

RESULTS

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Various chromosomal aberrations are observed in the bone marrow of rats treated with the following non-steroidal anti-inflammatory drugs : indocid, voltaren, curazolidine and profenid. Both numerical and structural types are identified and quantitated relative to non treated control.

Structural aberrations :

Include chromatid gap (Fig. 5), break (Fig. 6), deletion (Fig 7a,b) ring (Fig. 8) and chromatid fragmentation (Fig. 9).

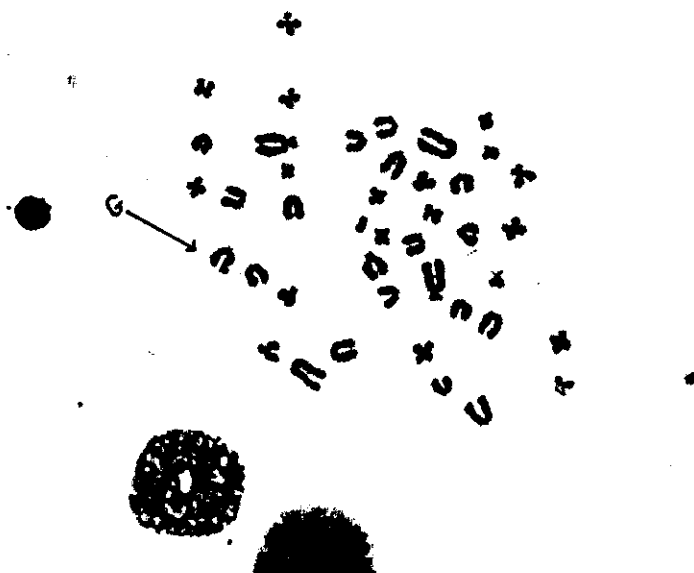


Fig. (5): Metaphase spread showing chromatid gap in bone marrow of rat treated with non steroidal anti-inflammatory drugs.

(Giemsa stain X 1000)



Fig. (6): Metaphase spread showing chromatid break in bone marrow cells of rat treated with non-steroidal anti-inflammatory drugs.

(Giemsa stain X 1000)

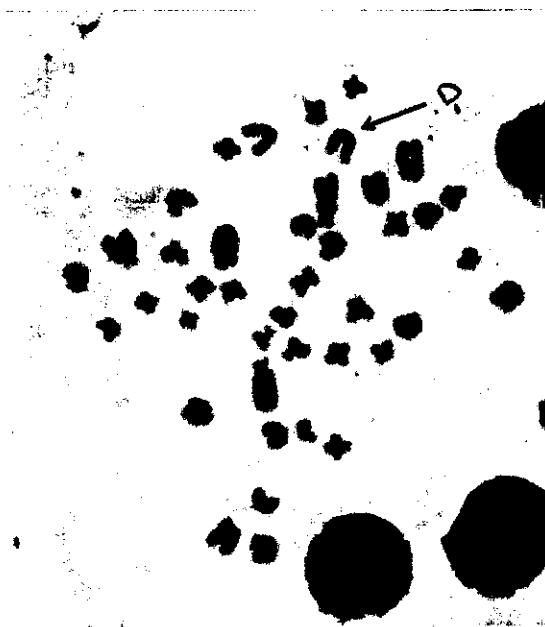


Fig. (7) : Metaphase spread showing deletion in bone marrow cells treated with non steroidal anti-inflammatory drugs.

(Giemsa stain X 1000)



Fig. (8): Metaphase spread showing a ring in bone marrow cells of rat treated with non steroidal anti-inflammatory drugs.

(Giemsa stain X 1000)

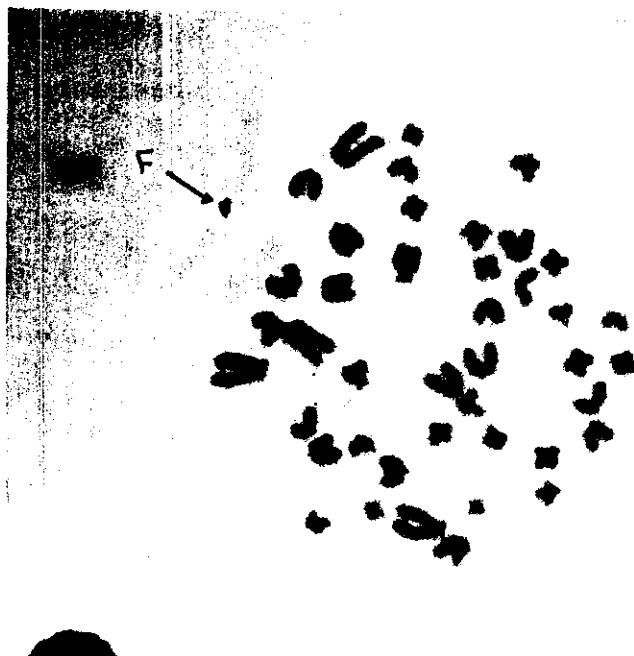


Fig. (9): Metaphase spread of rats showing a fragment in bone marrow treated with non steroidal anti-inflammatory drugs.

(Giemsa stain X 1000)

Generally the data for breaks, fragments and deletion were combined. This is possible because the phenomena are related.

Numerical aberrations :

The stickiness is considered as a sort of chromosomal "agglutination" of unknown nature which resulted in a pycnotic or sticky appearance of chromosomes. Stickiness may give rise to sticky adhesions between two or more chromosomes and to formation of "sticky bridges" at anaphase. Numerical aberrations usually arise, when the chromosomes or chromatids associated in such adhesions move to opposite spindle pole (Fig. 10).



Fig. (10): Metaphase spread of rats showing sticky chromosome in bone marrow cells treated with non-steroidal anti-inflammatory drugs.
(Giemsa stain X 1000)

curazolidine (4.8 ± 0.663) and profeind (15.6 ± 3.234) is higher than the corresponding control (1.4 ± 0.245).

In female rats, however, the difference is significantly higher than control (2.2 ± 0.374). The mean number of chromosomes showing gaps was evident on treatment with indocid (8.2 ± 1.8), voltaren (7.75 ± 1.108), curazolidine (7.6 ± 1.208) and profeind (14.6 ± 5.525).

Combining the values for both sexes, however, indicated that the mean number of chromosomes with gaps is higher than control with all drugs used.

A-II Chromatid break :

Table (2) and Fig. (12, 13) show the break and deletion combined together. In this table the mean value in 50 metaphase spreads is highly significant when the

values obtained from males and females are combined together, in all treated rats compared with control group. Separate values for male and female treated groups are also statistically significant from that of control group.

A-3 Chromosomal ring :

Table (3) and Fig. (14) show the chromatid ring in cells from the bone marrow of rats treated with the four non steroidal anti-inflammatory drugs. The mean value of ring chromosome in 50 metaphase spreads is significantly higher for both male and female in all treated rats than control. Also, the mean value for male or female is higher than that of control in indocid, voltaren, profenid and male treated by curazolidine but not significant in case of female treated with the drug.

Mitotic index :

Table (4) and Fig. (15) show the mitotic index (number of dividing cells per 1000) of bone marrow of laboratory rats under the effect of four non-steroidal anti-inflammatory drugs. It shows statistically non significant increase in the mean value of treated animals than the control.

Table (1) : Number of bone marrow cells per 50 metaphase nuclei with chromatid gaps. From rats treated⁽¹⁾ with anti-inflammatory drugs.

Treatment		Rat Number					Mean $\pm$ S.E.	Level of significance (P <)(3)
		1	2	3	4	5		
Control	M	1	2	1	2	1	1.4 $\pm$ 0.245	
							1.8 $\pm$ 0.249 ⁽²⁾	
	F	3	3	2	2	1	2.2 $\pm$ 0.374	
Indocid	M	4	6	13	10	4	7.4 $\pm$ 1.778	.01
							7.8 $\pm$ 1.200	.005
	F	4	6	6	12	13	8.2 $\pm$ 1.800	.01
Voltaren	M	6	5	6	5	4	5.2 $\pm$ 0.374	.005
							5.7 $\pm$ 0.869	.005
	F	7	6	7	11	0	7.75 $\pm$ 1.108	.005
Curazolidine	M	7	5	5	4	3	4.8 $\pm$ 0.663	0.005
							6.2 $\pm$ 0.799	.005
	F	11	9	6	8	4	7.6 $\pm$ 1.208	.005
Profenid	M	13	20	10	9	26	15.6 $\pm$ 3.234	.005
							14.2 $\pm$ 2.471	.005
	F	3	8	9	25	19	14.6 $\pm$ 5.525	.01

M = Male

F = Female

- (1) Each drug was administered for 32 days as described in material and methods.
 (2) The intermediate value represents the mean for both sexes.
 (3) Using student (t) test.

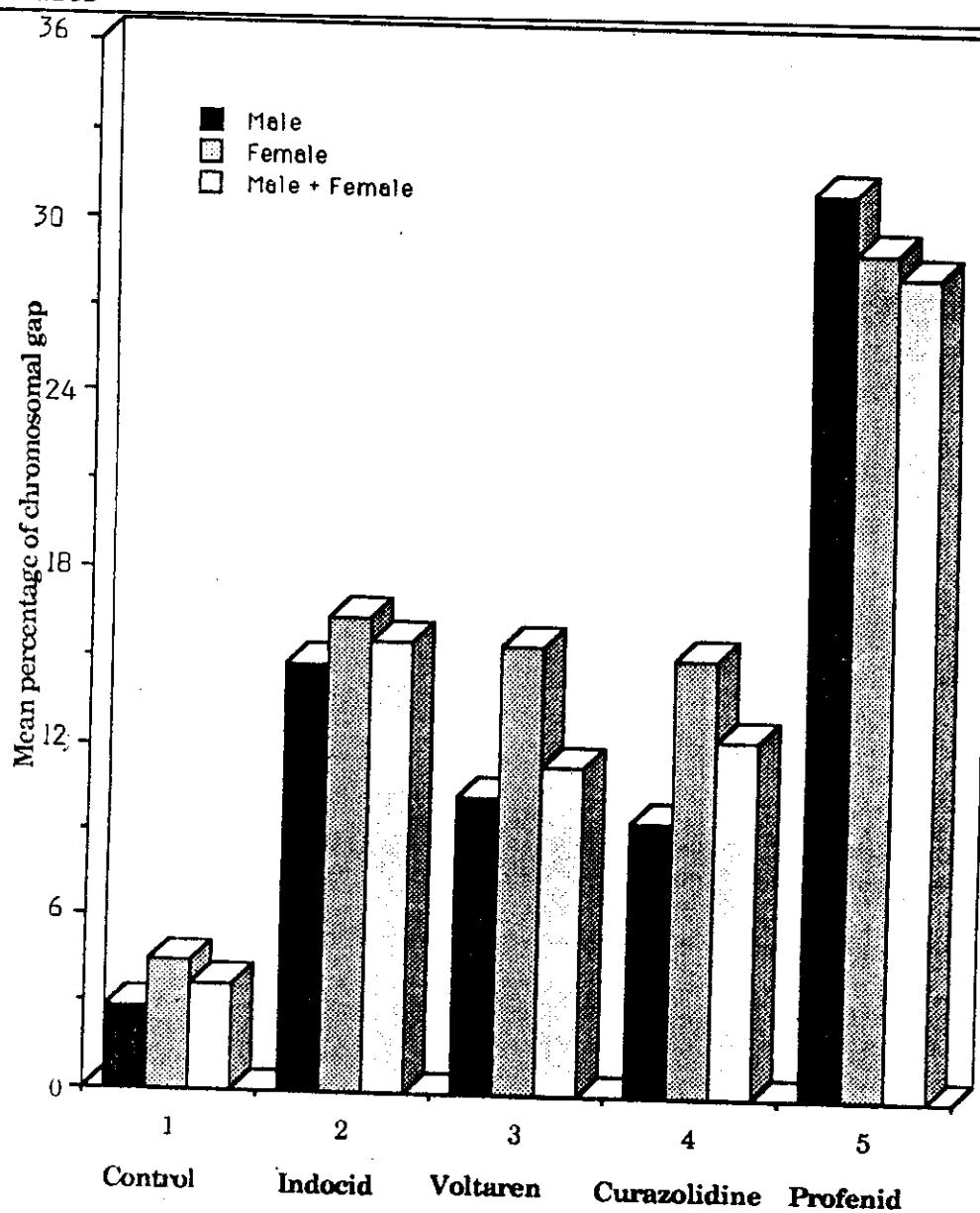


Fig. (11) Mean percentage of chromosomal gap observed in rat bone marrow after treatment with nonsteroidal anti-inflammatory drugs

Table (2) : Number of bone marrow cells per 50 metaphase nuclei having breaks and deletions From rats treated⁽¹⁾ with anti-inflammatory drugs.

