CHAPTER - 6

SUMMARY

6. SUMMARY

In view of the paucity of extant pharmacological data on goat tissues in general and goat spleen in particular, a study was undertaken to investigate some adrenergic and cholinergic mechanisms in goat isolated spleen and some other goat tissues.

6.1. Splenic strip

6.1.1. Noradrenaline (NA; 0.85×10^{-9} M - 3.82×10^{-8} M) and adrenaline (Adr; 0.27×10^{-9} - 1.7×10^{-8} M) elicited concentration-related contractions of goat isolated spleen strips. The contractions were blocked by phentolamine (1.26×10^{-8} M - 8.3×10^{-7} M) in a competitive manner. The pA2 values of phentolamine obtained with NA and Adr were 8.0 and 8.06 respectively and are close to those reported in the literature (Gulati et al., 1968; Sanders et al., 1975) indicating the similarity of goat spleen alpha-receptor with that present in other tissues.

6.1.2. Cocaine (3×10^{-5} M) failed to potentiate response to NA and Adr.

6.1.3. The NA content of the goat spleen was 13.72±0.18 nmoles/g. of tissue. Goat spleen strips incubated with various concentrations of NA (0.59×10^{-6} M - 2.36×10^{-5} M) failed to take up NA. It is possible that if sympathetic nerves exist in goat spleen they lack $uptake_1$ mechanism. Alternatively it is possible that sympathetic nerves are absent and the results could be accounted for due to the presence of chromaffin tissues.

6.1.4. Tyramine (1.07×10^{-5} M - 3.46×10^{-4} M) elicited reproducible concentration-related contractions and there was no tachyphylaxis. Tyramine-induced contractions were blocked by phentolamine (1.86×10^{-8} M). Prior exposure of the tissues to high concentrations of tyramine (0.83×10^{-3} M) or naphazoline (8.13×10^{-4} M) desensitized it to both these amines, but not to NA. Prior exposure of the tissue to a high concentration NA (1.63×10^{-4}M) desensitized it to NA, but not to tyramine or naphazoline. It would appear that tyramine acts on alpha-adrenoceptor at site which is different from the one on which NA acts.

6.1.5. Isoprenaline (ISO; 9×10^{-7} M - 3.6×10^{-6} M) failed to produce any effect per se or any relaxation of KCl-induced spasm. Higher concentrations of ISO (1.63×10^{-5} M - 2.58×10^{-4} M) per se produced concentration-related contraction which was blocked completely and irreversibly by phenoxybenzamine (0.32×10^{-6} M) suggesting alpha-receptor stimulating action of ISO.

6.1.6. Acetylcholine (ACh; 1.68×10^{-7} M - 3.38×10^{-5} M) produced concentration related contractions. The contractions were not potentiated by physostigmine (7.72×10^{-6} M) suggesting the absence of the enzyme AChE; this conclusion was supported by the failure of spectrophotometric measurements to detect AChE. ACh-induced contractions were competitively blocked by atropine (4.32×10^{-8} M - 4.32×10^{-7} M). The pA_2 value of atropine was 7.6 which was somewhat less than that reported in literature (Schild, 1947) . This result suggests the presence of muscarinic receptors in goat spleen and that atropine has less affinity for muscarinic receptor of this tissue than for those of other tissues reported in the literature(Schild, 1947).

6.1.7. 5-hydroxytryptamine (5-HT; 3.94×10^{-6} M - 6.31×10^{-5} M) elicited concentration-related contractions but showed tachyphylaxis when cumulative concentration-response curve pannels were repeated at 60 min intervals. However, EC_{50} concentrations of 5-HT elicited reproducible contractile responses repeated at intervals of 30 minutes. Phentolamine, xylocaine and cyproheptadine blocked EC_{50} responses. These results suggest that responses to 5-HT may atleast partly be direct on 5-HT receptors, and partly through release of NA and support the proposal of Innes (1962) made for cat spleen.

