S U M M A R Y

In the present study, it was found that metoclopramide produced in the isolated rabbit's jejunal smooth muscle preparations an initial inhibitory response in the amplitude of contraction followed by a marked stimulant action, when administered in doses varying between 0.5 ug/ml to 32 ug/ml. The inhibitory action of metoclopramide was found to be greater in larger doses varying from 64 ug/ml to 128 ug/ml.

In addition, it was found that metoclopramide produced only a stimulant action on the isolated rabbit's duodenal smooth muscles when given in doses varying between 0.5 ug/ml and 2 ug/ml.

Similar increase in the tone and also the amplitude of the isolated guinea pig ileal smooth muscle was demonstrated when metoclopramide was administered in doses varying from 4 ug/ml to 128 ug/ml. Such stimulant actions were found to be not dose dependent.

Concerning the nature of the biphasic inhibitory and stimulant actions of metoclopramide, a study was performed on the isolated rabbit's jejunal smooth muscle,

where it was found that the inhibitory action is mostly due to a direct depressant action and does not implicate stimulation of the alpha and beta adrenergic receptors.

In contrast, it was found that the stimulant action of metoclopramide was cholinergic in origin.

However, from the data presented in the present work, it is evident that metoclopramide sensitizes the isolated rabbit's jejunal smooth muscle to the action of acetylcholine when administered in doses 0.1 ug/ml to 0.8 ug/ml. And also the guinea pig ileal smooth muscle when administered in doses varying from 0.4 ug/ml to 32 ug/ml. Such effect was completely abolished by atropine.

By contrast, small doses of metoclopramide varying between 0.1 ug/ml to 0.2 ug/ml and larger doses varying between 64 ug/ml to 128 ug/ml were found to produce an inhibitory action on acetylcholine induced contractions on the guinea pig ileal smooth muscle preparation.

Moreover, similar sensitization of guinea pig ileal smooth muscle to histamine was demonstrated in this work when metoclopramide was administered in doses varying between 0.1 ug/ml to 0.4 ug/ml.

In contrast larger doses of metoclopramide ranging between 16 ug/ml to 128 ug/ml produced an inhibitory action on the histamine.

Concerning the interaction of metoclopramide with 5-hydroxytryptamine on the isolated rat fundus strip preparations, they were always inhibitory and metoclopramide never potentiated but completely prevented the effect of 5-hydroxytryptamine.

Metoclopramide is shown to antagonise the inhibitory responses to dopamine suggesting that the drug is a blocker of dopamine receptors in the gut.