Treatment		Break					Deletion					Mean of Total ± S.E.	Level of Signi- ficance (P <) (3)	
		1	2	3	4	5	1	2	3	4	5			
Control	M	1	0	2	0	1	8	1	2	2	7	4.8	± 1.59	
												5.3	± 1.897	(2)
	F	0	0	0	0	1	7	4	7	1	9	5.8	± 1.529	
Indocid	M	1	1	5	0	1	17	10	18	17	15	17	± 1.923	.005
												18.6	± 5.185	.05
	F	1	6	1	0	1	14	28	13	22	15	20.2	± 3.72	.01
Voltaren	M	0	5	0	4	6	16	22	24	23	24	24.8	± 2.395	.005
												25.4	± 6.936	.01
	F	0	3	0	2	6	20	22	27	25	25	26	± 1.788	.005
Curazolidine	M	0	4	0	2	3	18	14	15	8	9	14.6	± 1.599	.005
												15.2	± 4.218	.05
	F	2	4	0	1	5	9	23	7	8	22	16.2	± 4.454	.05
Profenid	M	2	7	3	2	2	28	33	34	24	41	35.2	± 3.152	.005
												37.2	± 10.365	.005
	F	4	8	3	1	3	26	35	31	42	43	39.2	± 3.056	.005

M = Male

F = Female

- (1) Each drug was administered for 32 days as described in material and methods.
 (2) The intermediate value represents the mean for both sexes.
 (3) Using student (t) test.

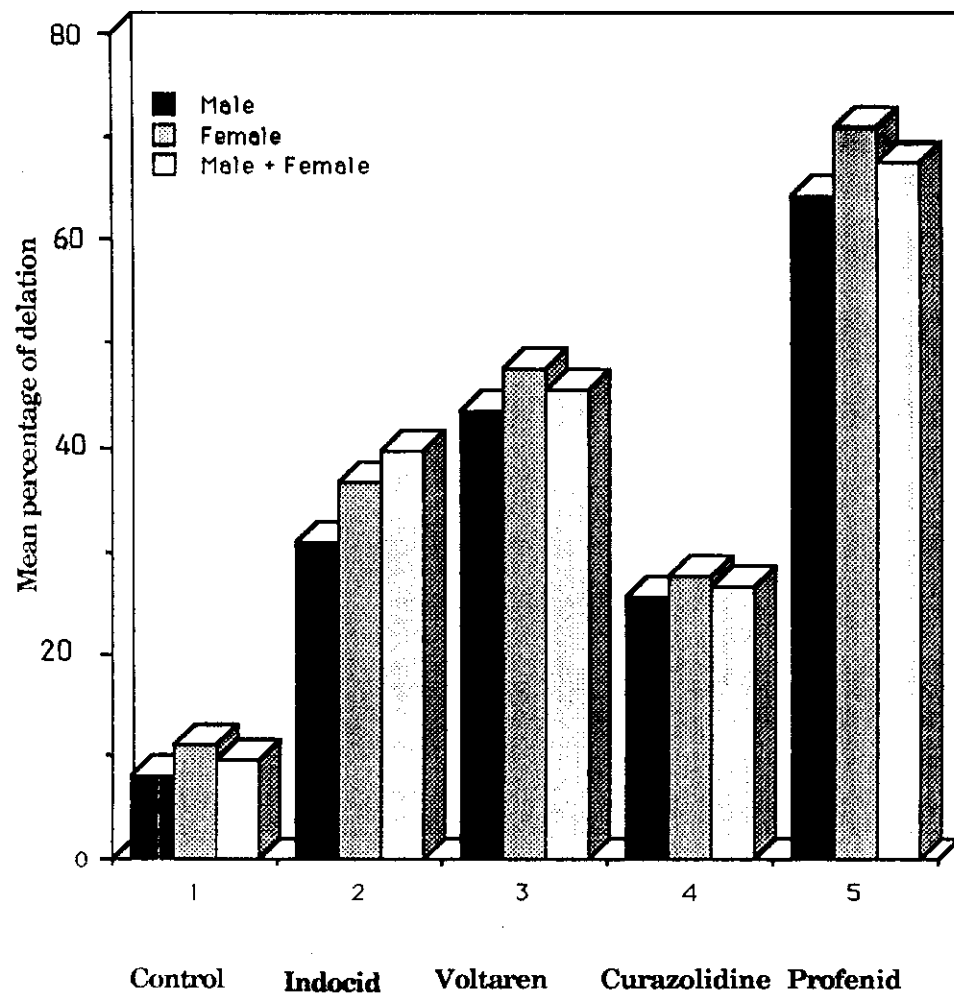


Fig. (12) Mean percentage of delation observed in rat bone marrow after treatment with nonsteroidal anti-inflammatory drugs

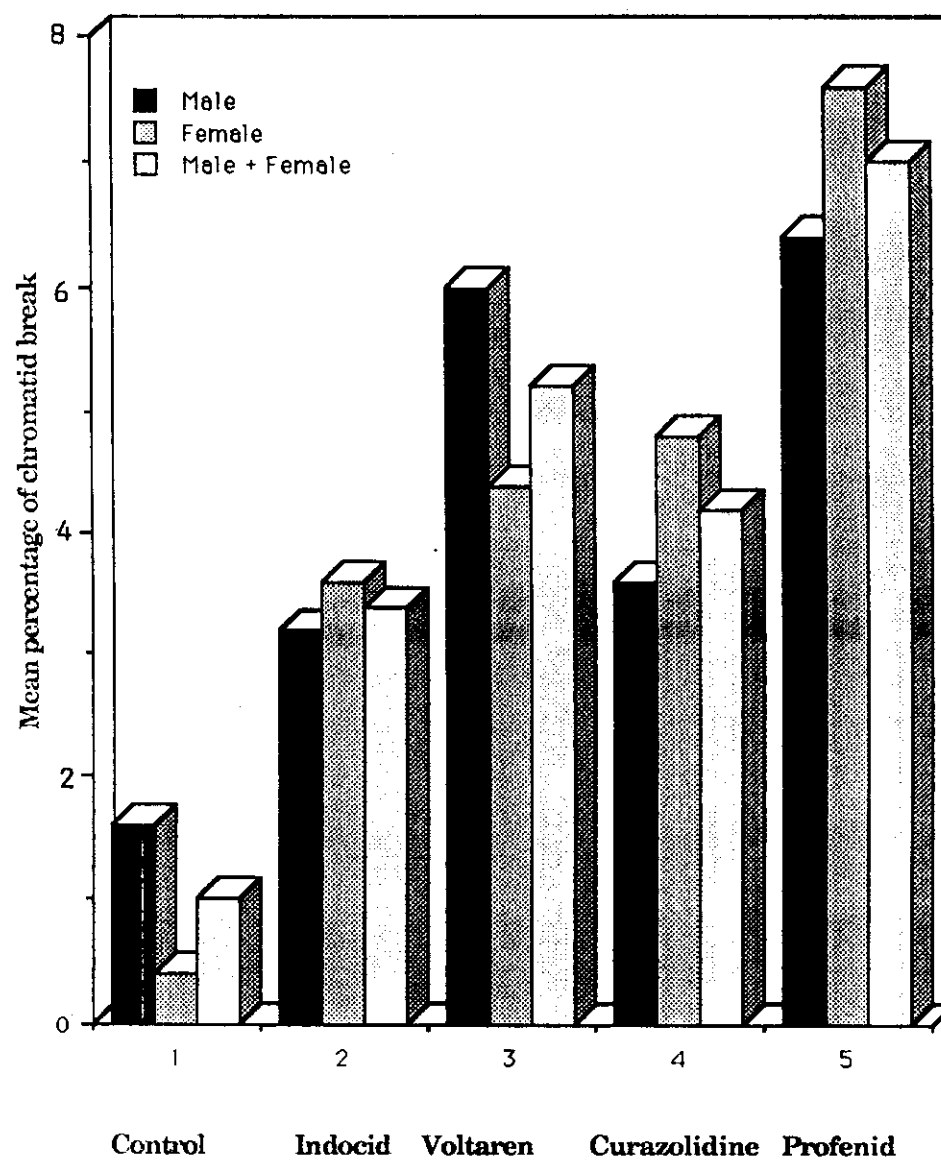


Fig. (13) Mean percentage of Chromatid break observed in rat bone marrow after treatment with nonsteroidal anti-inflammatory drugs

Table (3) : Number of bone marrow cells per 50 metaphase nuclei having ring.
From rats treated⁽¹⁾ with non steroid anti-inflammatory drugs.

Treatment		Rat Number					Mean $\pm$ S.E.	Level of significance (P <) ⁽³⁾
		1	2	3	4	5		
Control	M	1	0	0	0	0	0.2 $\pm$ 0.20	
							0.2 $\pm$ 0.133 (2)	
	F	0	0	0	1	0	0.2 $\pm$ 0.20	
Indocid	M	1	3	3	5	5	3.4 $\pm$ 0.75	.005
							3.5 $\pm$ 0.562	.005
	F	2	2	7	4	3	3.6 $\pm$ 0.93	.01
Voltaren	M	2	4	7	8	5	5.2 $\pm$ 1.07	.005
							5.0 $\pm$ 0.714	.005
	F	1	6	4	7	6	4.8 $\pm$ 1.07	.005
Curazolidine	M	17	7	4	3	4	3.8 $\pm$ 0.97	.01
							3.2 $\pm$ 0.879	.005
	F	8	0	1	0	4	3.25 $\pm$ 1.79	N.S.
Profenid	M	3	5	5	5	5	4.6 $\pm$ 0.4	.005
							6.5 $\pm$ 1.249	.005
	F	11	14	10	6	1	8.4 $\pm$ 2.25	.01

M = Male

F = Female

- (1) Each drug was administered for 32 days as described in material and methods.
 (2) The intermediate value represents the mean for both sexes.
 (3) Using student (t) test.

Table (4) : Mitotic index in bone marrow of laboratory rats treated with non steroidal anti-inflammatory drugs.⁽¹⁾

Treatment		Rat Number					Mean $\pm$ S.E.	Level of significance (P <) (3)
		1	2	3	4	5		
Control	M	226	150	102	127	297	180.4 $\pm$ 35.775	
	F	250	115	142	142	275	182.6 $\pm$ 22.74 (2) 179.4 $\pm$ 34.509	
Indocid	M	206	143	136	158	130	154.6 $\pm$ 13.673	
	F	231	229	216	200	189	183.8 $\pm$ 12.292 213.0 $\pm$ 8.162	
Voltaren	M	223	225	205	184	213	210 $\pm$ 7.430	
	F	169	188	201	145	195	194.8 $\pm$ 7.809 179.6 $\pm$ 10.186	
Curazolidine	M	267	102	269	204	173	203 $\pm$ 31.268	
	F	220	262	207	310	118	213.2 $\pm$ 21.336 223.4 $\pm$ 31.921	
Profenid	M	222	217	291	194	158	216.4 $\pm$ 35.221	
	F	183	197	191	214	147	201.4 $\pm$ 12.569 186.4 $\pm$ 11.089	

M = Male

F = Female

- (1) Each drug was administered for 32 days as described in material and methods.
 (2) The intermediate value represents the mean for both sexes.
 (3) Using student (t) test.

