

followed by  $-18^{\circ}\text{C}$  (93.8%) and  $4^{\circ}\text{C}$  (88.9%). Among the different groups tested, *Vibrio*, *Pseudomonas* and *Acinetobacter*, were isolated at all the three temperatures and they constituted the major flora. Of them *Vibrio* was not influenced by the variation in storage temperature and all the strains were TMAO reducers. *Pseudomonas* and *Acinetobacter* were influenced by the change in the storage temperature. *Acinetobacter* recorded decrease in the percentage of TMAO reducers along with decrease in temperature (table 1). *Pseudomonas* recorded a higher percentage of TMAO reducers at  $-18^{\circ}\text{C}$  (93.6%) than at  $4^{\circ}\text{C}$  (83.3%), although it formed the dominant flora during storage at  $4^{\circ}\text{C}$ .

TMAO reduction to TMA by *Vibrio*<sup>8,9</sup>, *Pseudomonas*<sup>10,11</sup> and members of Enterobacteriaceae<sup>8</sup> is known. TMAO reduction by species of *Alcaligenes*, *Micrococcus*, *Bacillus* and *Corynebacterium* is not reported earlier. Occurrence of these groups in *P. indicus* during storage and their ability to reduce TMAO to TMA suggest that they are the potential spoilers of prawn, as TMAO-TMA reduction is considered one among the reliable test for detecting and characterizing spoilage bacteria<sup>10</sup>. The presence of higher percentage of *Vibrio*, *Pseudomonas* and *Acinetobacter* in prawns during storage at various temperatures and the presence of the maximum percentage of TMAO-TMA reducers in these groups, suggest their dominant role in the rapid deterioration of prawns, and increase in the TMA content during storage.

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## ACTION OF HALOPERIDOL ON MEIOTIC CHROMOSOMES OF MALE MICE

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IN view of the emphasis on evaluation of cytogenetic effects of all new and established drugs, the authors had studied the effects of Haloperidol, an extensively used antipsychotic and anxiolytic agent, on somatic chromosomes of mice and reported a negative clastogenic and mitoclastic property<sup>1</sup>. Further, observations on meiotic chromosomes which are regarded as a test of the potential mutagenicity of chemicals in mammals<sup>2</sup> yield additional information. Hence investigations on these lines have been carried out to study the effects of Haloperidol and the results are reported in this paper.

Haloperidol (Serenace) was administered orally at doses of 0.312, 0.624 and 1.248  $\mu\text{g}$  in 0.5 ml of sterile distilled water to Swiss albino male mice belonging to 8–10 week age group and weighing 25 g on an average. Single and cumulative series have been employed; in the latter, the same doses of the drug were fed consecutively for 15 days at 24 hr intervals<sup>1</sup>. The doses computed on body weight basis correspond to human therapeutic levels. Animals belonging to control group were fed with an equal volume of distilled water and processed simultaneously. Animals were sacrificed after 24 hr and at weekly intervals upto the fifth week in single dose series, and after the same periods in cumulative treatments following last day of drug administration. Testes were processed by the standard air-drying technique for obtaining meiotic chromosome preparations and stained with Giemsa. One

hundred well-spread diakinesis-metaphase I stages of meiosis per dose per period were analysed in either series. Results have been statistically evaluated<sup>3</sup>.

Table I furnishes the quantitative details on various types of aberrations recorded in control and treated animals belonging to the two series. The percentage of gaps, breaks/fragments and multivalent associations (translocations) observed in the treated animals are very low and statistically nonsignificant. These indicate a non-clastogenic nature of the drug. Polyploids

(tetraploids) were noted at all treatment periods in both series and none of them is statistically significant. Frequencies of polyploids are known to vary and may occur to a maximum of 6% even in untreated animals<sup>4,5</sup>. Occurrence of these at diakinesis-metaphase I is regarded as an artifact due to fusion of two adjoining cells during preparation<sup>4</sup> or may be due to irregular segregation of spermatogonia and/or nuclear fusion of two or more primary spermatocytes<sup>5</sup>. In the present study polyploids do not exceed

Table I Chromosomal aberrations induced by Haloperidol in meiotic cells of male mice

