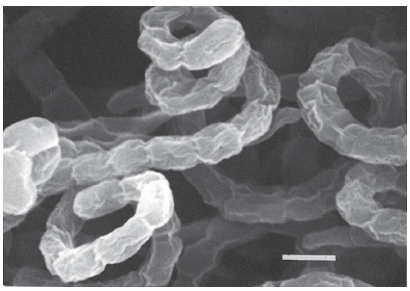
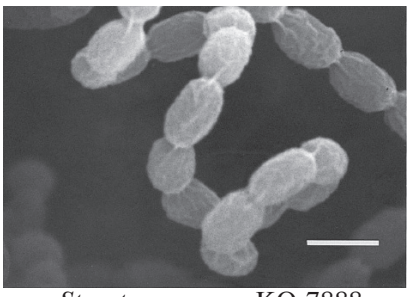
Phthoxazolin

1. Discovery, producing organisms and structures[1-7)]

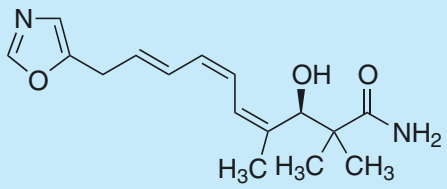
Phthoxazolin A was isolated from the culture broth of the actinomycete strain OM-5714 while screening for cellulose biosynthesis inhibitors. Phthoxazolins B, C, and D were isolated from the culture broth of the actinomycete strain KO-7888 while screening for triene compounds. Inthomycin A and CL22T were later reported to have the same structure as phthoxazolin A[6,7)]. The total synthesis of phthoxazolin was reported by Whiting *et al*.[8)] (See Appendix-I).



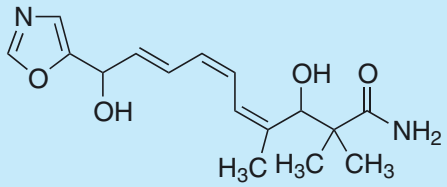
Streptomyces sp. OM-5714



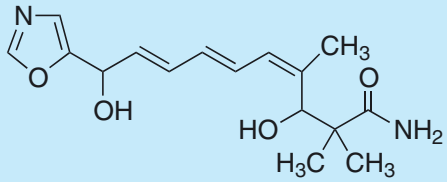
Streptomyces sp. KO-7888



Phthoxazolin A



Phthoxazolins B & C
(Phthoxazolins B and C are diastereomers)



Phthoxazolin D

2. Physical data (Phthoxazolin A)

Pale yellow powder. $C_{16}H_{22}N_2O_3$; mol wt 290.37. Sol. in DMSO, MeOH, $CHCl_3$. Insol. in H_2O, hexane.

3. Biological activity[1,2,9,10)]

1) Phthoxazolins are active against a strain of phytopathogenic fungi, *Phytophthora* sp., but are inactive against other bacteria and fungi tested. Phthoxazolin A is a potent herbicide, and inhibits its cellulose synthesis in cell-free and resting cell systems.[1,2)]

Cellulose synthase inhibition and herbicidal activity of phthoxazolin A

Compound	Amount μg/ml (mM)*	Anti-*Phytophthora* activity (inhibition zone, mm)	Growth inhibition of radish seedlings (%)	Inhibition (%) of cellulose biosynthesis in *Acetobacter xylinum*	
				Resting cell system	Cell-free system
Phthoxazolin A	100 (0.34)	31	100	47	69
	10 (0.03)	11	30	30	27

* to be read as μg per tube for herbicidal activity

3) Other biological activities[9,10)]
Phthoxazolin A inhibited prostate cancer growth.

4. Production by phosphate ion-depressed fermentation[2)]
Phthoxazolin A is produced under phosphate ion-depressed fermentation conditions. [Refer to "Development of ammonium ion- and phosphate ion-depressed fermentations" (p. 413)].

Phthoxazolin A production in media with and without added allophane

Production medium	Phthoxazolin A (μg/ml) None	+ Allophane (0.5%)
A	<5	95
B	<5	79
C	<5	90

Medium A: Soluble starch 2.0%, glycerol 0.5%, wheat germ 1.0%, meat extract 0.3%, dry yeast 0.3%, and $CaCO_3$ 0.3%; pH 7.5.
Medium B: Lactose 1.0%, glycerol 0.5%, pectin 0.5%, NZ-amine 0.5%, dry yeast 1.0%, and $CaCO_3$ 0.3%; pH 6.7.
Medium C: Starch 2.4%, glucose 0.1%, peptone 0.3%, meat extract 0.3%, yeast extract 0.5%, $CaCO_3$ 0.4%, and trace salt solution 0.5% (v/v); pH 7.0. The trace salt solution contains (each at 1 g/L): $FeSO_4 \cdot 7H_2O$, $MnCl_2 \cdot 4H_2O$, $ZnSO_4 \cdot 7H_2O$, $CuSO_4 \cdot 5H_2O$, and $CoCl_2 \cdot 6H_2O$; pH 6.7.

5. References

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