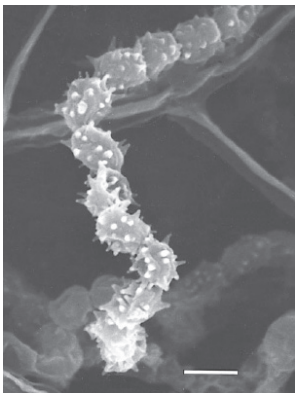
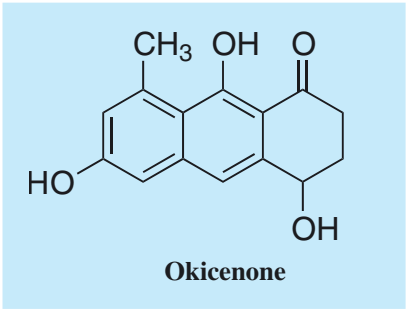
Okicenone

1. Discovery, producing organism and structure[1,2)]

Okicenone isolated from the culture broth of an actinomycete strain KO-3599, was found to be a growth inhibitor of mammalian tumor cells *in vitro*. The total synthesis of okicenone has been reported by Snider *et al*.[3)] (See Appendix-I).



Streptomyces sp. KO-3599



Okicenone

2. Physical data[1)]

Pale yellow needles. $C_{15}H_{14}O_4$; mol wt 258.09. Sol. in EtOAc, MeOH, $CHCl_3$. Insol. in H_2O.

3. Biological activity[1)]

1) Cytotoxicities of okicenone against tumor cells

Cell line	IC_{50} (μM)
HeLa S_3	2.05
B16 melanoma	2.56
P388 leukemia	11.2
P388/ADM^R	42.6
H69 human lung carcinoma	> 48.4

2) Antimicrobial spectrum

Okicenone showed no antimicrobial activity at a concentration of 1 mg/ml when tested against; *Xanthomonas oryzae* KB 88, *Candida albicans* KF 1, *Saccharomyces sake* KF 26, *Mucor racemosus* IFO 4581, *Pyricularia oryzae* KF 180, *Aspergillus niger* ATCC 6275, *Staphylococcus aureus* FDA 209P, *Bacillus subtilis* PCI 219, *Escherichia coli* NIHJ, *E. coli* NIHJ JC-2, *Pseudomonas aeruginosa* P3, *Micrococcus luteus* PCI 1001, *Bacteroides fragilis* KB 169, *Mycobacterium smegmatis* ATCC 607 and *Acholeplasma laidlawii* PG 8.

3) Inhibit Hu protein R activity[4)]

Okicenone inhibits Hu protein R (HuR) with nanomolar affinity. The mRNA-binding Huproteins are important for stabilization of short-lived (A+U)-rich element (ARE)-controlled mRNAs. Okicenone interferes with HuR RNA binding trafficking, cytokine expression and T-cell activation.

4. References

1. [468] K. Komiyama *et al., J. Antibiot.* **44**, 814-818 (1991)
2. [469] S. Funayama *et al., J. Antibiot.* **44**, 819-823 (1991)
3. B. -B. Snider *et al., J. Org. Chem.* **58**, 3185-3187 (1993)
4. M. Auer *et al., Nat. Chembiol.* **3**, 508-515 (2007)