EFFECT OF BRUFEN AN ANTI-INFLAMMATORY DRUG ON MICE SPERMATOCYTES

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ALONG with increase in population there is also an increase in the incidence of several human diseases. In the process of curing them there appears to be almost an indiscriminate use of drugs. Although the body can eliminate many of the drugs taken some may cause other deleterious effects. Evaluation of mutagenic potential of various drugs is regarded as of cardinal importance to reduce the genotoxicity and genetic load in man.

The common non-steroidal anti-inflammatory drugs which are in the medical practice are, tromaril, phenylbutazone, brufen and indomethacin. There is little or no information available about their mutagenic potential. Therefore, in the present study one of the non-steroidal anti-inflammatory drugs namely brufen (2-(4 iso butyphenyl) propionic acid) was studied for its mutagenic potential in terms of chromosomal aberrations in mouse spermatocytes. Meiotic chromosomes were scored for each type of aberrations at 7, 15 and 30 days of treatment to examine the effect on early and late spermatogenic cycle.

Mice (5–6 weeks old) were grouped into 6 animals in each group. Each group was orally administered with 210, 420 and 630 mg of brufen/kg body weight which corresponded to the 1/4, 1/2 and 3/4 of LD50, for the time indicated above. The metaphase chromosomes of the spermatocytes of the testicular cells were prepared[1–3] and 500–600 meiotic metaphases per group were scored for numerical and structural aberrations as described earlier[4, 5]. Statistical analysis was carried out using χ^2 test.

Analysis of meiotic metaphases gives a direct morphological evidence of genetic alterations in the cells. Results obtained are presented in table 1. The total percentages of anomalies after 7 days of treatment were 14.14, 19.55 and 22.56 for 210, 420 and 630 mg respectively, which were significantly higher than the control value of 10.35%. In regard to the individual aberrations euploids, aneuploids and univalents (*xy* and autosomal) were significantly elevated at 420 and 630 mg/kg body wt. At 210 mg dose none of the individual aberrations was significant.

Administration of the drug for 15 days resulted in a statistically significant increase of total aberrations with a frequency of 16.0%, 20.9% and 23.4% with the above 3 doses, as compared to the control value of 12.1%. As observed in 7-day treatment euploids, aneuploids and univalents were significant at the two higher doses only. The dose of 210 mg of brufen was administered for 30 days as the other two higher doses were found to be lethal or toxic when administered for longer periods. The incidence of total aberrations was 27.69% which was significant of over 13.62% as compared to control frequency. As observed in 7- and

Table 1 *Frequency of chromosomal aberrations in spermatocytes of mice administered with brufen*

Duration of treatment	Dose mg/kg body wt.	Total meta-phases	Normal II		Abnormal II		Eupolidy		Aneuploidy		Univalency		Translocations	
			No	%	No	%	No	%	No	%	No	%	No	%
7 days	0	570	511	89.6	59	10.3	21	3.6	14	2.4	24	4.2	0	0
	210	622	534	85.8	88	14.1*	29	4.6	22	3.5	37	5.9	0	0
	420	670	539	80.4	131	19.5**	44	6.5*	36	5.3**	49	7.3**	2	0.30
	630	585	453	77.4	132	22.5**	50	8.5**	35	5.9	47	8.0**	0	0
15 days	0	562	494	87.9	68	12.1	24	4.2	12	2.1	32	5.6	0	0
	210	575	483	84.0	92	16.0*	34	5.9	20	3.4	37	6.4	1	0.17
	420	564	446	79.0	118	20.9**	46	8.1*	29	5.1**	43	7.6	0	0
	630	558	438	76.5	131	23.4**	45	8.0**	34	6.0**	52	9.3**	0	0
30 days	0	580	501	86.3	79	13.6	25	4.3	18	3.1	36	6.2	0	0
	210	603	436	72.3	167	27.6*	51	8.4**	29	4.8**	85	14.1**	2	0.32

Note:– 1. Aneuploidy included hypoploidy (16 II, 17 II, 18 II and 19 II) and hyper diploidy (21 II, 22 II, 23 II).
2. Euploidy included 40 II, 60 II, 80 II and 100 II.
3. Univalencies included autosomal and Sex (X, Y) Chromosomes
4. Translocations included rings and chains.
5. * Significant at 5% level; ** Significant at 1% level.

15-day treatment individual chromosomal aberrations were highly significant.

Translocations were observed only in few of the drug-treated groups at frequencies which were insignificant and no translocations were observed in control animals. In control animals, total anomalies increased from 10.35% to 13.11% from 7 to 30 days. The anomalies exhibited in control animals were not due to the inoculation of drug but were thought to be spontaneous in origin[4-6]. The increase in the anomalies from 7 to 30 days could be attributed to the ageing of the animals[6].

The mechanism of production of the above anomalies is thought to be due to irregular cell divisions, nuclear fusion disturbance in mitotic spindle formation, selective or complete endo reduplication, lysis of certain chromosomes, asynapsis, desynapsis, structural rearrangements and deletions[7, 8]. It is not understood as to how brufen induces chromosome anomalies.

Analyses of the data showed that an increase in the concentration of the drug and duration of the treatment enhanced the incidence of chromosome aberrations. Thus it may be concluded that administration of brufen induced chromosome anomalies in spermatocytes of mice at higher doses.

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PSEUDO-NEOPLASTIC CONDITION "HAMARTOMA" IN *SYNODUS INDICUS*

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A PSEUDONEOPLASTIC condition known as "hamartoma" was reported for the first time in the lizard fish *Synodus indicus* (Class: Osteichthys; Order: Myctophiformes: Family: Synodontidae) from Indian waters.

During our investigation on the diseases of fishes of Porto Novo coast, 1653 fish belonging to 35 different species were autopsied for disease diagnosis. Incidentally, a peculiar disease manifestation was observed only in one out of 132 fish examined which belonged to the species *Synodus indicus*. The fish was caught from the nearshore waters of the Bay of Bengal at Porto Novo (Lat. 11°29′N; Long. 79°46′E) during March 1983. Apparently, the fish appeared healthy without any external sign of the disease, but when autopsied, a prominent pathological condition was observed. Gross pathological examination showed an abnormal growth of flattened tongue-shaped (approximately 1 cm × 2 cm) growth attached to the inside of the ventral body wall just posterior to the gill arch (figure 1).

The lesion was dissected and fixed in 10% neutral formalin embedded in paraffin wax, sectioned at 7 μ thickness and stained with haematoxylin and eosin. Histopathological examination was made by Dr John C. Harshbarger, Director, Registry of Tumour in Lower animals (RTLA), U.S.A., who diagnosed it as "hamartoma" and the material was evaluated and accessioned as RTLA 3299 of National Museum of Natural History, U.S.A.

According to the 26th edition of Dorlands's as well as Stedman's (24th edition) medical dictionaries, the diagnostic term "hamartoma" means a benign tumour-like nodule composed of an outgrowth of mature cells and tissues that normally occur in the affected part, but often with one element predominating and are not likely to result in compression of adjacent tissue (in contrast to neoplastic tissue). Pathological examination of the lesion in *Synodus indicus* revealed that the lesion consisted of skeletal muscles oriented as rows of muscle bundles separated by connective tissue fasciae. The muscle fibres were striated and appeared normal. In most places, the muscle bundles had an orderly appearance (figure 2).