SUMMARY
AND
CONCLUSION
1. A new series of sulphonylurea derivatives comprising of 45 compounds was initially screened for their hypoglycaemic properties on the normal fasting blood sugar level (F.B.S.) of albino rats. Chlorpropamide was used as the standard reference drug.

2. Structure activity relationship was established on F.B.S. Five, more potent compounds were selected for detailed investigations regarding their mechanism of action and general pharmacological properties.

3. Of all the compounds tested compounds 4 and 13 were found to be more potent as hypoglycaemic agents on fasting blood sugar level. The magnitude of hypoglycaemic action was comparable to chlorpropamide but the total duration of action was greater than that of chlorpropamide. The hypoglycaemic action ran parallel to the blood concentrations of these compounds.

4. Both intravenous and oral glucose tolerance curves were modified by all the compounds tested. Compounds 4 and 13 were found to be most potent in increasing the magnitude of glucose tolerance. Though the results were
comparable with chlorpropamide, compound 13 had a longer duration of action.

5. In experimental diabetes produced by alloxan most compounds tested were effective but compounds 4 and 13 produced antidiabetic action in a shorter time. The results were comparable to chlorpropamide.

6. Anterior pituitary induced experimental diabetes was partially antagonised by most of the compounds tested indicating their action against glyconeogenesis and catabolism induced by anterior pituitary extracts.

7. Adrenaline induced hyperglycaemia was slightly antagonised by most of the compounds including the reference drug chlorpropamide.

8. Most compounds showed increased uptake of glucose by the rat diaphragm and diminished glycogenolysis by rat liver slices. Thus indicating additional peripheral sites in the mechanism of their hypoglycaemic action.

9. None of the compounds tested exhibited any marked pharmacodynamic actions except some hypertensive action and neuromuscular blockade
at a very high dosage level. No toxicity was seen, acute or chronic with any of the compound tested even on prolonged administration with very high doses.

10. It is concluded that the sulphonylurea compounds tested produce their hypoglycaemic action essentially by stimulating beta cells of pancreas, but partially through their peripheral action i.e. increased glucose uptake by the tissues and diminished glycogenolysis. Some of the compounds in the present series viz. compound 4 (1-(p-chlorobenzyl)-3-(p-bromobenzenesulphonyl) urea) and compound 13 (1-(p-chlorobenzyl)-3-(p-chlorobenzenesulphonyl) urea) have hypoglycaemic action comparable to chlorpropamide but the duration of action of new compounds is greater than chlorpropamide. It is postulated that some of these compounds may ultimately find their use in clinical practice since they have the added advantage of longer duration of action.