culmorum*.
Reference: [24]

18. ISOMARTICIN. $C_{18}H_{16}O_9$ MW 376
Brown prisms, m.p. 168-169 C. $[\alpha]_D^{25}$ + 26^o ($CHCl_3$). λ_{max}^{EtOH} 227, 306, 497 nm. Phytotoxic to tomato cuttings, 8 µg/g. LD_{50} *Botrytis allii* Munn, >500 µg/ml. Inhibits *Bacillus subtilis*, 7 µg/ml. Inhibits anaerobic decarboxylation of pyruvate, 248 µg/ml; oxidative decarboxylation of α-ketoglutarate, 750 µg/ml.



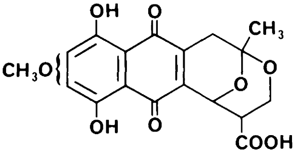
Source: *Fusarium martii* var. *pisi*. References: [23, 25]

19. JAVANICIN, SOLANIONE (5,8-Dihydroxy-6-methoxy-2-methyl-3,2'-oxo-propyl-1,4-naphthaquinone). $C_{15}H_{14}O_6$ MW 290 Red crystals, m.p. 208 C d. $\lambda_{max}^{CHCl_3}$ 307, 510 nm. Antibiotic for gram-positive and acid-fast microorganisms. LD_{50} mice, i.p. >500 mg/kg. Phytotoxic to tomato cuttings, 60 µg/ml. Inhibits anaerobic decarboxylation of pyruvate, 29 µg/ml; oxidative decarboyxlation of α-ketoglutarate, 87 µg/ml. Insecticidal activity against *Calliphora erythrocephala*.



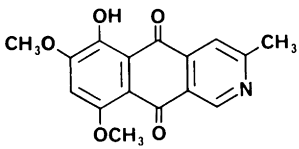
Source: *Fusarium javanicum*, *F. solani*.
References: [1, 22, 23, 26]

20. MARTICIN. $C_{18}H_{16}O_9$ MW 376
Dark red needles, m.p. 200-201 C. $[\alpha]_D^{25}$ + 132^o ($CHCl_3$). λ_{max}^{EtOH} 227, 305, 497 nm. Phytotoxic to tomato cuttings, 8 µg/g. LD_{50} *Botrytis allii* Munn, >500 µg/ml. Inhibits *Bacillus subtilis*, 7 µg/ml. Inhibits anaeorbic decarboxylation of pyruvate, 248 µg/ml; oxidative decarboxylation of α-ketoglutarate, 750 µg/ml.



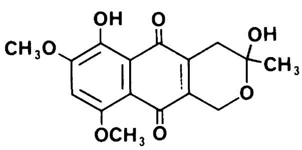
Source: *Fusarium martii* var. *pisi*.
References: [23, 25]

21. 8-O-METHYLBOSTRYCOIDIN. $C_{16}H_{13}NO_5$ MW 299 m.p. 215-216 C. λ_{max} 247.5, 318, 480 nm ($\varepsilon_{mol.}$ 4.5, 3.92, 3.83, respectively); $\lambda_{max}^{CH_3OH(H^+)}$ 227, 262, 310, 510 nm ($\varepsilon_{mol.}$ 4.32, 4.20, 3.88, 3.73, respectively); $\lambda_{max}^{CH_3OH(OH^-)}$ 259, 306, 546 nm ($\varepsilon_{mol.}$ 4.44, 3.82, 4.0, respectively).



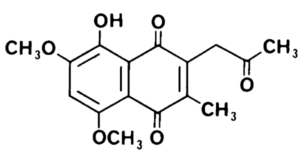
Source: *Fusarium moniliforme* MRC 602, *F. moniliforme* var. *subglutinans* MRC 604. Reference: [27]

22. 8-O-METHYLFUSARUBIN. $C_{16}H_{16}O_7$ MW 320 m.p. 138-139 C. λ_{max} 226, 282.5, 484, 510, 550 sh nm ($\varepsilon_{mol.}$ 4.48, 4.05, 3.83, 3.80, 3.49, respectively).



