**RESULTS**  $(^{\gamma\gamma})$ 

# **RESULTS**

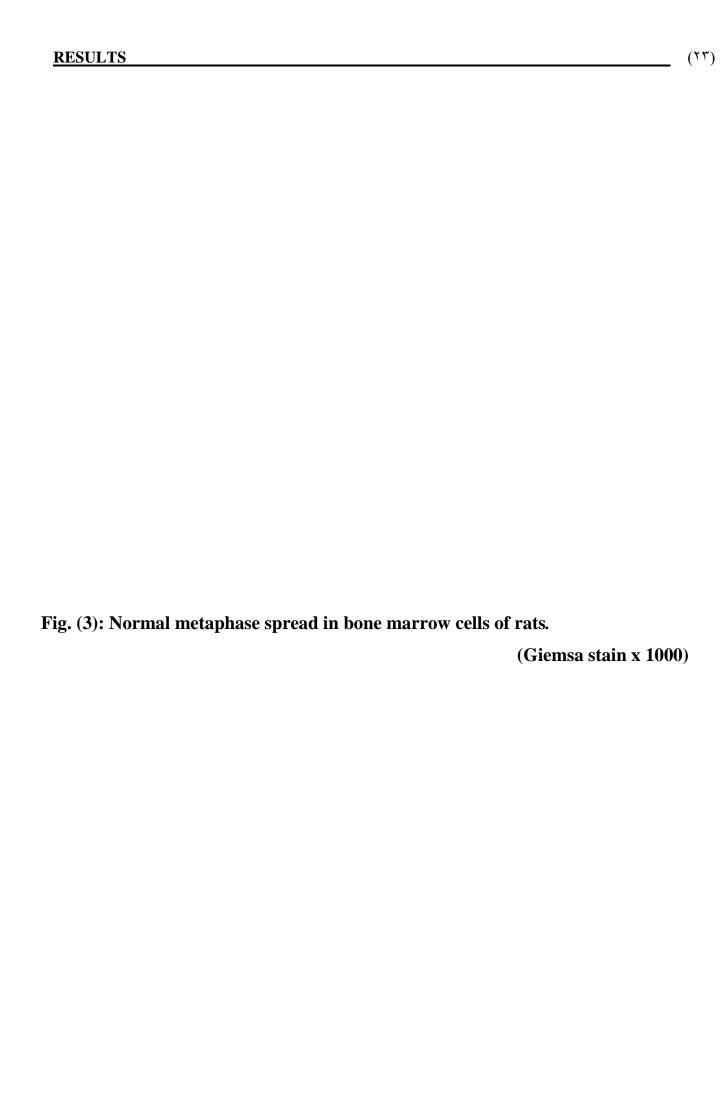
Various chromosomal aberrations are observed in the bone marrow cells of both male and female rats treated with different doses of lornoxicam. Both numerical and structural types of aberrations are identified and quantitated relative to none-treated control which have 42 chromosomes and represented in (Fig. 3).

#### **I-Structural aberrations:**

Include chromatid deletion (Fig. 4), chromatid gap (Fig. 5), break (Fig. 6), fragmentation (Fig. 7), centric fusion (Fig. 8), centromeric attenuation (Fig. 9) and end to end association (Fig. 10).

### **II-Numerical aberrations:**

Include euploidy and aneuploidy. The stickness 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 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. 11).



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Fig. (4): Metaphase spread showing deletion (D) in bone marrow cells of rats treated with the NSAID lornoxicam.

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Fig. (5): Metaphase spread showing gap (G) in bone marrow cells of rats treated with the NSAID lornoxicam.

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Fig. (6): Metaphase spread showing break (B) in bone marrow cells of rats treated with the NSAID lornoxicam.

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Fig. (7): Metaphase spread showing fragment (F) in bone marrow cells of rats treated with the NSAID lornoxicam.

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Fig. (8): Metaphase spread showing centric fusion (CF) in bone marrow cells of rats treated with the NSAID lornoxicam.

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Fig. (9): Metaphase spread showing centromeric attenuation (CA) in bone marrow cells of rats treated with the NSAID lornoxicam.

(Giemsa stain x 1000)

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Fig. (10): Metaphase spread showing end to end association (EE) in bone marrow cells of rats treated with the NSAID lornoxicam.

(Giemsa stain x 1000)

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Fig. (11): Metaphase spread showing sticky (S) in bone marrow cells of rats treated with the NSAID lornoxicam.

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# A-Structural aberration:

#### 1-Deletion:

Table (1), Fig. (12), shows the mean values of chromatid deletion in 50 metaphases of female rats treated with different doses of lornoxicam. It represents a significant difference between the control and the treated animal groups. The treatment with 1/5 LD50 of lornoxicam revealed higher significant values of deletion after 12 hrs, 24 hrs, 48 hrs and 5 days when compared with the control values. The administration of both 1/10 and 1/20 LD50 of lornoxicam increased the deletion values significantly in the whole trial period except at 24 hrs.

Also chromatid deletion of male rats treated with the same doses of lornoxicam represented significant higher values than control animals during the whole experiment (Table 2, Fig. 13)

### 2-Chromatid gaps:

The mean values of chromatid gaps showed the same pattern in both females and males (Fig. 14 and 15).