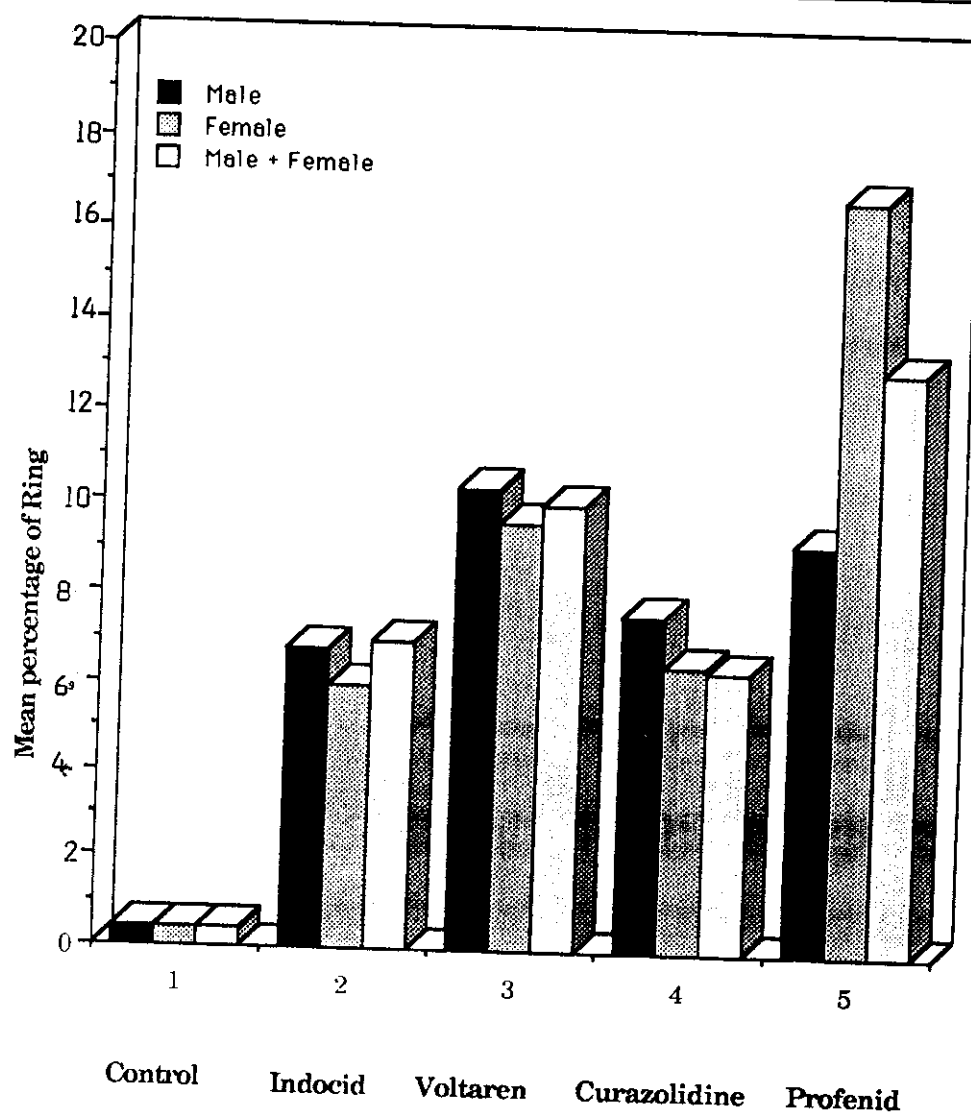


Fig. (14) Mean percentage of Ring observed in rat bone marrow after treatment with nonsteroidal anti-inflammatory drugs

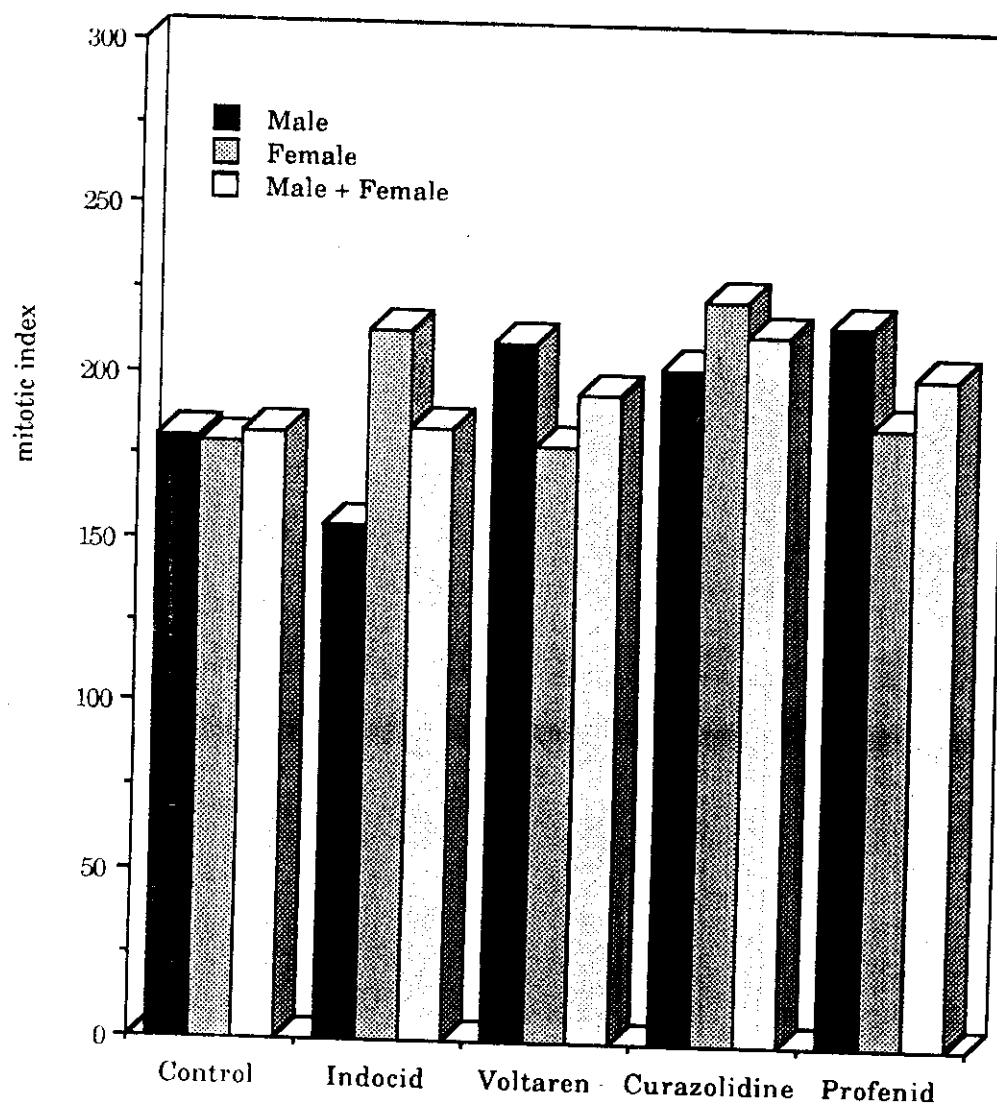


Fig. (15) Mitotic index in rat bone marrow after treatment with non steroidal anti-inflammatory drugs.

B. Numerical aberration :**B-1 Chromatid stickiness :**

Table (5) and Figure (16) show the chromatid stickiness in cells from the bone marrow of rats treated with the four non steroidal anti-inflammatory drugs. The mean value for cells with chromosomal stickiness per 50 metaphase spreads is not statistically significant in case of indocid, voltaren or in male treated with curazolidine and profenid. However, the difference is significant in values obtained for case of female and combined male and female treated curazolidine and profenid.

B.2. Aneuploidy :

Table (6) and Figure (17) show that the number of cells containing trisomic chromosomes per 50 metaphase spreads is numerically higher than control. The difference, however, is not statistically significant for indocid treated animals and males treated with curazolidine.

Table (7) and Figure (18) show that the number of cells with monosomic chromosomes are significantly higher in animals of either sexes or pooled sexes for all treated groups compared with control.

Table (5) : Number of bone marrow cells per 50 metaphase nuclei having sticky chromosome (1) from rats treated with non steroidal anti-inflammatory drugs.

Treatment		Rat Number					Mean $\pm$ S.E.	Level of significance (P <)(3)
		1	2	3	4	5		
Control	M	3	3	4	4	1	3 $\pm$ 0.547	
							3 $\pm$ 0.33 (2)	
	F	3	4	2	4	2	2 $\pm$ 0.45	
Indocid	M	1	8	4	8	8	5.8 $\pm$ 1.428	N.S.
							4.6 $\pm$ 0.819	N.S.
	F	3	4	2	5	3	3.4 $\pm$ 0.51	N.S.
Voltaren	M	4	2	3	3	1	2.6 $\pm$ 0.51	N.S.
							4 $\pm$ 0.745	N.S.
	F	6	3	3	6	9	5.4 $\pm$ 1.122	N.S.
Curazolidine	M	4	4	6	6	2	4.4 $\pm$ 0.748	N.S.
							4 $\pm$ 0.394	.01
	F	4	3	3	4	4	3.6 $\pm$ 0.245	.005
Profenid	M	2	5	4	9	8	5.6 $\pm$ 1.288	N.S.
							5.5 $\pm$ 0.718	.05
	F	5	8	3	6	5	5.4 $\pm$ 0.812	.01

M = Male

F = Female

- (1) Each drug was administered for 32 days as described in material and methods.
 (2) The intermediate value represents the mean for both sexes.
 (3) Using student (t) test.

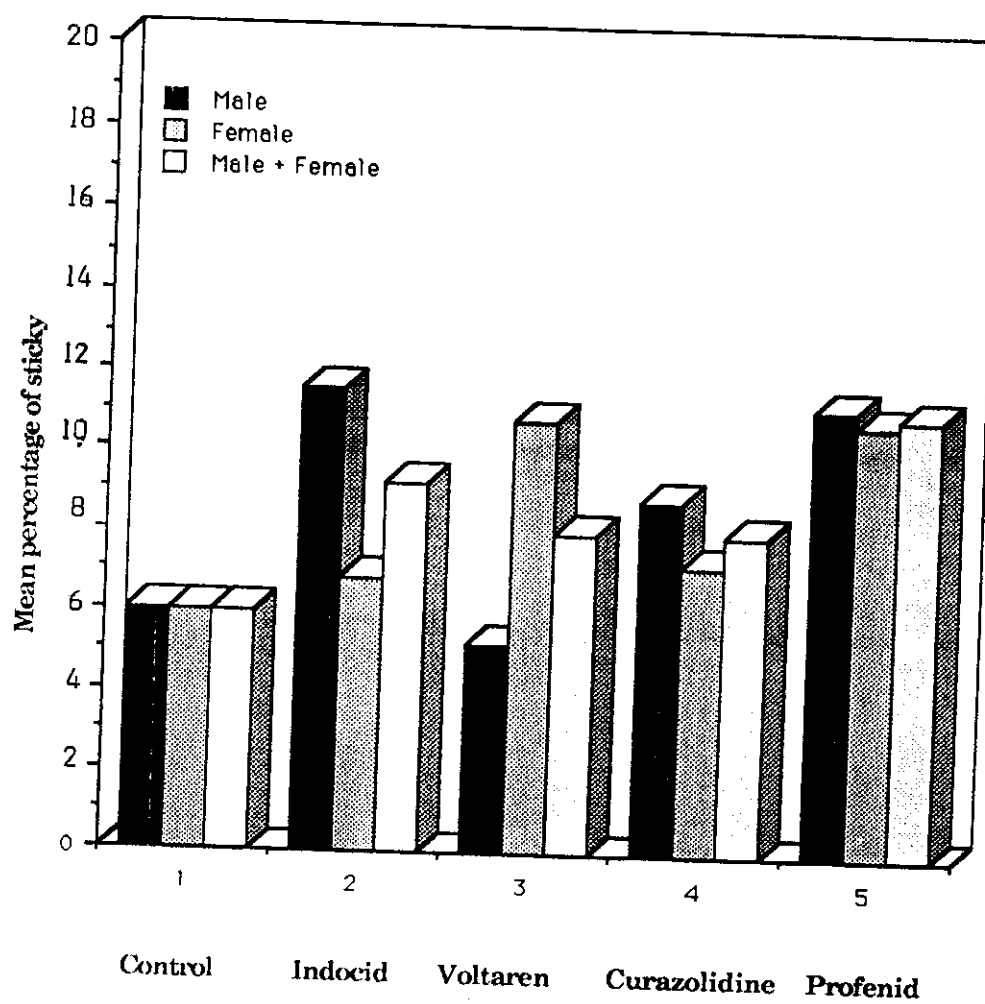


Fig. (16). Mean percentage of stickiness observed in rat bone marrow after treatment with non steroidal anti-inflammatory drugs.

