SUMMARY AND CONCLUSIONS

Domperidone is a new antiemetic drug of novel chemical structure. It is free from most of the side effects usually observed with the neuroleptic antiemetic drugs. Furthermore, it differs from metoclopramide in only possessing a peripheral site of action.

The present study is carried out to explore the mechanism of action of domperidone as gastrokinetic agent. In addition, study of its interaction with acetylcholine, histamine, barium chloride, 5-hydroxy-tryptamine and dopamine. Experiments were carried out on isolated rabbit intestine, guinea pig ileum, rat fundus and on the intestinal motility of the intact rabbits.

Results obtained in the present study pointed out that domperidone possesses a stimulant action on the G.I.T. motility mediated through stimulation of nicotinic receptors of parasympathetic ganglia of the intramural myenteric plexus. This observation is backed by the finding that such stimulant action is blocked by the ganglion blocker nicotine and chlorisondamine on both isolated and intact preparations respectively.

Domperidone was also found more or less to modulate the action of acetylcholine. It also attenuates the stimulant action of barium chloride, histamine and 5-hydroxytryptamine on the isolated rabbit's intestine, guinea pig ileum and rat fundus strips respectively. This attenuation is most probably due to a non-specific blocking property of relatively large doses of domperidone. Regarding dopamine, domperidone was found to antagonise the inhibitory action of dopamine both in-vitro and in-vivo intestinal preparations through blockade of specific dopamine receptors in the G.I.T. This antidopamine action might contribute to the gastrokinetic effect of the drug and to the antiemetic property of the drug.

In conclusion, domperidone was found to possess the following pharmacological actions:

a- Stimulant action of gastrointestinal motility most probably mediated through stimulation of central cholinergic (nicotinic) receptors of the myenteric intramural parasympathetic ganglia.

b- More or less mild attenuation of the acetylcholine stimulant action.