A significant increase was observed at all intervals and after the treatment of all doses except the doses of 1/20 LD50 and 1/5 LD50 at 5 days in females (Table 2), and the dose of 1/20 LD50 at 12hrs in males (Table 3).

The highest values of gap was observed at 5 days of 1/10LD50 of lornoxicam exposure, in both females and males, also gap data recorded a very sharp increase after 12 hrs in both females and males exposed to 1/5 LD50 lornoxicam.

# 3. Chromatid breaks:

Table (3), Figure (16), shows the mean values of chromatid break in 50 metaphases of female rats treated with different doses of lornoxicam, it represents a

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significant difference between the control and the treated animal groups given 1/20 LD50 after all time of treatment, while at 1/10 LD50 only at 24hrs, at the same time at 1/5 LD50 (the higher dose) there is a significant difference at 12 hrs and 5 days.

Table (3), Figure (17), showed the mean values of chromatid break in 50 metaphases of male rats treated with different doses of lornoxicam, it represents a significant difference between the control and the treated animal groups given 1/20 LD50 and 1/10 LD50 at 48hrs and 5 days, while at 1/5 LD50 at all periods.

### 4-Fragmentation:

The mean values of fragments showed the same pattern in both males and females (Fig. 18 & 19). A highly significant increase was observed at all intervals and after the treatment of all doses with the exception of the dose of 1/20 LD50 at 12hrs which represents only a significant difference (Table 4).

### 5-Centric fusion:

A significant increase was observed at all intervals and after the treatment of the doses of 1/10 LD50 and 1/5 LD50 in both females and males (Fig. 20 and 21). While, the exposure of the animals to a dose of 1/20 LD50 showed a significant increase only at 12hrs in females and at 12hrs and 48hrs in males (Table 5).

## **6-Centromeric attenuation:**

Figure (22) and figure (23) showed the mean values of centromeric attenuation in 50 metaphases of females and males, respectively, treated with different doses of lornoxicam. It represented highly significant increase of treated animal groups than the control in both females and males. The doses of 1/20 LD50 at 12hrs in females and 1/20 LD50 at 12hrs, 24hrs and 48hrs in males recorded no significant differences (Table 6).

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## 7-End to end association:

Figure (24) and (25) showed the mean values of end to end association in 50 metaphases of both females and males ,respectively, the mean values of treated groups in both females and males represented a higher significant increase than in the control group (Table 7).

## **B-Numerical aberrations:**

### 1-Chromatid stickiness:

The mean values of chromatid stickiness in cells of bone marrow of females rats treated with three doses of lornoxicam were significantly higher than after 12hrs, 48hrs and 5 days and were significant after 24 hrs (Table 8, Fig. 26).

In males rats, the mean values for cells with chromosomal stickiness per 50 metaphases were highly significant than control for all doses at all periods of time except 1/20 LD50 and 1/10 LD50 at 12hrs (Table 8, Fig. 27).

## 2-Aneuploidy:

Table (9), figure (28), shows the number of cells with monosomic chromosomes of female rats, it shows that there is a high significant difference with the dose of 1/10 LD50 at 5 days and a significant difference with the doses of 1/20 LD50 at 5 days and 1/10 LD50 at 48hrs.

Table (9), figure (29), shows the number of cells with monosomic chromosomes of male rats, it shows that there is a high significant difference only with the dose of 1/10LD50 at 5 days and a significant difference only with the doses of 1/20 and 1/10 LD50 at 5 days.

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### Cells with one type of aberrations:

The mean values of treated groups in females rats represented highly significant increase than in control group for cells with one type of aberrations, it is clear that there is highly significant difference between the control and the treated animals with a dose of 1/10 LD50 at 24hrs and48 hrs and with a dose of 1/20 and 1/5 LD50 at 5 days (Table 10,fig. 30).

Table (10), figure (31), shows the cells with one type of aberrations in male rats, it is clear that there is highly significant difference between the control and all the treated animals with a dose of 1/20 LD50 except at 12hrs and at 5 days with the doses of

1/10 LD50 and 1/5 LD50.

#### Cells with more than one type of aberrations:

Table (11), figure. (32), shows the cells with more than one type of aberrations in female rats, it is clear that there is highly significant difference between the control and all the treated animals with all doses except of 1/20 LD50 at 5 days and of 1/10 LD50 at 48 hrs and 48 hrs and 5 days.

Table (11), figure (33), shows the cells with more than one type of aberrations in male rats, it is clear that there is a high significant difference between the control and all the treated animals with all doses except of 1/20 LD50 at 5 days and of 1/10 LD50 and 1/5 LD50 at 48 hrs.

## Mitotic index:

Table (12), figure (34), and figure (35) show the mitotic index (number of dividing cells per 1000 cells) of female and male rats, respectively, treated with

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different doses of lornoxicam. It is clear that the mean values of mitotic index decreased after 12hrs of injection at all doses, then it regain increased gradually after all times of injections.

Table (13), figure (36) and table (14), figure (37) show the total structural aberrations occurred in female and male rats, respectively, of treated groups. There is highly significant difference between control and all treated animal groups.

Table (14) and table (15) summarize the mean percentage of chromosomal abnormalities observed in the bone marrow cells of female and male rats, respectively, after treatment with different doses of lornoxicam.

Table (16) and table (17) summarize the monosomic and mitotic index observed in the bone marrow cells of female and male rats, respectively, after treatment with different doses of lornoxicam.