Table (6): The number of trisomic cells per 50 metaphase spreads of laboratory rats treated⁽¹⁾ with non steroidal anti-inflammatory drugs.

Treatment		Rat Number					Mean $\pm$ S.E.	Level of significance (P <)(3)
		1	2	3	4	5		
Control	M	1	2	-	-	2	1 $\pm$ 0.44 0.8 $\pm$ 0.29 (2) 0.6 $\pm$ 0.4	
	F	-	2	-	-	1		
Indocid	M	4	-	1	1	1	1.4 $\pm$ 0.67 1.3 $\pm$ 0.36 1.2 $\pm$ 0.37	N.S N.S. N.S.
	F	2	2	1	1	-		
Voltaren	M	1	2	4	3	7	3.4 $\pm$ 1.02 3.4 $\pm$ 0.58 3.4 $\pm$ 0.68	N.S .005 .01
	F	1	4	5	3	4		
Curazolidine	M	2	2	4	7	1	3.2 $\pm$ 1.07 3.2 $\pm$ 0.65 3.2 $\pm$ 0.86	N.S .005 .005
	F	-	5	3	4	4		
Profenid	M	-	3	8	2	7	.5 $\pm$ 1.47 4.1 $\pm$ 0.98 5.25 $\pm$ 1.25	.05 .005 .01
	F	-	5	8	2	6		

M = Male

F = Female

- (1) Each drug was administered for 32 days as described in material and methods.
 (2) The intermediate value represents the mean for both sexes.
 (3) Using student (t) test.

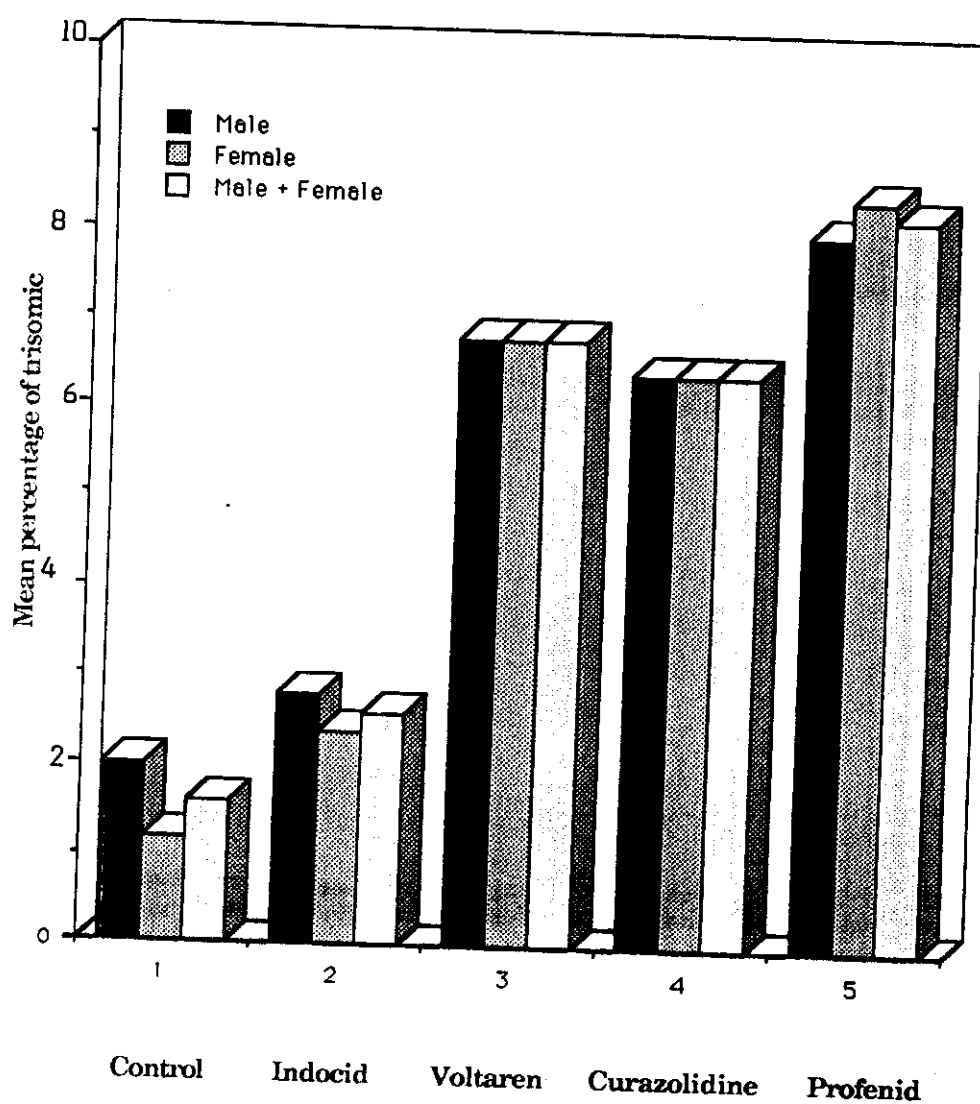


Fig. (17) Mean percentage of numerical aberration (trisomic) observed in rat bone marrow after treatment with nonsteroidal anti-inflammatory drugs

Table (7): The number of monosomic cells per 50 metaphase spreads of laboratory rats treated⁽¹⁾ with non steroidal anti-inflammatory drugs.

Treatment		Rat Number					Mean $\pm$ S.E.	Level of significance (P <)(3)
		1	2	3	4	5		
Control	M	6	4	2	5	4	4.2 $\pm$ 0.66	
							4.9 $\pm$ 1.66 (2)	
	F	3	5	6	9	5	5.6 $\pm$ 0.97	
Indocid	M	10	15	19	9	16	13.8 $\pm$ 1.88	.055
							13.3 $\pm$ 1.14	.055
	F	12	13	14	8	17	12.8 $\pm$ 1.64	.005
Voltaren	M	14	9	6	7	8	8.8 $\pm$ 1.39	.05
							8.8 $\pm$ 0.85	.005
	F	12	11	7	8	6	8.8 $\pm$ 1.16	.05
Curazolidine	M	12	10	15	11	12	12 $\pm$ 0.83	.005
							13 $\pm$ 1.45	.005
	F	25	8	12	12	13	14 $\pm$ 2.88	.05
Profenid	M	9	17	12	13	8	11.8 $\pm$ 1.59	.005
							11.7 $\pm$ 1.01	.005
	F	15	15	10	10	8	11.6 $\pm$ 1.43	.01

M = Male

F = Female

- (1) Each drug was administered for 32 days as described in material and methods.
 (2) The intermediate value represents the mean for both sexes.
 (3) Using student (t) test.

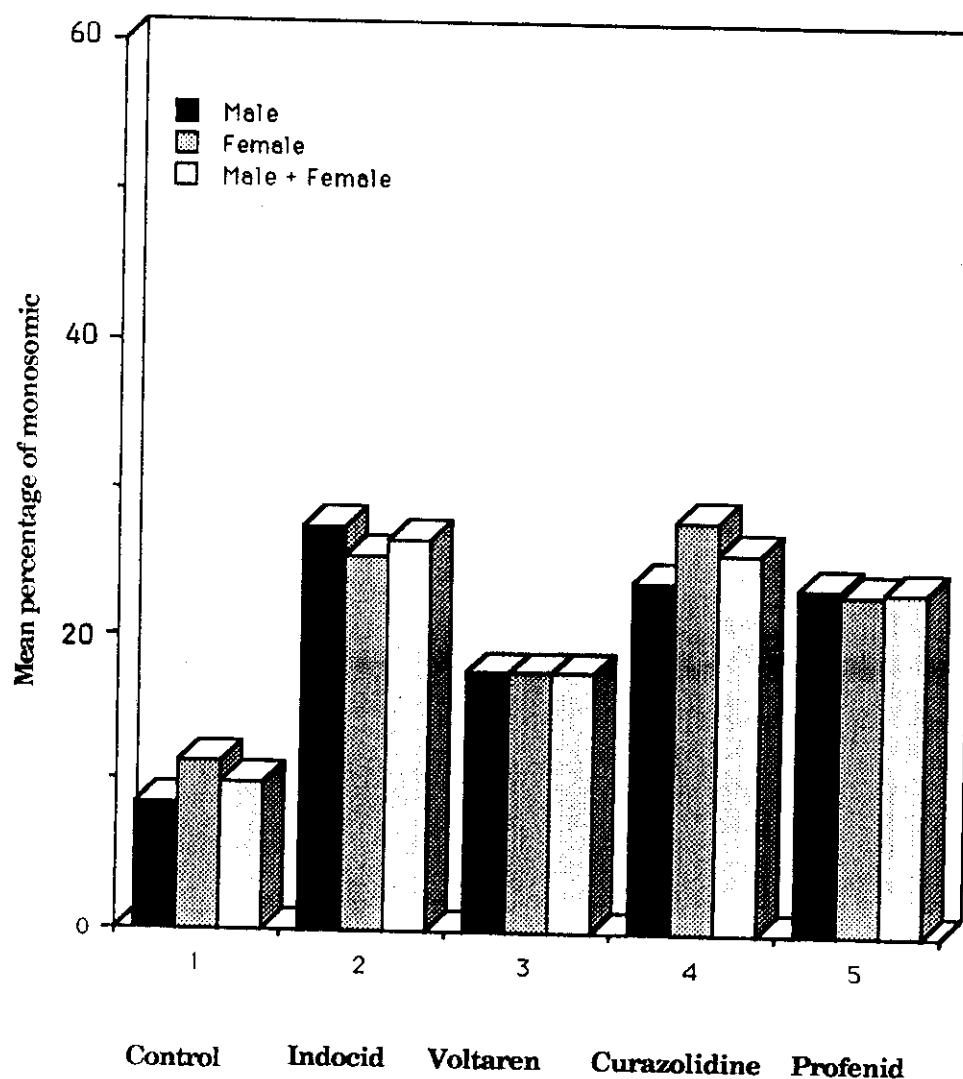


Fig. (18) Mean percentage of numerical aberration (Monosomic) observed in rat bone marrow after treatment with nonsteroidal anti-inflammatory drugs

Cells with only one type of aberration (table 8 and Figure 17) : In all drugs used, the number of cells showing one type of aberration is significantly higher in case of male and female combined together than that of control. The means for each sex alone almost follows the above pattern.

Cells with more than one type of aberration :

Table (9) and figure (20) show that for all treated groups, there is a highly significant difference than control when values for male and female are combined.

In male, the difference from the control is significant in indocid and voltaren treated and highly significant in curazolidine and profenid treated animals. The difference is highly significant in females treated with indocid and profenid and significant in voltaren treated but non significant in females treated with curazolidine.

Table (10) and Figure (21) represent the total damaged cells in the bone marrow of control rats and those treated with non steroidal anti-inflammatory drugs. It is clear that the mean number of aberrant cells from female rats is higher than those from male. There is a highly significant difference between the values obtained for treated animals and control.

Table (8): Cells with one type of aberration per 50 metaphase spreads of bone marrow of laboratory rats treated⁽¹⁾ with non steroidal anti-inflammatory drugs.