6.1.8. In the Ca^{++}-free medium containing EDTA (1×10^{-5} M) there was significant inhibition of responses to 5-HT (7.29×10^{-5} M) and KCl (2.69×10^{-2}M). However, responses to NA (7.74×10^{-8} M) and tyramine (5.46×10^{-6} M) were not altered significantly. These results are in accord with earlier reports in the literature that contraction with K^{+} is mainly dependent upon extracellular Ca^{++} permeability, contractions with 5-HT is partially dependent upon extracellular Ca^{++} while contractions with NA are mainly dependent upon intracellular Ca^{++} through release from bound sites (Kalsner et al., 1970; Huggins and Weiss, 1968; Hinke, 1965; Jhamnadas and Nash, 1967).

6.1.9. The concentration-response curve of histamine (1.63×10^{-7} M - 5.21×10^{-5} M) was competitively antagonized by different concentrations of H_1 receptor blocker antazoline (1.99×10^{-9} M - 1.99×10^{-8} M) in a concentration-related manner, but was not altered by atropine (1.44×10^{-5} M) hexamethonium (2.76×10^{-5} M) and phentolamine (6.30×10^{-6} M) added together in the bath. The pA_2 value of antazoline was 8.84 which is about 1 log unit higher than values reported in the earlier literature (Reuse, 1948; Gulati et al., 1968) suggesting higher affinity of antazoline for goat-spleen H_1-receptors.

6.2. Aortic strip

6.2.1. NA (0.52×10^{-8} M - 1.92×10^{-7} M) elicited concentration-related contractile effect which was not altered significantly by cocaine (3.0×10^{-5} M) or reserpine (5.43×10^{-6} M). The NA content of goat aorta was 6.8 ± 0.36 nMoles/g of tissue. No significant increase in NA accumulation was obtained on incubating goat aorta with different concentrations of NA for 1, 5 and 15 min time periods. These results suggest that both the possibilities entertained for goat spleen (see 6.1.3) may also hold for goat aorta.

6.2.2. Responses to NA were inhibited by 6.3×10^{-8} M phentolamine suggesting alpha-receptor action of NA on goat aorta.

6.2.3. No measurable responses to tyramine (4.24×10^{-5} M - 3.39×10^{-6} M) were obtained, precluding further experiments.

6.3. Tracheal chain

6.3.1. ISO (2.25×10^{-9} M - 1.44×10^{-7} M) produced concentration-related relaxant effects in tracheal chain preparations contracted with pilocarpine (3.70×10^{-6} M) or with KCl (1.36×10^{-2} M). Different concentrations of propranolol could inhibit relaxant effect of ISO in a competitive manner suggesting beta-receptor action of ISO on goat trachea. The pA_2 value of propranolol was 7.78 and is close to values for this beta-receptor blocker reported by others (Takagi and Takayanagi; 1970; Gulati et al., 1973; Ariens, 1967; Wesserman and Bernard, 1974) suggesting that beta-receptors of this tissue are similar to those of other tissues.

6.3.2. No modification of responses to ISO (2.25×10^{-9} M - 1.44×10^{-7} M) by phenoxybenzamine was observed and it is, therefore, suggested that both presynaptic and postsynaptic alpha-receptors may be absent in goat-trachea.

6.3.3. Normetanephrine (2.73×10^{-5} M) potentiated responses to ISO (2.25×10^{-9} M - 1.44×10^{-7} M). Since normetanephrine is a prototype $uptake_2$ blocker, it is suggested that $uptake_2$ mechanism for catecholamine disposition exists in this tissue.

6.3.4. Lowering of bath temperature from 37 °C ± 0.5 °C to 22 °C ± 0.5 °C potentiated responses to ISO (2.25×10^{-9} M - 1.44×10^{-7} M); this may be due to a generalized inhibitory action of lower temperature on enzyme activity.

6.3.5. The contraction due to submaximal concentration of histamine (1.0×10^{-5} M) was not significantly affected by H_2-receptor blocker metiamide (2.72×10^{-5} M) but was completely blocked by H_1-receptor blocker mepyramine (2.50×10^{-6} M) suggesting the presence of only H_1-receptors in goat trachea.

6.3.6. Submaximal concentration of histamine (1.0×10^{-5} M) did not produce any relaxation of the spasm induced by KCl (1.36×10^{-2} M) indicating the absence of H_2-receptors in goat trachea.