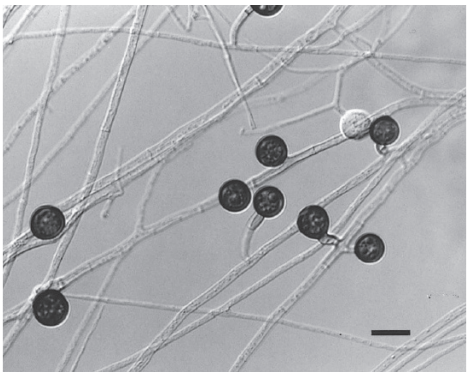
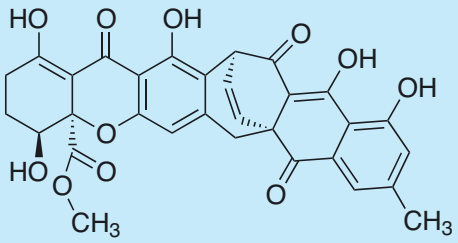
Xanthoquinodin

1. Discovery, producing organism and structures[1-4)]

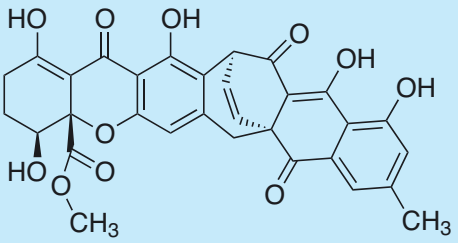
Xanthoquinodins were isolated from the culture broth of *Humicola* fungal strain FO-888 and recognized by a cell-based assay as anticoccidial agents.



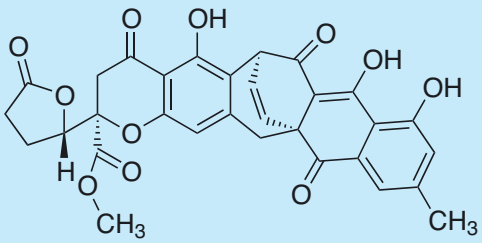
Humicola sp. FO-888
Bar: 20 μm



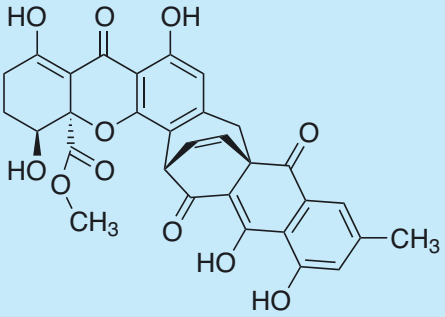
Xanthoquinodin A1



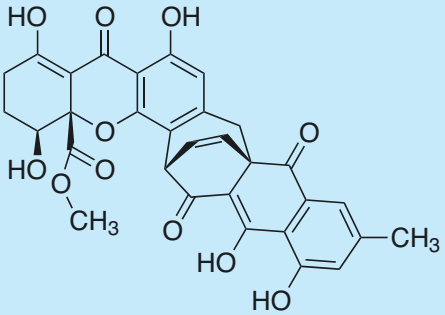
Xanthoquinodin A2



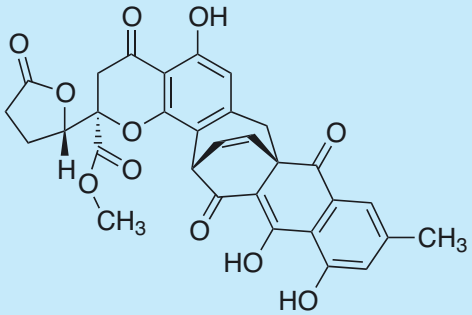
Xanthoquinodin A3



Xanthoquinodin B1



Xanthoquinodin B2



Xanthoquinodin B2

2. Physical data (Xanthoquinodin A1)[1)]
Yellow powder; $C_{31}H_{24}O_{11}$; MW 572.13; Sol. in MeOH, $CHCl_3$. Insol. in H_2O.

3. Biological activity[1,4,7)]
1) Anticoccidial activity[1,4)]
An *in vitro* assay system was established using BHK-21 cells as a host and monensin-resistant *Eimeria tenella* as a parasitic protozoan.

