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Rifampicin Induced Chromatid Exchanges in Mouse Bone Marrow Cells

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ABSTRACT Mice were injected i.p. with Single dose of 0.5, 2.5, 5 mg/kg body of weight of rifampicin. Cells were sampled for mitotic chromosome analysis 4, 16 and 24 h after treatment. The maximal yield of chromosome type aberrations induced was found 24 h after treatment. More than 60% of the cells carried at least one chromatid exchange. The majority of these were exchanges derived from breaks in the centromeric heterochromatin.

Rifampicin is an antibiotic which inhibits INA dependent RNA synthesis *in-vivo* in prokaryotes but non in eukaryotic origin. Hence the effects of rifampicin have been studied mainly in lower organisms. At higher concentrations, the drug inhibits RNA chain elongation, as well as, initiation, although at lower concentration only the chain initiation step is inhibited (Nakamura and Yura, 1976). Rifampicin forms a complex with β sub unit of the enzyme (Zilling et al., 1970) thereby blocking RNA chain initiation (Sippel and Hartman, 1968). Although some biochemical effects of this drug have been studied, the cytological and crytoplasmic effects of this drug, especially eukaryotic systems, have not yet been elucidated. The present investigation deals with the effects of rifampicin in mouse bone marrow cells.

MATERIAL AND METHODS

As many as three sets each containing three mice were injected intraperitoneally with rifampicin (disloved in distilled water) at 0.5, 2.5 and 5 mg/kg body weight. The first set of mice was sacrificed after 4 h, the second set after 16 h and third set after 24 h. The mice received an injection of colchicine 4 mg/kg three hours before sacrificing. Control mice received distilled water colchicine injections. The bone marrow suspension was collected and hypotonic treatment and cell swelling were done in usual way (Ghosh and Ghosh, 1969). Slides were prepared by air drying technique and stained with giemsa. Microscopic analysis was carried for each concentration and time duration and 150 metaphases were observed for treated groups and 300 for control animals. The mitoses were analysed for chromatid type aberrations such as gaps, breaks and exchanges. The selection was based on uniform staining quality, lack of overlapping chromosomes and chromosome number (40 + 2).

RESULTS

Different types of aberrations induced by rifampicin have been presented in table 1. Cells with only gaps were significantly more frequent in the experimental groups than in control groups. Cells with only breaks were not frequent. The majority of the effected cells contained chromatid exchanges. Presence of translocations and ring chromosomes are also a notable feature. The lowest dose yielded a maximum number of exchanges 16 h after treatment. Whereas the maximum number for highest dose occured at 24 h.

DISCUSSION

In eukaryotic systems cytological and cytogenetic effects of different antibiotic type have been studied, but they produce different types of aberrations and the reaction mechanisms are also different. Nogalomycin inter-

Table 1 : Frequencies of different types of chromatid aberrations induced by Rifampicin in mouse bone marrow cells

Dose mg/kg	*Time (h)*	*Number of animals*	*Total no. of of cells observed*	*Number of cells with gaps*	*Number of cells with breaks*	*Number of cells with exchanges*	*Percentage of exchanges*
0.5	4	3	150	8	1	1	0.67
	16	3	150	5	1	20	11.00
	24	3	150	2	1	13	9.00
Control		3	300	1	1	2	0.01
2.5	4	3	150	6	0	2	0.36
	16	3	150	4	2	50	31.00
	24	3	150	5	2	55	35.00
Control		3	300	1	0	2	0.01
5.0	4	3	150	0	2	3	1.33
	16	3	150	6	1	62	44.00
	24	3	150	3	2	75	55.00
Control		3	300	1	0	0	0.00

feres with DNA directed RNA synthesis by bindng to the DNA primer of eukaryotes (Bhuyan and Smith, 1965). But mitomycin-c inhibits DNA synthesis by directly acting upon the DNA and producing compementary strands of the double helix (Iyer and Szybalsi, 1963). Like nogalomycine DNA directed RNA polymerase ativity is inhibited by rifampicin but only in prokaryotic systems (Nakamura and Yura, 1976). The present study shows a positive chromosome breaking effect of the drug in mouse bone marrow chromosomes. Rifampicin induced symmetrical and asymmetrical exchanges of chromatids. The positive correlation with respect to dose and durations confirm the clastogenicity of the drug. From the appearance of the exchanges it can be concluded that the breakage leading to those exchanges occur in the centromeric heterochromatin (Vadhuri et al., 1984).

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