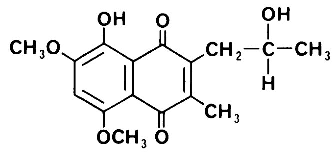
Source: *Fusarium moniliforme* MRC 602, *F. moniliforme* var. *subglutinans* MRC 604. Reference: [27]

23. 8-O-METHYLJAVANICIN. $C_{16}H_{16}O_6$ MW 304, m.p. 197-198 C. λ_{max} 226, 282.5, 482, 510, 550 sh nm ($\varepsilon_{mol.}$ 4.56, 4.04, 3.80, 3.75, 3.80, respectively).



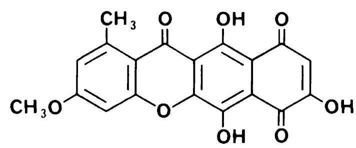
Source: *Fusarium moniliforme* MRC 602. Reference: [27]

24. 8-O-METHYLSOLANIOL. $C_{16}H_{18}O_6$ MW 306 m.p. 152-154 C. λ_{max} 226, 285, 476, 510 sh nm ($\varepsilon_{mol.}$ 4.49, 4.025, 3.82, 3.69, respectively).



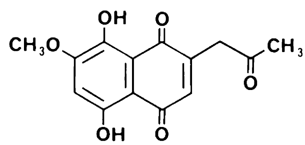
Source: *Fusarium moniliforme* MRC 602. Reference: [27]

25. NORBIKAVERIN. $C_{19}H_{12}O_8$ MW 368 m.p. >350 C d. $\lambda_{max}^{CHCl_3}$ 253, 273, 320, 515, 550 nm.



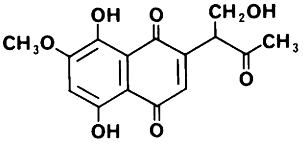
Source: *Gibberella fujikuroi* ACC 917. Reference: [11]

26. NORJAVANICIN (5,8-Dihydroxy-6-methoxy-3-2'-oxopropyl-1,4-naphthaquinone). $C_{14}H_{12}O_6$ MW 276 Red needles, m.p. 200-204 C. Phytotoxic to tomato cuttings, 90 µg/ml. LD_{50}, *Botrytis allii* Munn, 10 µg/ml. Inhibits *Bacillus subtilis*, 1 µg/ml. Inhibits anaerobic decarboxylation of pyruvate, 3 µg/ml; oxidative decarboxylation of α-ketoglutarate, 31 µg/ml.



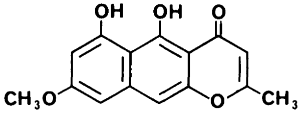
Source: *Fusarium martii* var. *pisi* M 808, *F. solani* M 898. References: [23, 28]

27. NOVARUBIN. $C_{15}H_{14}O_7$ MW 306
Red crystals, m.p. 162 C. Phytotoxic to tomato cuttings, 35 µg/ml. LD_{50} Botrytis allii Munn, 5 µg/ml. Inhibits Bacillus subtilis, 0.5 µg/ml. Inhibits anaerobic decarboxylation of pyruvate 4 µg/ml; oxidative decarboxylation of α-ketoglutarate, 31 µg/ml.



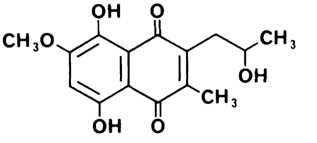
Source: Fusarium martii var. pisi M 808, F. solani M 898.
Reference: [23]

28. RUBROFUSARIN (5,6-Dihydroxy-8-methoxy-2-methyl-benzochromen-4-one). $C_{15}H_{12}O_5$ MW 272
Orange-red needles, m.p. 210-211 C. λ_{max}^{EtOH} 225.5, 278, 327, 344, 410 nm.



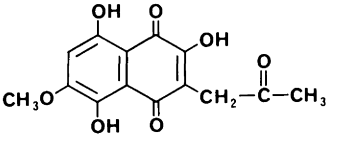
Source: Fusarium culmorum, F. graminearum, Gibberella zeae.
References: [2, 29-33]

29. SOLANIOL (5,8-Dihydroxy-3-(2'-hydroxypropyl)-6-methoxy-2-methyl-1,4-naphthaquinone). $C_{15}H_{16}O_6$
MW 292 Dark red needles, m.p. 190-194 C d. $[\alpha]_D^{25}$ + 122° (CH_3OH). $\lambda_{max}^{dioxane}$ 227, 304, 472, 500, 556 nm.