Treatment		Rat Number					Mean $\pm$ S.E.	Level of significance (P <)(3)
		1	2	3	4	5		
Control	M	9	3	5	4	5	5.2 $\pm$ 1.020 6.1 $\pm$ 0.69 (2) 7 $\pm$ 0.836	
	F	9	7	7	4	8		
Indocid	M	15	19	28	18	22	20.4 $\pm$ 2.204 20 $\pm$ 1.174 19.6 $\pm$ 1.122	.005 .005 .005
	F	22	22	20	17	17		
Voltaren	M	21	42	29	25	27	25.2 $\pm$ 1.356 24.8 $\pm$ 1.031 24.4 $\pm$ 1.691	.005 .005 .005
	F	23	22	31	24	22		
Curazolidine	M	20	21	31	32	20	24.8 $\pm$ 2.746 26.7 $\pm$ 1.660 28.6 $\pm$ 1.749	.005 .005 .005
	F	24	30	33	31	25		
Profenid	M	30	24	28	21	21	24.8 $\pm$ 1.827 25.7 $\pm$ 1.802 26.6 $\pm$ 3.295	.005 .005 .005
	F	22	19	23	35	34		

M = Male

F = Female

- (1) Each drug was administered for 32 days as described in material and methods.
 (2) The intermediate value represents the mean for both sexes.
 (3) Using student (t) test.

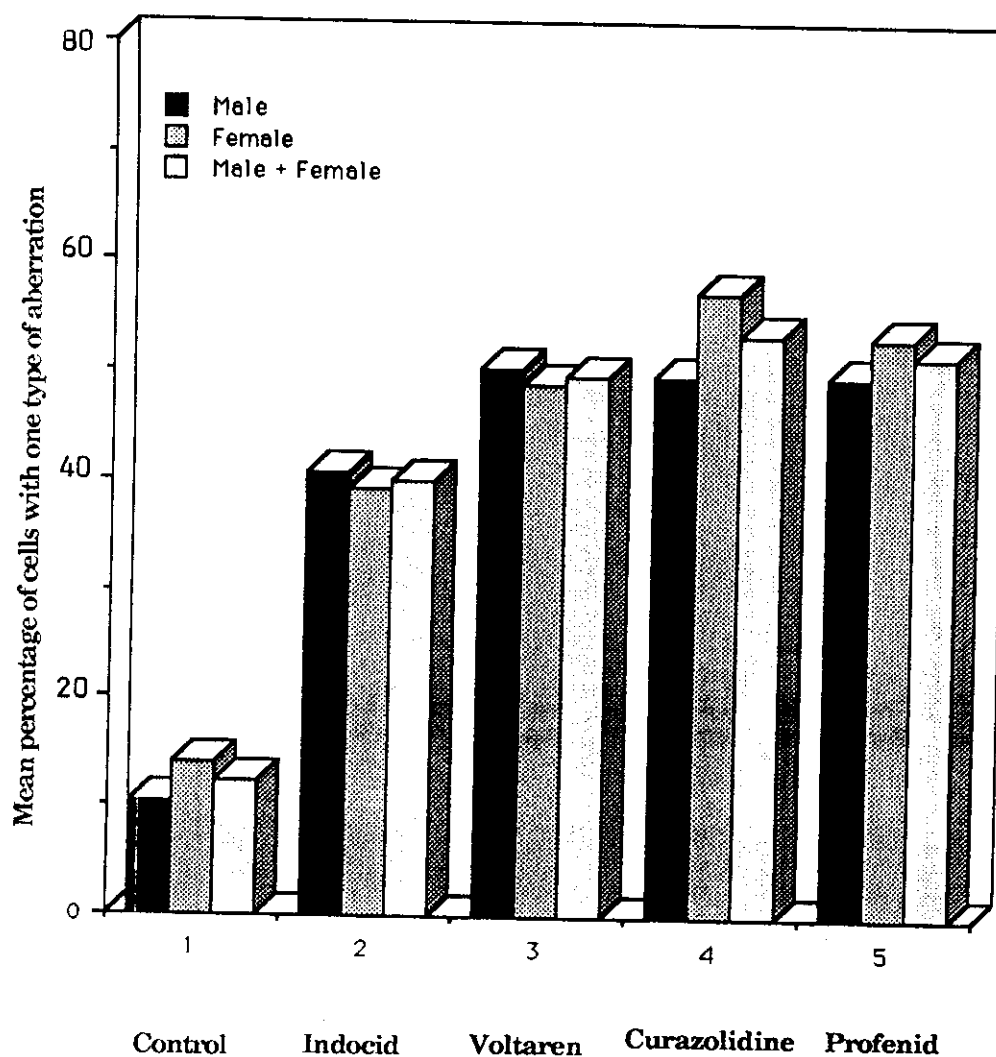


Fig. (19) Mean percentage of cells with one type of aberration observed in rat bone marrow after treatment with nonsteroidal anti-inflammatory drugs

Table (9): Cells with mor than one type of aberration in 50 metaphase spreads of bone marrow of laboratory rats treated⁽¹⁾ with non steroidal anti-inflammatory drugs.

Treatment		Rat Number					Mean $\pm$ S.E.	Level of significance (P <)(3)
		1	2	3	4	5		
Control	M	1	0	0	0	2	0.6 $\pm$ 0.40	
							0.5 $\pm$ 0.223 (2)	
	F	0	0	1	0	1	0.4 $\pm$ 0.25	
Indocid	M	4	1	4	6	1	3.2 $\pm$ 0.97	.05
							4.4 $\pm$ 0.858	.005
	F	2	8	3	8	7	5.6 $\pm$ 1.29	.005
Voltaren	M	1	7	4	2	7	4.2 $\pm$ 1.24	.05
							4.4 $\pm$ 0.991	.005
	F	1	7	0	7	8	4.6 $\pm$ 1.69	.05
Curazolidine	M	3	5	4	2	5	3.8 $\pm$ 0.58	.005
							3 $\pm$ 0.557	.005
	F	3	2	1	0	5	2.2 $\pm$ 0.86	N.S.
Profenid	M	10	19	12	10	26	15.4 $\pm$ 3.13	.005
							15.7 $\pm$ 2.03	.005
	F	6	21	14	23	16	16 $\pm$ 2.98	.005

M = Male

F = Female

- (1) Each drug was administered for 32 days as described in material and methods.
 (2) The intermediate value represents the mean for both sexes.
 (3) Using student (t) test.

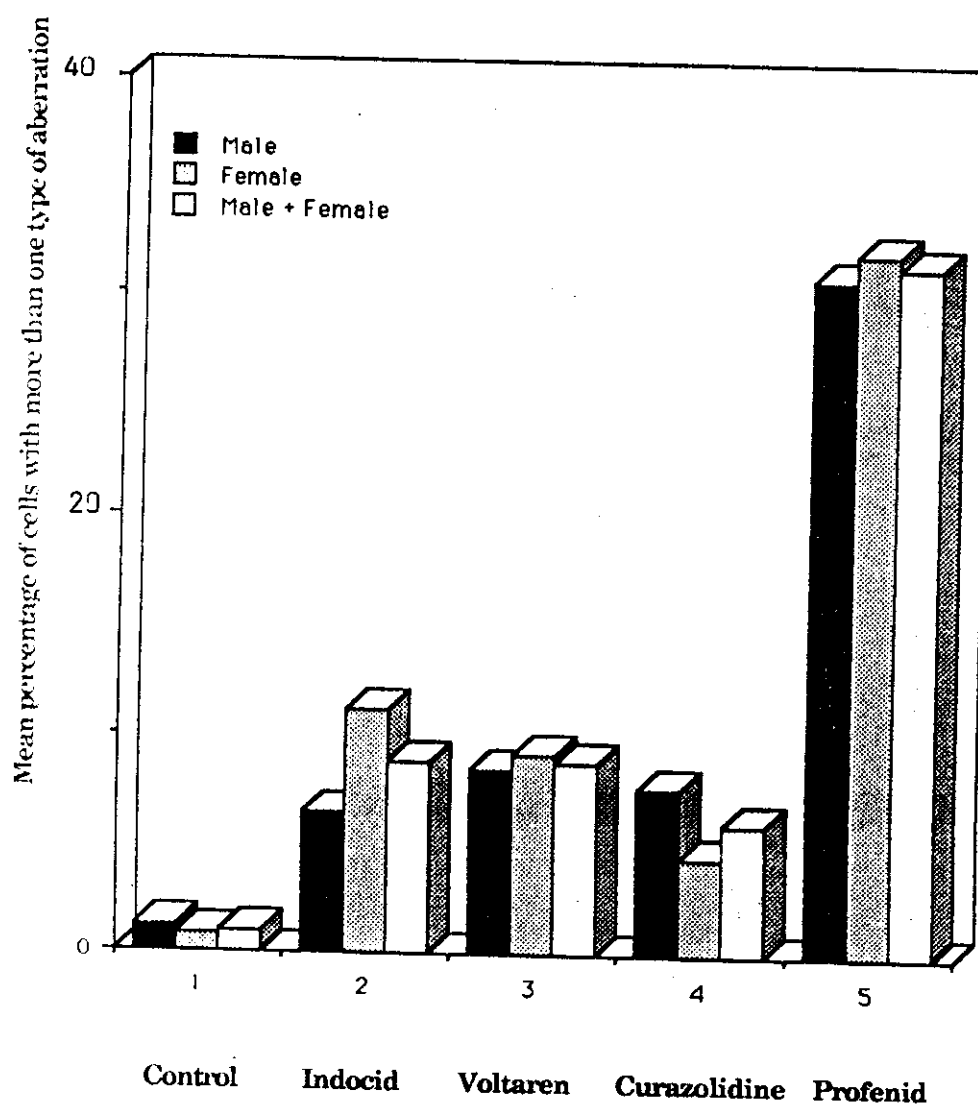


Fig. (20) Mean percentage of cells with more than one type of aberration observed in rat bone marrow after treatment with nonsteroidal anti-inflammatory drugs

Table (10): Incidence of aberrated chromosomes in bone marrow per 50 metaphase nuclei from rats treated⁽¹⁾ with non steroidal anti-inflammatory drugs.

Treatment		Rat Number					Mean $\pm$ S.E.	Level of significance (P <) (3)
		1	2	3	4	5		
Control	M	14	6	9	9	11	9.8 $\pm$ 1.32	
							11 $\pm$ 0.894 (2)	
	F	12	11	14	9	15	12.2 $\pm$ 1.07	
Indocid	M	32	31	49	42	35	37.8 $\pm$ 3.39	.005
							37.9 $\pm$ 2.20	.005
	F	30	37	33	48	42	38 $\pm$ 3.20	.005
Voltaren	M	31	49	50	51	63	48.8 $\pm$ 5.12	.005
							49.0 $\pm$ 2.820	.005
	F	40	48	46	55	57	49.2 $\pm$ 3.08	.005
Curazolidine	M	34	37	53	36	48	41.6 $\pm$ 3.75	.005
							44.1 $\pm$ 2.873	.005
	F	36	44	50	62	41	46.6 $\pm$ 4.46	.005
Profenid	M	55	98	90	116	119	95.6 $\pm$ 11.50	.005
							98.9 $\pm$ 7.165	.005
	F	73	95	96	126	121	102.2 $\pm$ 9.65	.005

M = Male

F = Female

- (1) Each drug was administered for 32 days as described in material and methods.
 (2) The intermediate value represents the mean for both sexes.
 (3) Using student (t) test.