Compound	Minimum effective concentration (μM)		Specificity
	Anticoccidial activity (A)*	Cytotoxicity (C)**	C/A
Xanthoquinodin A1	0.035	3.50	100
Xanthoquinodin A2	0.035	0.35	10
Xanthoquinodin A3	0.035	3.5 0	100
Xanthoquinodin B1	0.035	3.50	100
Xanthoquinodin B2	0.035	3.50	100
Xanthoquinodin B3	0.035	3.50	100

* No mature shizonts were observed in the cells at the indicated drug concentration or higher.
** No BHK-21 cells were observed at the indicated drug concentration or higher.

2) Antimicrobial activity[1,4)]
Xanthoquinodin A1 showed antimicrobial activity against *Bacillus subtilis, Micrococcus luteus, Staphylococcus aureus, Acholoplasma laidlawli* and *Bacteroides fragilis* at 1 mg/ml using the paper disc method.

3) *In vivo* anticoccidial activity xanthoquinodin A1 was evaluated in an assay of monensin-resistant *E. tenella* from chicks.[1,4)]

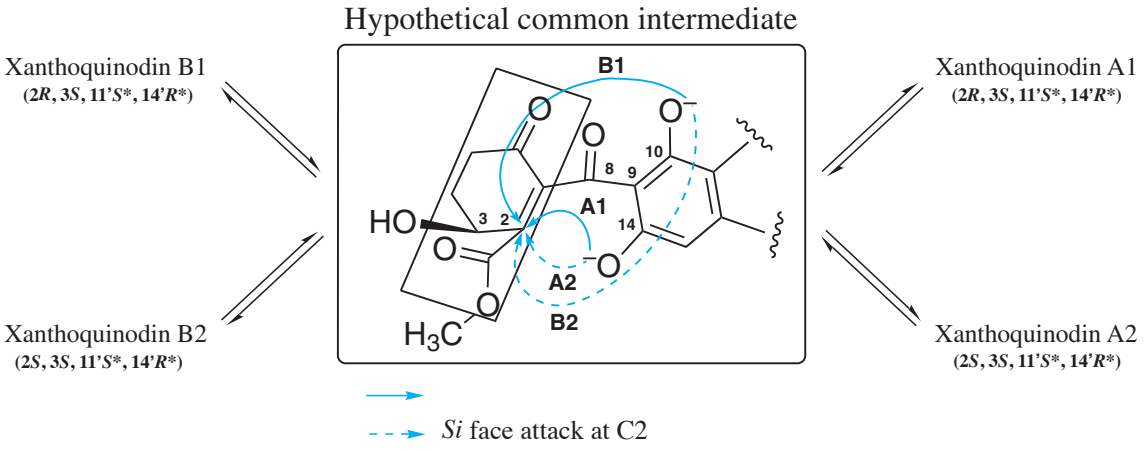
Treatment	A Mortality (%)	B Weight gain (%)	C Cecal lesion score	D Oocyst score	ACI*
Uninfected, unmedicated	0	100.0	0	0	—
Infected, unmedicated	20	64.5	40	40	—
Xanthoquinodin A1, 25.0 ppm	0	64.5	0	0	164.5
Monensin, 80.0 ppm	0	71.9	34	10	127.9

*ACI = 100 - A + B - C - D

4) Cytotoxic activity[7)]
The cytotoxic acticvity of xanthoquinodins A1, A2 and A3 was tested against HL-60, SMMC-7721, A-549, MCF-7, and SW480 human cancer cell lines.

