CONCLUSIONS :

Streptomycin, kanamycin, viomycin, neomycin and paromomycin inhibited the spontaneous contractions of the guinea pig ileum. These antibiotics antagonised competitively the contractile response to acetylcholine of the guinea pig ileum and the frog rectus abdominis muscle.

Unlike the antibiotics, the degradation products, streptidine and streptamine induced contractions of the guinea pig ileum. The stimulant action on the ileum was blocked by atropine (10 ng/ml) and hexamethonium (10 µg/ml) indicating a parasympathomimetic action. Though streptidine potentiated the spontaneous contractions of the guinea pig ileum, it antagonised the contractile response to acetylcholine of the guinea pig ileum and the frog rectus abdominis muscle. Streptamine however, potentiated the contractile response to acetylcholine of the frog rectus abdominis muscle.

Thus the presence of additional amino groups in streptidine mask the acetylcholine-like action of streptamine and contribute to its antiacetylcholine action. The presence of amino acids as in

viomycin or sugar residues as in other antibiotics stabilises the antiacetylcholine action.

The antibiotics depressed the isolated rabbit heart while the degradation products had stimulant action. The stimulant action of the degradation products was not observed in hearts obtained from reserpine treated rabbits, indicating an indirect sympathomimetic action.

The amino acids or the sugar residues present in the antibiotics seem to mask the indirect sympathomimetic action and contribute to the inhibitory action. This was confirmed by the effects on blood pressure of anaesthetised cat and dog in which streptidine and streptamine (20 mg/kg) both elicited a pressor response while the antibiotics (20 mg/kg) lowered the blood pressure.

The antibiotics (10 mg/kg) injected repeatedly every 10 min lowered the blood pressure of cat. The degradation products administered in a similar way raised the blood pressure initially and subsequently lowered it.

The antibiotics and the degradation products changed the vasodepressor response to histamine into a biphasic one and potentiated the pressor

component of the biphasic response to McN-A-343 and the pressor response to DMPP. The fall in blood pressure in response to vagus stimulation was inhibited and the vagal escape was facilitated. The responses to exogenously administered adrenaline and noradrenaline were not affected significantly by the antibiotics or the degradation products.

The modification of responses to histamine, McN-A-343, DMPP and vagus stimulation could not be due to sensitisation of the cardio vascular system to effects of released adrenaline and noradrenaline, to inhibition of the up-take mechanism of these amines or to inhibition of monoamino-oxidase enzyme since the responses to exogenously administered adrenaline and noradrenaline were uneffected. By a process of exclusion, it is suggested that the modified responses following the antibiotics and the degradation products were probably due to increased release of sympathonimetic amines like adrenaline and noradrenaline.

The contractions of the nictitating membrane in response to stimulation of the preganglionic superior cervical fibres were not affected by the antibiotics. Streptidine and streptamine both potentiated the contractile response of the

nictitating membrane. However, the potentiation was not comparable ($P < 0.05$) to the potentiated pressor responses to McN-A-343 and DMPP ($P < 0.01$ in both cases). This suggested that the antibiotics and the degradation products did not affect the release of acetylcholine.

The degradation products, streptidine and streptamine both possessed parasympathomimetic action and indirect sympathomimetic action. These effects were not observed with the antibiotics. However, the similarities in the chemical structure (presence of guanido group) of the antibiotics and the degradation products are well reflected in their other biological actions presented in the investigation.

The results suggest that the pharmacological actions of the antibiotics are mainly manifested by the central core of the molecule of the antibiotics containing the guanido groups which is probably also responsible for various toxic manifestations of the antibiotics reported in the literature.