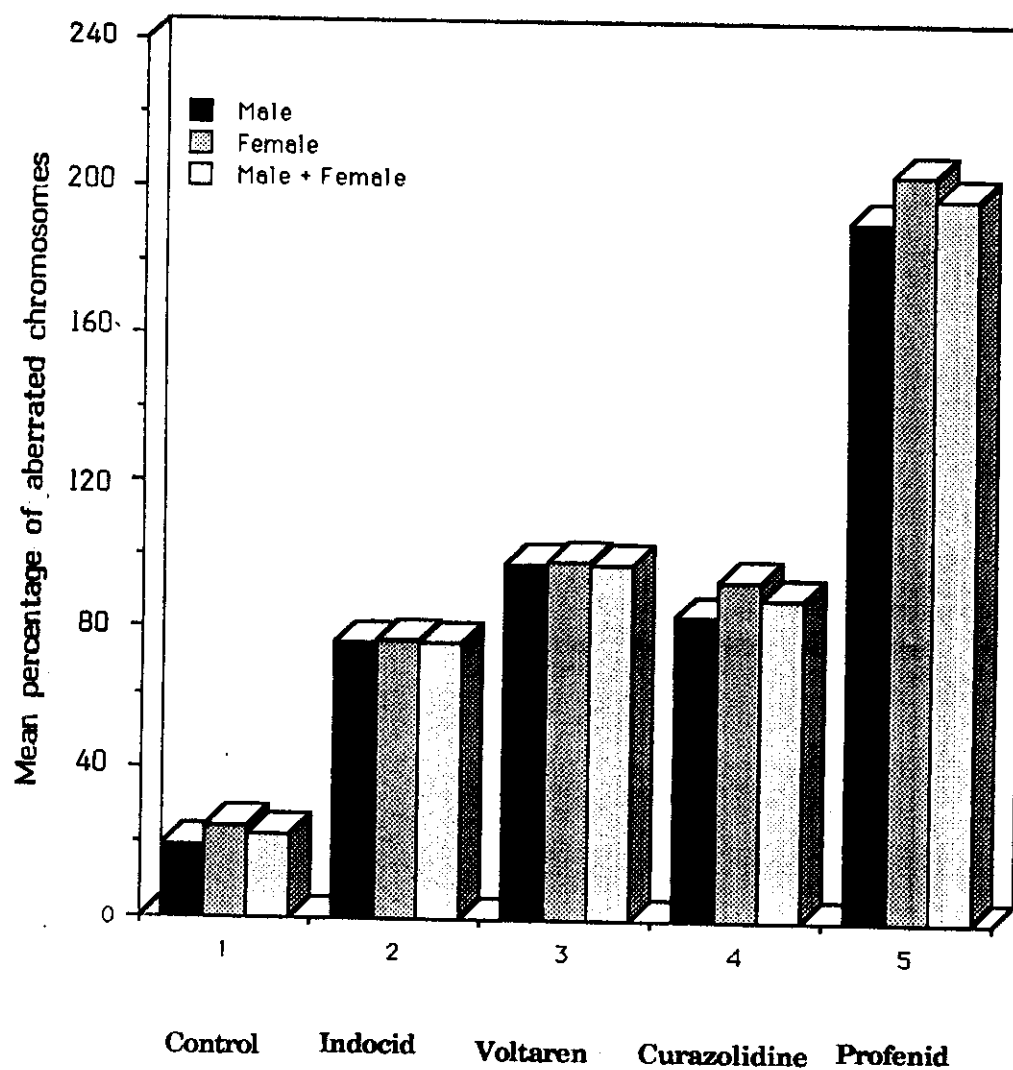


Fig. (21) Mean percentage of aberrated chromosome observed in rat bone marrow after treatment with nonsteroidal anti-inflammatory drugs

Table (11) summarizes the mean percentage of chromosomal abnormalities observed in rat bone marrow after treatment with non steroidal anti-inflammatory drugs.

Table (12) and Figure (22) shows mitotic activity after treatment of animals for 24 h, 48 h, 5 days and 32 days. The difference in values for different durations is not statistically significant. However, there is a significant difference between values obtained from treated animals and control (except for animals treated for 32 days).

Table (13) and Figure (23) show the mean number of nuclei with chromosomal aberrations in female rats treated with phenylbutazone for 24 h, 48 h, 5 days and 32 days. There is a significant difference between cells with structural aberrations in all treated animals compared with control. However, for numerical aberrations, the difference is significant only in case of 24 hours, 5 day and 32 day treatments. The intertreatment difference in numerical aberrations is significantly only between 5 day and 32 day treated animals.

Table (11): Average number of nuclei with chromosomal abnormalities observed in 50 metaphase spreads of rat bone marrow after treatment with non steroidal anti-inflammatory drugs.

observation		Control	Indocid	Voltarene	Curazolidine	Profenid
Chromatid gaps	M	1.4 $\pm$ 0.24	7.4 $\pm$ 1.778	5.2 $\pm$ 0.374	4.8 $\pm$ 0.663	15.6 $\pm$ 3.234
	M+F	1.8 $\pm$ 0.24	7.8 $\pm$ 1.2	5.7 $\pm$ 0.869	6.2 $\pm$ 0.799	14.2 $\pm$ 2.471
	F	2.2 $\pm$ 0.37	8.2 $\pm$ 1.80	7.75 $\pm$ 1.108	7.6 $\pm$ 1.208	14.6 $\pm$ 6.525
Deletion	M	4 $\pm$ 1.45	15.4 $\pm$ 1.44	21.8 $\pm$ 1.50	12.8 $\pm$ 1.88	32 $\pm$ 2.88
	M+F	4.8 $\pm$ 0.979	16.9 $\pm$ 1.589	22.8 $\pm$ 0.975	13.3 $\pm$ 1.909	33.7 $\pm$ 2.118
	F	5.6 $\pm$ 1.40	18.4 $\pm$ 2.88	23.8 $\pm$ 1.24	13.8 $\pm$ 3.57	35.4 $\pm$ 3.23
Chromatid breaks	M	0.8 $\pm$ 0.374	1.6 $\pm$ 0.372	3 $\pm$ 1.265	1.8 $\pm$ 0.800	3.2 $\pm$ 0.969
	M+F	0.5 $\pm$ 0.224	1.7 $\pm$ 0.651	2.6 $\pm$ 0.806	2.1 $\pm$ 0.586	3.5 $\pm$ 0.705
	F	0.2 $\pm$ 0.199	1.8 $\pm$ 1.068	2.2 $\pm$ 1.113	2.4 $\pm$ 0.927	3.8 $\pm$ 1.157
Ring	M	0.2 $\pm$ 0.20	3.4 $\pm$ 0.75	5.2 $\pm$ 1.07	3.8 $\pm$ 0.97	4.6 $\pm$ 0.4
	M+F	0.2 $\pm$ 0.133	3.5 $\pm$ 0.562	5 $\pm$ 0.714	3.2 $\pm$ 0.879	6.5 $\pm$ 1.249
	F	0.2 $\pm$ 0.20	3.6 $\pm$ 0.93	4.8 $\pm$ 1.07	3.25 $\pm$ 1.79	8.4 $\pm$ 2.25
Sticky	M	3 $\pm$ 0.547	5.8 $\pm$ 1.428	2.6 $\pm$ 0.51	4.4 $\pm$ 0.748	5.6 $\pm$ 1.288
	M+F	3 $\pm$ 0.33	4.6 $\pm$ 0.819	4 $\pm$ 0.745	4 $\pm$ 0.394	5.5 $\pm$ 0.718
	F	3 $\pm$ 0.45	3.4 $\pm$ 0.51	4.5 $\pm$ 1.122	3.6 $\pm$ 0.245	5.4 $\pm$ 0.812
incidence of aberrated chromosomes	M	9.8 $\pm$ 1.32	37.8 $\pm$ 3.39	48.8 $\pm$ 5.12	41.6 $\pm$ 3.75	95.6 $\pm$ 11.5
	M+F	11 $\pm$ 0.894	37.9 $\pm$ 2.20	49 $\pm$ 2.82	44.1 $\pm$ 2.873	98.9 $\pm$ 7.165
	F	12.2 $\pm$ 1.07	38.0 $\pm$ 3.20	49.2 $\pm$ 3.08	46.6 $\pm$ 4.46	102.0 $\pm$ 9.65
Cells with one abnormality	M	5.2 $\pm$ 1.020	20.4 $\pm$ 2.204	25.2 $\pm$ 1.356	24.8 $\pm$ 2.746	24.8 $\pm$ 1.827
	M+F	6.1 $\pm$ 0.69	20 $\pm$ 1.179	24.8 $\pm$ 1.031	26.7 $\pm$ 1.66	25.7 $\pm$ 1.802
	F	7 $\pm$ 0.836	19.6 $\pm$ 1.122	24.4 $\pm$ 1.691	28.6 $\pm$ 1.749	26.6 $\pm$ 3.295
Cells with more than one abnormality	M	0.6 $\pm$ 0.40	3.2 $\pm$ 0.9	4.2 $\pm$ 1.24	3.8 $\pm$ 0.58	15.4 $\pm$ 3.13
	M+F	0.5 $\pm$ 0.223	4.4 $\pm$ 0.858	4.4 $\pm$ 0.991	3 $\pm$ 0.557	15.7 $\pm$ 2.03
	F	0.4 $\pm$ 0.25	5.6 $\pm$ 1.29	4.6 $\pm$ 1.69	2.2 $\pm$ 0.86	16.0 $\pm$ 2.98

M = Male

F = Female

Table (12): Mitotic index in bone marrow of laboratory rats treated with phenylbutazone

Treatment with phenyl- butazone	Rat number				Mean $\pm$ S.E	Level of significance	
	1	2	3	4		Control	Previous period
Control	226	150	102	127	151.25 $\pm$ 26.77		
24 hr	255	319	218	193	246.25 $\pm$ 27.39	0.05	
48 hr	265	232	255	253	251.25 $\pm$ 6.932	0.05	N.S
5 days	283	310	319	235	286.75 $\pm$ 18.87	0.01	N.S
32 days	267	102	269	204	210.5 $\pm$ 39.18	N.S	N.S

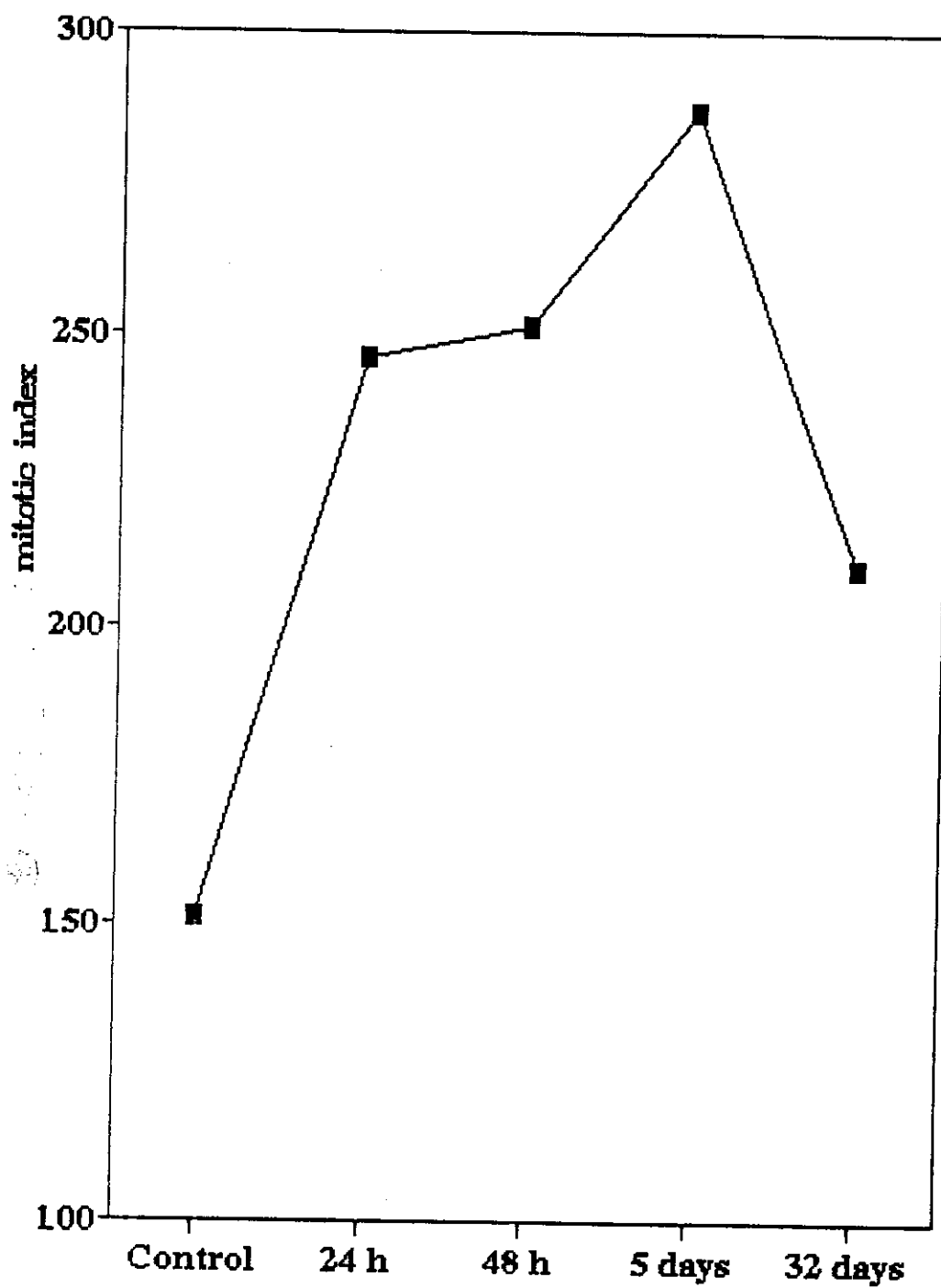


Fig. (22) : Mitotic index in rat bone marrow.
after treatment with curazolidine.