Human cancer cell lines	cytotoxicity IC_{50} (μM)				
	HL-60	SMMC-7721	A-549	MCF-7	SW480
xanthoquinodins A1	6.22	8.00	3.33	14.16	28.82
A2	5.50	6.77	4.04	20.80	>40
A3	4.18	16.73	15.27	7.47	15.49
cisplatin	1.86	6.13	7.27	15.27	16.23
paclitaxel	<0.008	<0.008	<0.008	<0.008	<0.008

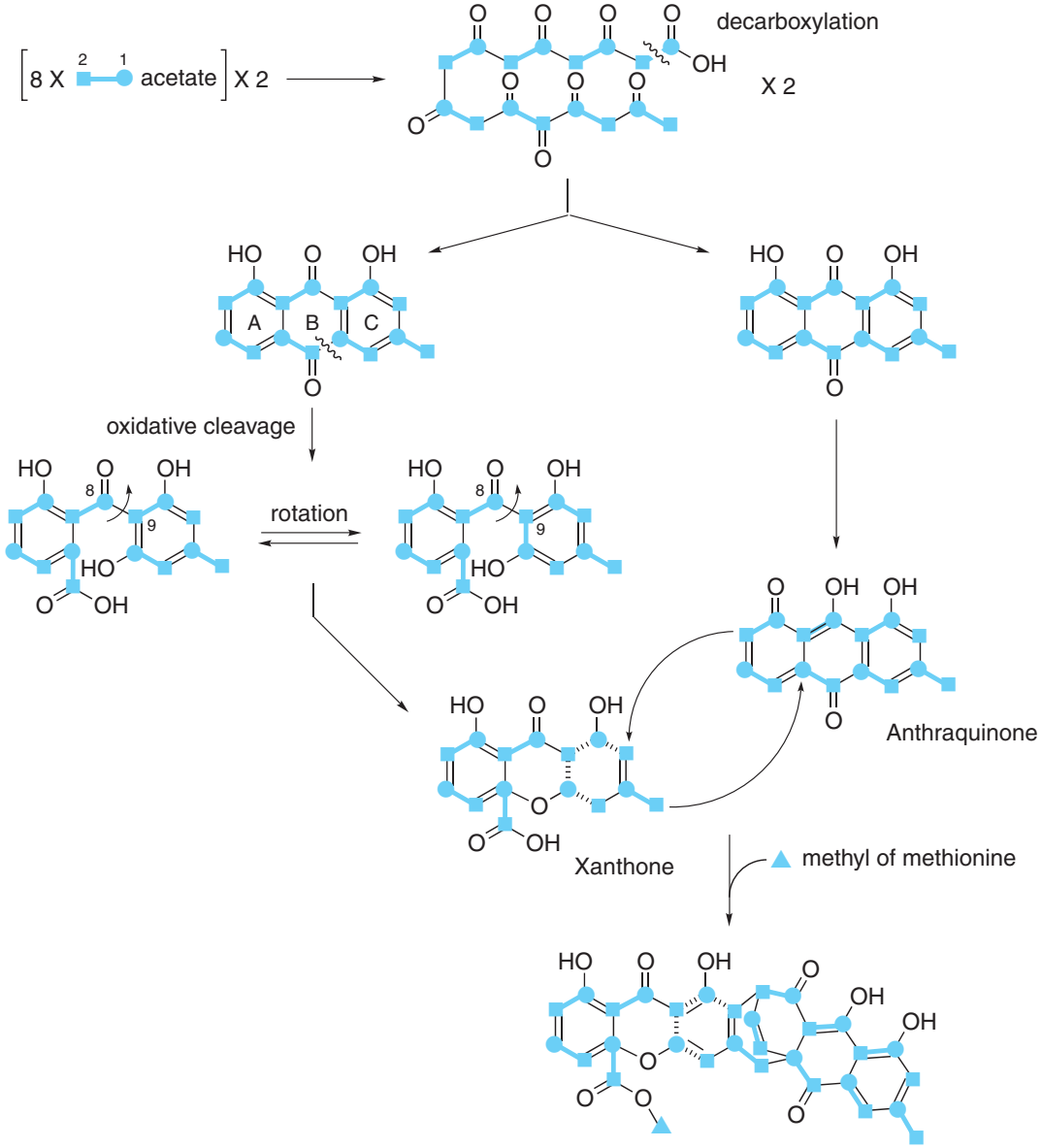
4. Stereochemistry[3)]



5. Biosynthesis[3)]

Xanthoquinodins are the first heterodimers in which octaketide-derived xanthone and anthraquinone monomers are connected in an "end-to-body" fashion.

In structurally related fungal toxins, beticolins[5)] and cebetins[6)], the anthraquinone and xanthone moieties are linked in an "end-to-end" fashion.



6. References

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