SUMMARY AND CONCLUSION

In the present study, the evaluation of the side effects induced by sodium valproate in epileptic patients was investigated. In addition, the effect of the drug on brain chemical neurotransmitters namely GABA and 5HT was studied to explain some of its side effects. Moreover, the teratogenic effect of the drug was studied.

To fulfill this aim, the present study included two parts:

a) **The clinical part** was to study the tolerability of sodium valproate in epileptic patients.
b) **The experimental part** was to explain the mode of action of sodium valproate and its effect on 2 chemical neurotransmitters namely GABA and 5HT and to explain some unwanted side effects. Moreover, to study its teratogenic effect.

The clinical part of this study was carried out on 20 epileptic patients, they were treated as out patients and were randomly allocated to sodium valproate (30-50 mg/kg/oral) for at least 3 months.

All the patients were both clinically and laboratory investigated before treatment and after 3 months of treatment. The findings, in the present study revealed that side effects were found in 35%; these unwanted effects included sedation (5%), headache (5%), tremors (10%), allergy (5%), gastrointestinal disturbance (10%), weight gain (20%) and appetite gain (10%).

facilitation of GAD, and this elevation of GABA may explain its anticonvulsant effect.

In addition, the increased release of GABA may explain weight gain and sedation in epileptic patients under valproate treatment.

Moreover, results of the present work revealed significant elevation of 5HT in cerebral cortex and midbrain, and this may result from increased tryptophan availability, MAO_B inhibition, and decreased transport of 5HIAA.

The elevated 5HT concentration in the cerebral cortex may add another explanation of the anticonvulsant effect of the drug. But, 5HT level was significantly reduced in thalamus, hypothalamus, this may be due to the poor concentration of the drug in this area. This may explain stimulant effect of valproate on appetite.

Regarding, the teratogenic effect of the drug, results of the present work revealed that, maternal administration of sodium valproate (400 mg/kg . oral /day) induced non-significant change in the resorption rate, number of implantation or number of live fetuses.

Moreover, external examination of fetuses revealed that 3 fetuses with short neck (15%). On examination of fetuses skeletons, there were 6 rats (30%) showed spina bifida, 3 (15%) were with absence of angle of mandible, and ossofic centers in upper and lower limbs this may be due to interference with folate metabolism.

From the present clinical and experimental findings, we may conclude that some of side effects of sodium valproate were dose dependent as sedation, headache and tremors, while others were due to both toxic reactions and non-dose-related idiosyncratic as rashes.

Some, unwanted effects may be due to change of the chemical neurotransmitters pattern as sedation and weight gain which may be due to increased concentration of GABA. Moreover, other unwanted effects as increased appetite may be due to lowering the concentration of 5HT in hypothalamus. In addition, the anticonvulsant effect of sodium valproate may be due to increase levels of cerebral GABA and 5HT.

The present work revealed that, the liver injury induced by valproate may be due to degeneration of hepatocytes caused by the drug or its metabolites.

Finally, the present work revealed a strong association in valproate treated experimental animals and incidence of spina bifida, this may be due to interference with folate metabolism. Moreover, other teratogenic effect like short neck, absence of angle of mandible, and absence of ossified centers in limbs were detected.