Source: Fusarium solani.
Reference: [34]

30. 2,5,8-TRIHYDROXY-6-METHOXY-3-(2'-OXO-PROPYL)-1,4-NAPHTHAQUINONE. $C_{14}H_{12}O_7$ MW 292 Red crystals, m.p. 231-234 C. λ_{max}^{EtOH} 212, 238, 261, 320, 470, 490, 520 nm ($\varepsilon_{mol.}$ 4.22, 4.14, 4.07, 3.88, 3.84, 3.82, 3.66, respectively).



Source: Fusarium solani.
Reference: [35]

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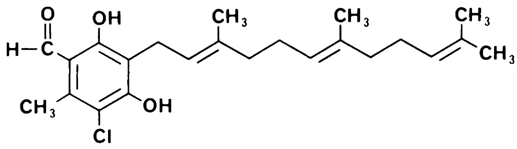
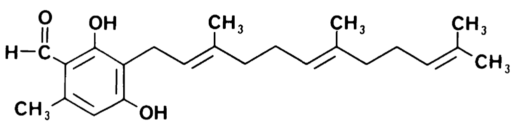
ANTIBIOTICS (1-16)

1. ANTIBIOTIC LL-Z1272 α.
$C_{23}H_{31}O_3Cl$ MW 390 m.p. 72.5-73 C. λ_{max} 228, 293, 345 nm. Anti-Tetrahymena pyriformis activity.



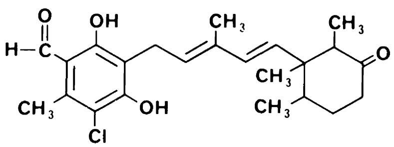
Source: Fusarium sp.
Reference: [1]

2. ANTIBIOTIC LL-Z1272 β.
$C_{23}H_{32}O_3$ MW 356 m.p. 97.5 C. λ_{max} 223, 233 sh, 297, 340 nm.



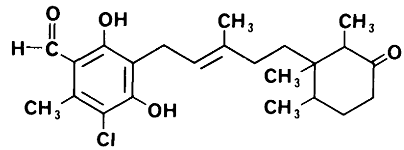
Source: Fusarium sp.
Reference: [1]

3. ANTIBIOTIC LL-Z1272 γ ASCOCHLORIN.
$C_{23}H_{29}O_4Cl$ MW 404 m.p. 172-173 C. $[\alpha]_D^{25}$ -31° (CH_3OH). λ_{max} 230, 293, 347 nm. Anti-Tetrahymena pyriformis activity.



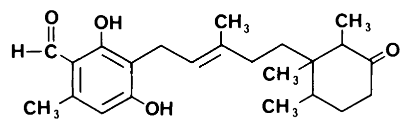
Source: Fusarium sp.
Reference: [1]

4. ANTIBIOTIC LL-Z1272 δ.
$C_{23}H_{31}O_4Cl$ MW 406 m.p. 129.5-130.5 C. $[\alpha]_D^{25}$ + 6° (CH_3OH). λ_{max} 231, 293, 346 nm. Anti-Tetrahymena pyriformis activity.



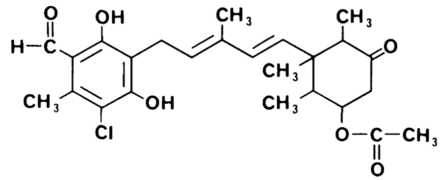
Source: Fusarium sp.
Reference: [1]

5. ANTIBIOTIC LL-Z1272 ε.
$C_{23}H_{32}O_4$ MW 372 m.p. 171.5-172.5 C. $[\alpha]_D^{25}$ + 6° (CH_3OH). λ_{max} 223, 233 sh, 295, 340 sh nm. Anti-Tetrahymena pyriformis activity.