Period and dose ( $\mu$ g)	Percentage of cells with												
	Structural aberrations								Univalents				
	Gaps		Breaks/fragments		Multi-valents		Poly-ploids		Sex chromosomal		Auto somal		
	SD	CD	SD	CD	SD	CD	SD	CD	SD	CD	SD	CD	
24 hr.													
Control	0	0	0	0	0	0	0	0	0	3	0	1	1
0.312	0	0	0	1	1	0	1	0	9	8*	3	2	
0.624	0	0	1	1	0	0	2	3	4	7*	5	4	
1.248	0	0	0	1	0	0	2	0	5	5*	2	2	
I week													
Control	0	0	0	0	0	0	0	0	1	2	3	1	
0.312	0	1	1	0	0	0	2	1	6	7	5	4	
0.624	0	0	0	1	0	0	1	0	7*	8	2	3	
1.248	0	0	0	1	0	0	0	0	18*	8	3	7*	
II week													
Control	0	0	0	0	0	0	0	0	4	6	1	1	
0.312	0	0	0	0	0	0	0	0	9	9	2	3	
0.624	0	0	0	2	0	0	1	3	3	8	0	2	
1.248	0	0	0	0	0	0	1	1	8	2	2	2	
III week													
Control	0	0	0	0	0	0	0	0	3	4	1	0	
0.312	0	1	1	0	0	0	3	1	8	5	1	0	
0.624	0	0	1	2	1	0	0	1	10	7	3	4*	
1.248	0	0	2	1	0	0	0	2	8	16*	4	2	
IV week													
Control	0	0	0	0	0	0	0	0	2	3	1	1	
0.312	0	1	0	1	0	0	1	1	3	3	2	3	
0.624	1	0	0	0	0	0	0	1	7	3	3	0	
1.248	0	0	0	0	0	0	0	0	9*	8	2	1	
V week													
Control	0	0	0	0	0	0	0	0	3	2	2	0	
0.312	0	0	0	1	0	1	0	1	12*	8	0	3	
0.624	0	1	1	0	0	0	1	1	9	6	2	5*	
1.248	0	0	0	0	0	0	1	1	9	8	2	5*	
Overall percentages													
Control	0	0	0	0	0	0	0	0	2.66	2.84	1.50	0.66	
Treated	0.06	0.22	0.39	0.66	0.11	0.06	0.88	0.94	8.00	7.00	2.39	2.89	

\* Significant at 5% level. SD: Single dose series; CD: Cumulative dose series.



3% and this suggests a negative mitoclastic activity of Haloperidol.

A significant feature was the elevated frequencies of behavioural aberrations<sup>5</sup> viz sex chromosomal and autosomal univalents following drug treatment, with a preponderance of the former. Lack of homologous segments and binding forces of chiasmata<sup>6</sup> may lead to an easy dissociation of the bivalent. Hence higher values of XY univalents are not surprising. Among the autosomal univalents the smallest pair was more often involved than others. The mechanism of induction of univalents and their consequences have been amply discussed and illustrated<sup>2,5,7-13</sup>. Spontaneous levels of these are known to be very high and vary widely<sup>5,8-10</sup>. Hence, the significance of induced univalency should be assessed by comparing them with the respective controls. Viewed from this angle XY and autosomal univalents induced by Haloperidol are significant only for some doses and periods, in either series. Besides these cells with more than one pair of univalents were also noted. The behavioural aberrations appear to be insignificant if a random or chance segregation leads to a normal distribution of univalents during metaphase, leading to the production of normal gametes. However, the possibility of its irregular distribution cannot be ruled out. The abnormalities have to be reckoned with as having some consequence and significance, if sex chromosomes are involved. In general presence of abnormalities till the fifth week in single dose series indicates that the drug or its metabolite/s may affect the various stages of spermatogenesis. Moreover the drug is known to be found in small quantities for several weeks following administration<sup>14</sup>. Overall percentages of aberrations induced by haloperidol show only marginal variation between single and cumulative treatments for any specific type of aberration.

Negative findings with haloperidol with respect to clastogenic and mitoclastic activity indicates non-hazardous nature of the drug at therapeutic levels. These observations made on germ cells corroborate the earlier report on somatic chromosomes of mouse<sup>1</sup>.

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#### DOSE RESPONSE RELATIONSHIPS FOR CHROMOSOME ABERRATIONS IN PERIPHERAL BLOOD LYMPHOCYTES AFTER CYTOSTATICS *IN VITRO*

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VINBLASTINE sulphate, an antineoplastic agent is often used in combination with other drugs in the treatment of Hodgkin's disease and a wide variety of carcinomas<sup>1-4</sup>. In the present investigation, an attempt