Table (13): Mean number of nuclei with chromosomal aberration per 50 meta-phase spreads of bone marrow cells of rats treated with phenylbutazone.

Treatment with Phenylbutazone	Structural					Numerical		
	Gap	Break	Deletion	Ring	Sticky	Total	Monosomic	Trisomic
Control	2.5 ± 0.29	0.75 ± 0.48	4.75 ± 1.436	0.25 ± 0.25	2.75 ± 0.49	11 ± 1.47	4.75 ± 0.629	0.5 ± 0.5
24. h	1.75 ± 0.629	1 ± 0.707	23.25 ± 1.887 ^(*)	1 ± 0.408	4 ± 0.408	31 ± 1.471 ^(*)	4.5 ± 0.28	3.5 ± 0.28 ^(*)
48 h.	2 ± 1.08	0.75 ± 0.48	19 ± 2.05 ^(*)	1.25 ± 0.48	5.0 ± 1.29	27.75 ± 2.858 ^(*)	6.0 ± 1.47	1.25 ± 0.27 ^(*)
5 days	2.75 ± 1.25	1.0 ± 0.41	17.75 ± 2.46 ^(*)	1.0 ± 0.41	4.25 ± 0.94	26.75 ± 4.768 ^(*)	8.25 ± 0.47 ^(*)	1.0 ± 0.40
32 days	8.5 ± 1.041 ^(*)	1.75 ± 0.85	11.75 ± 3.77	2.25 ± 1.931	3.5 ± 0.289	27.75 ± 5.22 ^(*)	11.25 ± 1.109 ^(*)	3 ± 1.08

(*) Significant between a value and control
 (**) P ≤ .05
 (***) P ≤ .01
 (****) P ≤ .005

(.) Significant between a value and previous value
 (..) P ≤ .01
 (...) P ≤ .005

Effect of non steroidal anti-inflammatory drugs on sperm head abnormality :

The sperms of control rats consist of the usual parts : the head and the tail. The head has a curved pointed tip and a broad base. The tail starts by a broad cylindrical part at the side of the broad base (Figure. 24). The abnormalities in the head region are mostly related to size or the shape of the hook.

If the hook is absent this is called lack hook (Figure 25). The head might be reduced in size it is called amorphous (Figure 26a,b,c). The hook might show an unusual curvature or banana like shape (Figure 27).

Table (14) and Figure (28) summarize the incidence of abnormality in the shape of sperms per 1000 after treatment with the different drugs. The average total abnormality is (88.2) for indocid (91.8) for voltaren (111.4) for curazolidine and (123.4) for profenid.

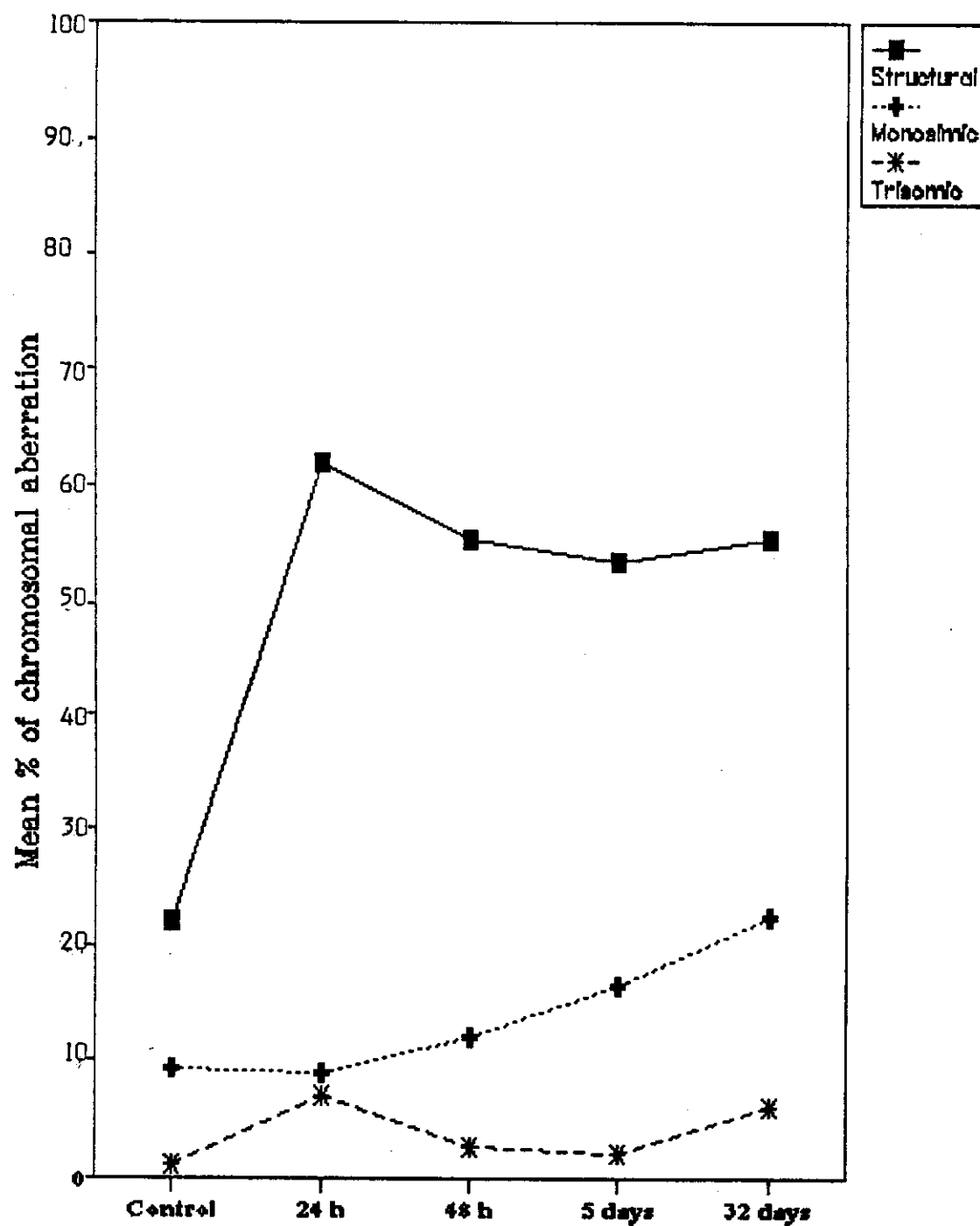


Fig. (23) : Mean percentage of chromosomal aberrations in rat bone marrow after treatment with curazolidine.

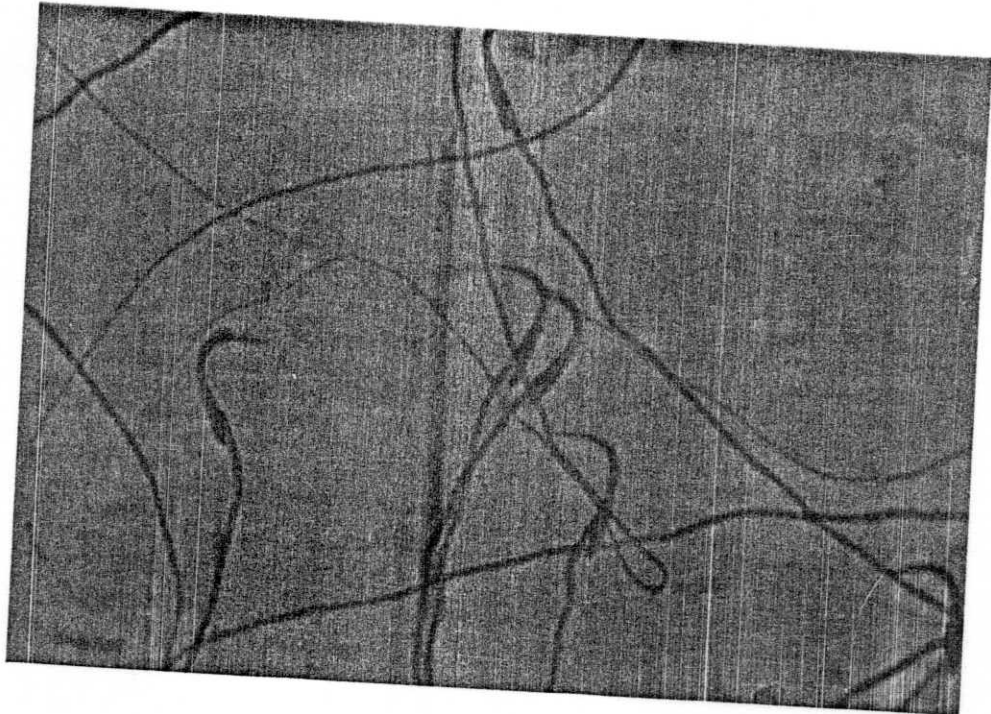


Fig. (24) : Normal sperm from a control group of rats.
(Eosin stain X 1000)

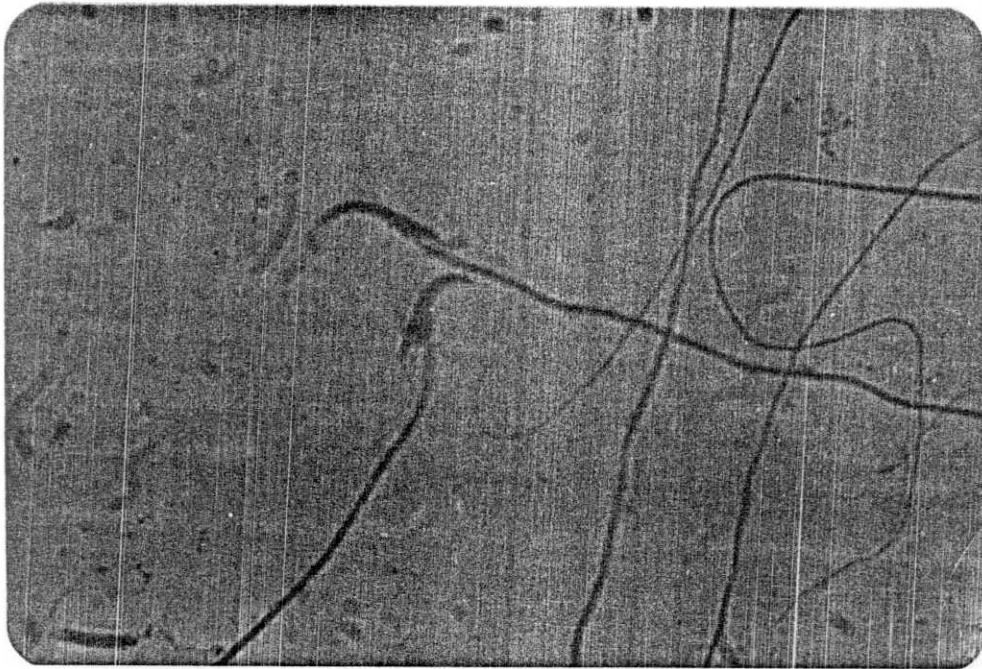


Fig. (25) : Sperm heads with a lost pointed hook (lack hook) in rats treated with non steroidal anti-inflammatory drugs.
(Eosin stain X 1000)