Source: Fusarium sp.
Reference: [1]

6. ANTIBIOTIC LL-Z1272 ζ.
$C_{25}H_{31}O_6Cl$ MW 462, m.p. 156.5-157 C. $[\alpha]_D^{25}$ -15° (CH_3OH). λ_{max} 239, 293, 347 nm. Anti-Tetrahymena pyriformis activity.

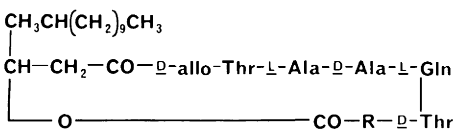


Source: Fusarium sp.
Reference: [1]

7. CYCLODEPSIPEPTIDE COMPLEX (CDPC).

R	%	MW	Formula
1-leucine	62.37	887	$C_{45}H_{73}N_7O_{11}$
Isoleucine	30.69	887	$C_{45}H_{73}N_7O_{11}$
Valine	6.93	873	$C_{44}H_{71}N_7O_{11}$

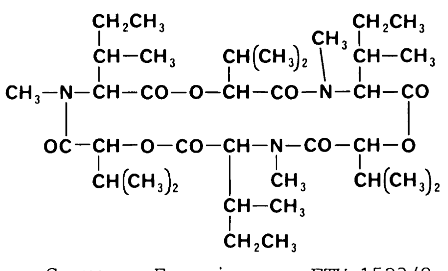
m.p. 206-208 C (for CDPC). CDPC inhibits germination of Penicillium digitatum conidia with swelling of conidia up to 10 diameters more than conidia incubated in a control media.



Source: Fusarium roseum NRRL 6227 F. tricinctum NRRL 3510.
References: [2, 3]

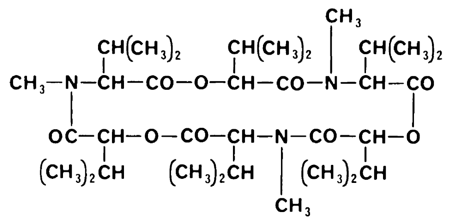
8. ENNIATIN A, LATERITIIN I.
$C_{36}H_{63}N_3O_9$ MW 681 m.p. 122 C. $[\alpha]_D^{18}$ -91.9^o ($CHCl_3$).

Active against gram-positive, gram-negative and acid-fast bacteria. Inhibits phytopathogenic fungi.



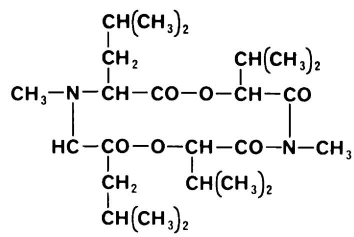
Source: Fusarium sp. ETH 1523/8.
References: [4,5]

9. ENNIATIN B, LATERITIIN II.
$C_{33}H_{57}N_3O_9$ MW 639 m.p. 174-176 C. $[\alpha]_D^{21}$ -108^o ($CHCl_3$).
Inhibits Mycobacterium phlei, 3 µg/ml; Mycobacterium paratuberculosis, 5 µg/ml. Activity against bacteria and phytopathogenic fungi weaker than Enniatin A.



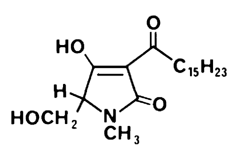
Source: Fusarium sp. ETH 4363 and ETH 1574. References: [5-7]

10. ENNIATIN C. $C_{24}H_{42}N_2O_6$ MW 454
m.p. 123 C. $[\alpha]_D^{22}$ -83^o ($CHCl_3$).



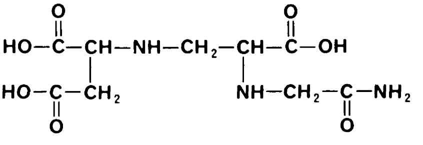
Source: Fusarium sp.
Reference: [8]

11. EQUISETIN, N-METHYLTETRAMIC ACID.
$C_{22}H_{31}NO_4$ MW 373 m.p. 65 C.
λ_{max}^{EtOH} 235, 250, 292 nm. Active against gram-positive, and acid-fast bacteria and Neisseria perflava. Lethal dose to mice, i.p., 63 mg/kg.



