SUMMARY AND CONCLUSION

The present work aimed to study the effect of chronic administration of some currently used NSAIDs, namely, indomethacin, piroxicam and diclofenac on the rate of mitosis and on the chromosomal pattern of bone marrow cells of albino rat.

Bone marrow samples used through this study were obtained from 200 albino rats. They were divided into 4 equal groups, each comprising 50 animals. In the first group, the animals were given indomethacin at a dose of 3 mg/kg daily. In the second group, the animals were given piroxicam at a dose of 1 mg/kg daily. In the third group, the animals were given diclofenac at a dose of 2 mg/kg daily. The three groups were given the drugs for 10,20,30, 45 and 60 days. In the fourth group, the animals were give 5% gum arabic aqueous solution daily for 10,20,30,45 and 60 days and were used as controls. Observations of the cell kinetics and cytogenetic changes of the bone marrow cells were carried out on 10 rats from each group after 10,20,30,45 or 60 doses of drug administration. The method of preparing metaphase spreads from bone marrow was used according to **Palmer et al. (1972)** and Giemsa stain was prepared according to the method described by **Genest and Auger (1963).**

For each rat, 500 cells were counted and the percentage of the transformed cells were calculated. For chromosomal analysis, 50 metaphases were examined for the presence of any chromosomal anomalies either structural or numerical, and the results were tabulated and tested using the Student t test. The results of the present study revealed the following :

1- The mean transformed cell percentage in control samples after 10,20,30,45 and 60 days were 24.28%±1.5623,23.96% ±2.0336, 23.66%±1.5762, 24.36%±1.8808 and 24.06%±1.8055 respectively and there was no significant statistical difference between them ($P<0.05$).

2- The mean transformed cell percentage in indomethacin samples after 10,20,30,45 and 60 days were 23.96% ± 1.7489, 22.98% ± 2.147, 22.2% ± 1.9067, 20.78% ± 1.6357 and 17.96% ± 2.2125 respectively and there was a high statistically significant reduction in the samples examined 45 and 60 days after drug administration ($P<0.001$). On the other hand, the samples examined 10,20 and 30 days after the drug administration revealed no significant statistical difference in comparison with the control ($P<0.05$).

3- The mean transformed cell percentage in piroxicam samples after 10,20,30,45 and 60 days were 23.8%±1.917, 22.96%±2.1602, 21.94%±2.1338, 21.22%±1.6179 and 18.26% ±2.2671 respectively and there was a high statistically significant reduction in the samples examined 45 and 60

days after drug administration (P <0.001). On the other hand, the samples examined 10,20 and 30 day after the drug administration revealed no significant statistical difference in comparison with the control (P <0.05).

4- The mean transformed cell percentage in diclofenac samples after 10,20,30,45 and 60 days were 24.44% ± 1.7074, 23.28%±2.0221, 22.66%±2.0773, 21.68% ± 1.9078 and 18.64% ± 2.3626 respectively and there was a high statistically significant reduction in the samples examined 45 and 60 days after the drug administration (P <0.001). On the other hand, the samples examined 10,20 and 30 days after the drug administration revealed no significant statistical difference in comparison with the control (P <0.05).

5- The total numbers of chromosomal aberrations in 500 examined cells for the controls including structural anomalies, aneuploidy and polyploidy were as follows :

a- After 10 days : 3 : 3 : 8

b- After 20 days : 3 : 4 : 7

c- After 30 days : 2 : 4 : 8

d- After 45 days : 2 : 3 : 8

e- After 60 days : 2 : 3 : 9

6- The total number of chromosomal aberrations for the indomethacin samples including structural anomalies, aneuploidy and polyploidy were as follows :

a- After 10 days : 2 : 4 : 7

b- After 20 days : 3 : 3 : 9

c- After 30 days : 4 : 5 : 11

d- After 45 days : 7 : 9 : 15

e- After 60 days : 9 : 13 : 19

7- The total number of chromosomal aberrations for the piroxicam samples including structural anomalies, aneuploidy and polyploidy were as follows :

a- After 10 days : 2 : 3 : 7

b- After 20 days : 3 : 3 : 8

c- After 30 days : 4 : 5 : 10

d- After 45 days : 8 : 9 : 14

e- After 60 days : 10 : 11 : 18

8- The total number of chromosomal aberrations for the diclofenac samples including structural anomalies, aneuploidy and polyploidy were as follows :

a- After 10 days : 2 : 3 : 8

b- After 20 days : 3 : 4 : 7

c- After 30 days : 3 : 5 : 9

d- After 45 days : 5 : 7 : 13

e- After 60 days : 9 : 11 : 17

9- The chromosomal aberrations in the studied groups examined 10,20 and 30 days revealed no significant statistical difference in comparison with the control ($P < 0.05$). On the other hand, the three drugs caused significant increase in chromosomal anomalies, structural and numerical, after drug administration for 45 and 60 days as compared to normal untreated controls ($P < 0.05$).

From the previous results it may be concluded that the significant decrease of transformed cells occurred 45 and 60 days after drug administration for indomethacin, piroxicam and diclofenac and the chromosomal aberrations found were statistically significant after these therapeutic daily administrations for 45 and 60 days. So, one may assume that the tested drugs exhibit their effect after 45 and 60 days of administration.

In addition, the choice of any of the drugs will be according to the sensitivity of the disease in question and/or according to the accomodation of the patient to the side effects since all drugs had nearly the same effect on the cell kinetics and the chromosomal pattern.