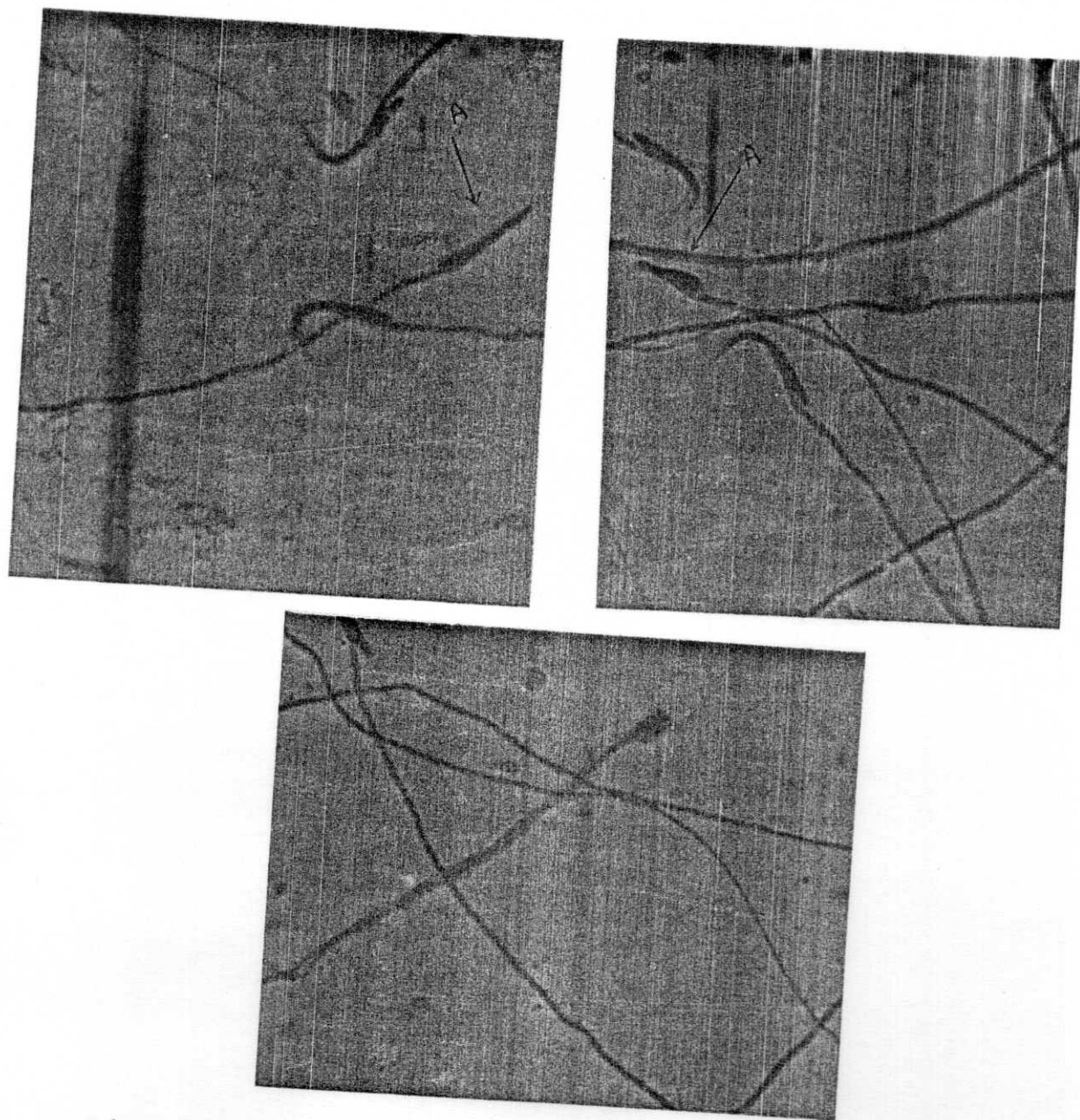


Fig. (26a, b, & c) : Amorphous sperm head of rats treated with non steroidal anti-inflammatory drugs.
(Eosin stain X 1000)

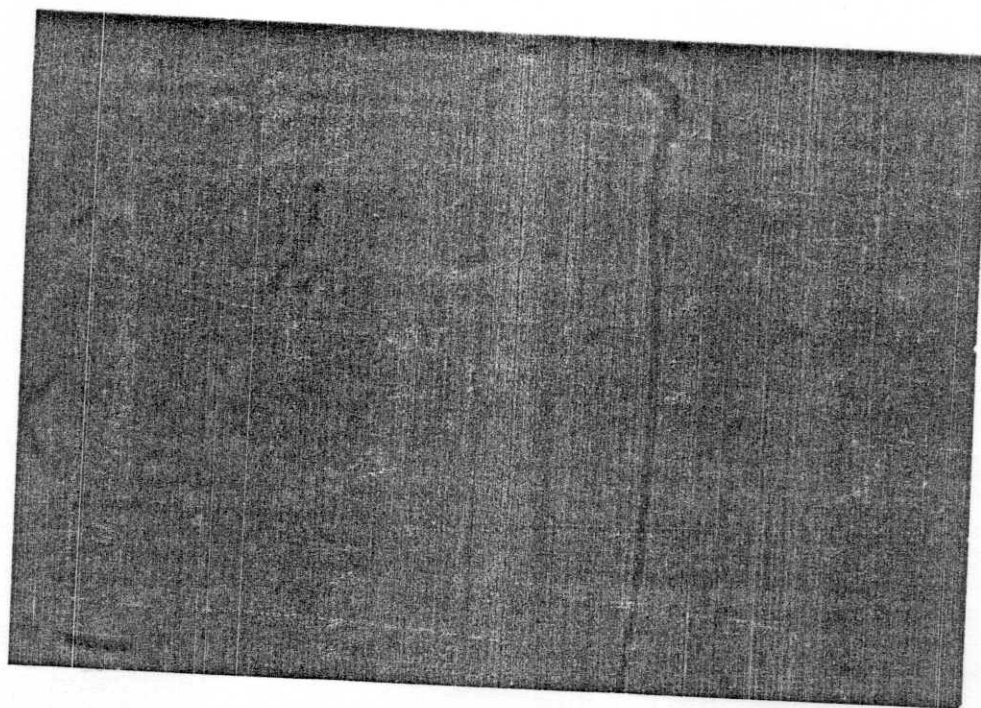


Fig. (27) : Banana like sperm head in rats treated with
non steroidal anti-inflammatory drugs.
(Eosin stain X 1000)

Table (14) : Incidence of the abnormally shaped sperms per thousand after treatment of nonsteroidal anti-inflammatory drugs.

	Normal sperm		abnormal sperms				Total	%
			Amorphous	Banana like	No Hook			
Control	976, 997 981, 972, 971	5, 2, 5 9, 9	9, 1, 1 4, 8	10, 0, 13 15, 12				
Mean $\pm$ SD	979.4 $\pm$ 10.6	6 $\pm$ 3	4.6 $\pm$ 3.78	10 $\pm$ 5.87	20.6 $\pm$ 10.6	2.06		
Indocid	926, 899 908, 919, 907	28, 39, 34 18, 27	16, 22, 13 24, 20	30, 40, 45 39, 46				
Mean $\pm$ SD	911.3 $\pm$ 10.66	29.2 $\pm$ 7.92	19 $\pm$ 4.47	40 $\pm$ 6.36	88.2 $\pm$ 10.66 ^(***)	8.82		
Voltaren	948, 896, 903 877, 917	19, 42, 39 63, 26	18, 14, 15 12, 14	15, 48, 43 48, 43				
Mean $\pm$ SD	908.2 $\pm$ 26.51	37.8 $\pm$ 16.93	14.6 $\pm$ 2.19	39.4 $\pm$ 13.87	91.8 $\pm$ 26.51 ^(***)	9.18		
Curazolidine	923, 878, 877 881, 884	19, 55, 52 41, 43	20, 15, 26 29, 27	38, 52, 45 49, 46				
Mean $\pm$ SD	888.6 $\pm$ 19.42	42 $\pm$ 14.14	23.4 $\pm$ 5.77	46.524	111.4 $\pm$ 19.42 ^(***)	11.4		
Profenid	924, 865, 869 847, 878	23, 49, 67 57, 55	33, 39, 28 33, 24	15, 47, 36 63, 43				
Mean $\pm$ SD	876.6 $\pm$ 28.80	51.2 $\pm$ 14.5	31.4 $\pm$ 5.68	40.8 $\pm$ 17.50	123.4 $\pm$ 28.8 ^(***)	12.34		

(***) Statistically significant (P < 0.005)

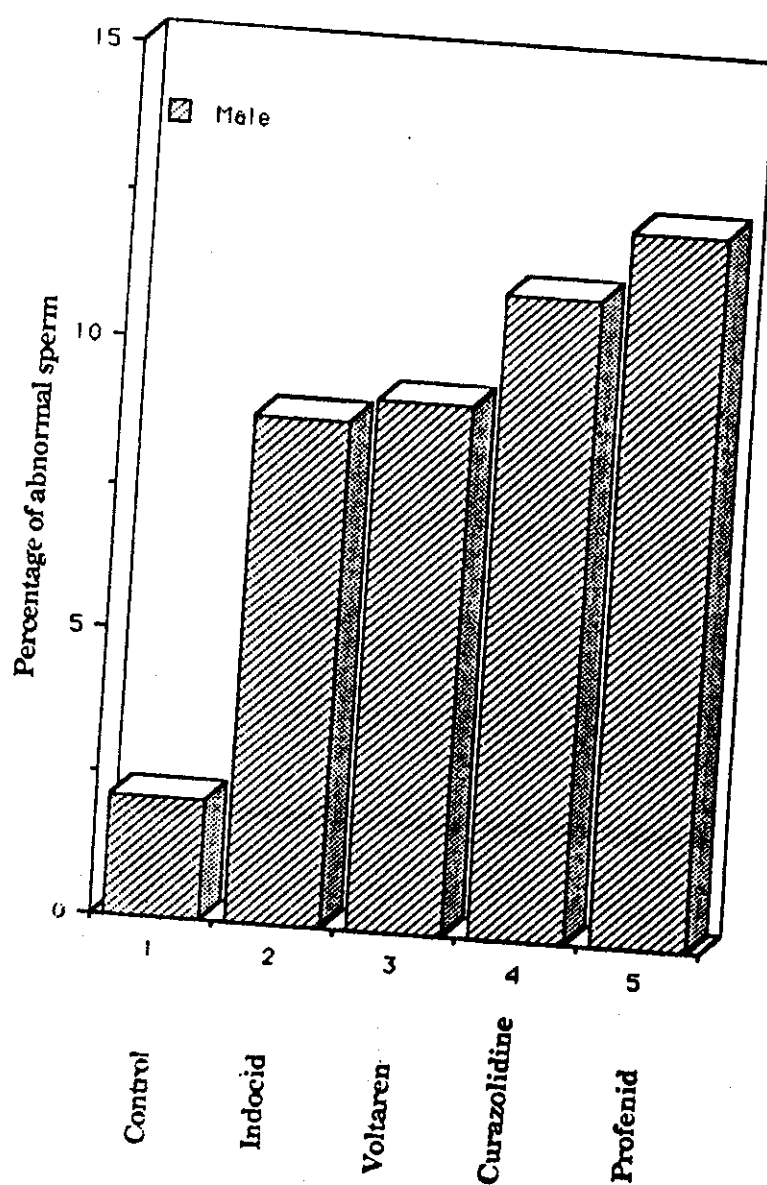


Fig. (28) Abnormally shaped sperms following treatment with nonsteroidal anti-inflammatory drugs