Source: *Fusarium equiseti* NRRL 5537. References: [9, 15]

12. LYCOMARASMIN. $C_9H_{15}N_3O_7$ MW 277 m.p. 227-229 C d. $[\alpha]_D^{20}$ -42^o to -48^o (H_2O, pH 7). Inhibits *Lactobacillus casei*. Tomato wilting toxin.



Source: *Fusarium lycopersici*. References: [10-13]

13. PHYTOTOXINS (Dehydrofusaric acid, Fusaric acid).

14. PIGMENTS (Avenacein Y, Bikaverin, Bostrycoidin, Cephalchromin, Fusarubin, Isomarticin, Javanicin, Marticin, Novarubin, Norjavanicin, Oxyjavanicin).

15. RAMIHYPHINS. MW 1192 Daltons, White amorphous compound. $\lambda_{max}^{CH_3OH}$ 210 nm. Active against pathogenic and saprophytic fungi. Stimulates branching of hyphae at subfungistatic concentrations.

STRUCTURE UNKNOWN

Source: *Fusarium* sp. S-435. Reference: [14]

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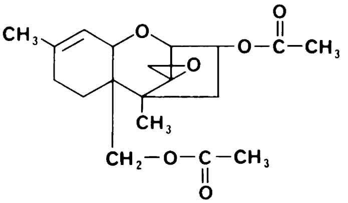
TRICHOTHECENES (1-48)

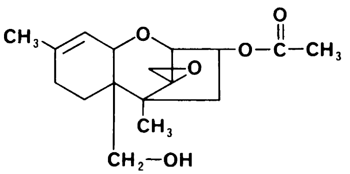
Calonectrin Derivatives (1-5)

1. CALONECTRIN (3α,15-Diacetoxy-12,13-epoxytrichothec-9-ene). $C_{19}H_{26}O_6$ MW 350 Prisms, m.p. 83-85 C. $[\alpha]_D^{27}$ + 14.6° ($CHCl_3$).



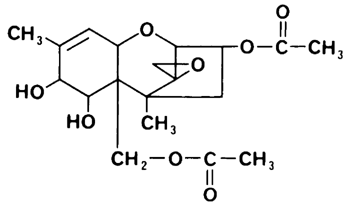
Source: Calonectria nivalis, Fusarium nivale CMI 14764 is F. culmorum (reference 42, page 7).
Reference: [1]

2. DEACETYLCALONECTRIN (3α-Acetoxy-15-hydroxy-12,13-epoxytrichothec-9-ene). $C_{17}H_{24}O_5$ MW 308 Prisms, m.p. 184-186 C. $[\alpha]_D^{27}$ + 11.2° ($CHCl_3$).



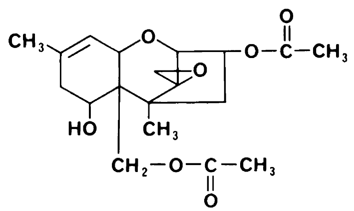
Source: Calonectria nivalis, Fusarium nivale CMI 14764 is F. culmorum (reference 42, page 7), F. roseum ATCC 28114.
References: [1, 3]

3. 7α,8α-DIHYDROXYCALONECTRIN (3α,15-Diacetoxy-7α,8α-dihydroxy-12,13-trichothec-9-ene). $C_{19}H_{26}O_8$ MW 382 m.p. 190.5-191.5 C. $[\alpha]_D^{26.8}$ + 7.13°.



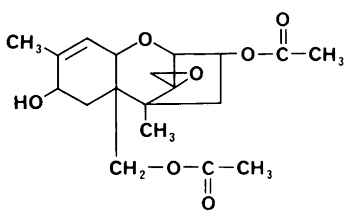
Source: Fusarium roseum ATCC 28114.
Reference: [2]

4. 7-HYDROXYCALONECTRIN. $C_{19}H_{26}O_7$ MW 366 m.p. 174-175 C. $[\alpha]_D^{23.2}$ -14.3°.



Source: Fusarium roseum ATCC 28114.
Reference: [3]

5. 8-HYDROXYCALONECTRIN. $C_{19}H_{26}O_7$ MW 366 m.p. 168-170 C. $[\alpha]_D^{21.3}$ -6.67°.



Source: Fusarium roseum ATCC 28114.
Reference: [3]