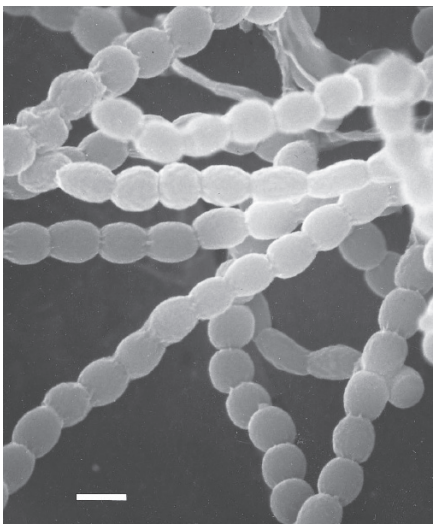
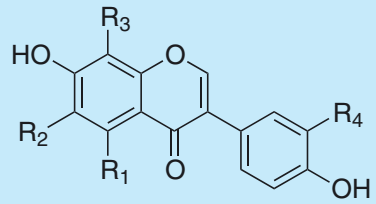
Isoflavone

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

Isoflavones were isolated from the culture broth of the actinomycete strain OH-1049 and recognized as antioxidant substances.



Streptomyces sp. OH-1049



Isoflavones

4',7,8-Trihydroxyisoflavone (1)

$R_1 = R_2 = R_4 = H$, $R_3 = OH$

3',4',7-Trihydroxyisoflavone (2)

$R_1 = R_2 = R_3 = H$, $R_4 = OH$

8-Chloro-3',4',5,7-tetrahydroxyisoflavone (3)

$R_1 = R_4 = OH$, $R_2 = H$, $R_3 = Cl$

2. Physical data (4',7,8-Trihydroxyisoflavone)[1)]

Colorless powder. $C_{15}H_{10}O_5$; mol wt 270.05. Sol. in MeOH.

3. Biological activity[1,3)]

A microsomal fraction of rat liver was incubated with NADPH, doxorubicin, and the sample solution. The lipid peroxide level was compared with the control. Antioxidant activity is shown as the inhibition percent of malondialdehyde generation[1,3)].

1) Antioxidant activity

Isoflavone	Inhibition %			
	Dose (mg/Kg) 20	4	0.8	0.16
1	100	100	100	40
2	100	100	70	41
3	100	100	80	32
4*	100	100	90	70
5**	77	20	6	6
α-Tocopherol	100	100	31	34

*: 4',6,7-Trihydroxyisoflavone, **: Daidzein.

2) Cytocidal activity against HeLa S3 cells[1)]

Isoflavone	IC_{50} (μg/ml)
1	12.5
2	6.3
3	25.0
4*	12.5
5**	3.2

*: 4',6,7-Trihydroxyisoflavone, **: Daidzein.

3) Antitumor activity of 4',7,8-trihydroxyisoflavone (**1**) *in vivo*[2)]

Tumor	Inoculum size and mice	Dose (mg/kg/day)	MSD	ILS (%)
IMC carcinoma	1x106 cells/CDF1		14.7	0
		25	17.7	20
		100	20.0	36
Sarcoma180	1x106 cells/ICR		11.0	0
		25	14.7	33
		100	26.3	139
P388 leukemia	1x105 cells/CDF1		9.0	0
		25	9.6	7
		100	10.0	11
P388/ADM leukemia	1x105 cells/CDF1		9.5	0
		25	10.0	5
		100	10.0	5

Samples were administered i.p. and tumor cells were maintained in acidic form by serial i.p. passaging in mice.

4) Effects of additives on the inhibitory activity of 4',7,8-Trihydroxyisoflavone against Helicobacter pylori urease[4)]

Compound	Additives	IC_{50}(mM)
4',7,8-Trihydroxyisoflavone	None	0.14
	+2-Mercaptoethanol	>1.48
	+Dithiothreitol	>1.48
Acetohydroxamic acid	None	0.017
	+2-Mercaptoethanol	0.019
	+Dithiothreitol	0.018

5) Isoflavones inhibit angiogenesis in the chicken chorioallantoic membrane. Densitomeric evaluation of blood vessel surfaces revealed in vivo antiangiogenic effects. Compared with negative controls that slightly inhibited in *vivo* angiogenesis by 6.30%, 4',7,8-Trihydroxy-isoflavone reduced angiogenesis by 24.42%.[5)]

4. References

1. [424] K. Komiyama *et al., J. Antibiot.* **42**, 1344-1349 (1989)
2. [425] S. Funayama *et al., J. Antibiot.* **42**, 1350-1355 (1989)
3. M. Uchiyama *et al., Anal. Biochem.* **86**, 271-278 (1978)
4. H. –L. Zhu *et al. Bioorg. Med. Chem.* **15**, 3703-3710 (2007)
5. N. Uchiyama *et al., British Journal of Nutrition* **93**. 317-323 (2005)