ANTITUMOR ACTIVITY OF KIJANIMICIN

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Kijanimicin is a novel tetronic acid structure[1,2] produced by *Actinomadura kijaniata* sp. nov.[3,4]. It has been reported to be inhibitory to Gram-positive bacteria and rodent malaria[4]. We have tested kijanimicin for antitumor effects in transplanted animal tumor systems.

The procedures used for *in vivo* mouse tumor inhibition tests generally followed the protocols established by the National Cancer Institute[5]. Kijanimicin, which is water soluble, was dissolved in saline and injected intraperitoneally into tumor bearing mice according to the schedules shown on the accompanying tables.

Table 1. Effect of kijanimicin on P-388 lymphatic leukemia.

Treatment schedule	Dose, i.p. (mg/kg/inj.)	Effect MST (% T/C)	Average weight change (g) Day 5
QD 1 → 9	64	150	−1.9
	32	156	−1.0
	16	139	−0.6
	8	111	−0.8
	4	111	−0.3
	2	106	−0.7
Day 1, 5 & 9	64	139	−1.5
	32	117	−1.1
	16	111	−1.0
	8	100	−0.3
	4	100	−1.0
	2	100	−0.4
Day 1	128	133	−1.8
	64	111	−1.5
	32	117	−1.4
	16	111	−0.8
	8	106	−1.3
	4	100	−0.8

Tumor inoculum: 10^6 ascites cells implanted i.p.
Host : CDF_1 ♀ mice.
Evaluation : MST=median survival time.
Effect : % T/C=(MST treated/MST control)×100.
Criteria : % T/C≥125 considered significant antitumor activity.

Table 2. Effect of kijanimicin on B16 melanoma.

Dose, i.p. (mg/kg/inj.)	Effect MST (% T/C)	Average weight change (g) Day 5
64	139	−1.5
32	130	−1.2
16	117	−0.8
8	117	−0.8
4	109	+0.2
2	100	+0.3

Tumor inoculum: 0.5 ml of a 10% brei, i.p.
Treatment : Once daily for nine injections.
Host : BDF_1 ♀ mice.
Evaluation : MST=median survival time.
Effect : % T/C=(MST treated/MST control)×100.
Criteria : % T/C≥125 considered significant antitumor activity.

The results of a test in which kijanimicin was administered on three different dose schedules to mice bearing P-388 leukemia are shown in Table 1. The maximum survival increase, T/C=156, was observed at 32 mg/kg/day on a daily ×9 schedule. Using the same schedule, slight inhibition of B16 melanoma was also seen, Table 2.

Two other antibiotics which may be related to kijanimicin, antlermicin[6,7] and the tetracarcins[8,9], have also been reported to inhibit tumor growth.

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