SUMMARY AND CONCLUSION

Diabetes is presently regarded as a syndrome rather than a disease. The syndrome of diabetes is characterized by disorders of metabolism of carbohydrates, protein and lipids due to insulin deficiency and/ or insulin resistance evolving from interaction of a variety of genetic and environmental factors. The root bark of *Salacia oblonga* Wall. has been reported to contain hypoglycaemic principles. Therefore it is pertinent to isolate the antidiabetic principles and study their ameliorating effects in diabetes induced deranged metabolism.

Activity in normal and diabetic rats

An antidiabetic principle of *S. oblonga* root bark was isolated by a bioguided solvent extraction. This active principle was found to be a petroleum ether extract being eluted by acetone, referred to as S. ob2. The S. ob2 (250 mg kg\(^{-1}\)) significantly lowered the fasting blood glucose in both normoglycaemic (22.5%) and STZ-induced moderately diabetic rats.

Long-term effects in diabetic rats

The activity of S. ob2 was compared to those of the effective doses of glibenclamide and insulin on one-month treatment. The activity of S. ob2 was comparable to that of glibenclamide. It improved the serum insulin level, body weight, haemoglobin, serum protein and controlled urine sugar, glycosylated haemoglobin, and blood urea in treated diabetic rats as is the case with glibenclamide and insulin. S. ob2 ameliorated some of the deranged enzymes such as hexokinase, glucose-6-phosphatase and lactate dehydrogenase. The lipogenic enzymes that were deranged in diabetes *viz.*, glucose-6-phosphate dehydrogenase,
malic enzyme, 6-phosphogluconate dehydrogenase and isocitrate dehydrogenase were also significantly ameliorated by S. ob2, glibenclamide and insulin in an increasing order. In the same way 14C-glucose incorporation into the liver glycogen was significantly increased in the liver of S. ob2, glibenclamide and insulin administered diabetic rats.

The deranged lipid levels (cholesterol, triacylglycerols, phospholipids and serum lipoprotein cholesterol) were improved by S. ob2 as is the case with other two drugs, the glibenclamide and insulin. The activities of some of the deranged enzymes involved in lipid metabolism such as HMG CoA reductase and lipoprotein lipase were significantly ameliorated. 14C-acetate incorporation studies in to the tissue cholesterol demonstrated that S. ob2, glibenclamide and insulin improved the dyslipidemia in diabetic rats.

The hypoglycaemic principle also ameliorated the STZ-diabetic induced lipid peroxidation. The concentration of lipid peroxides (thiobarbituric acid reactive substances, conjugated dienes and hydroperoxides) were significantly lowered in the S. ob2, glibenclamide and insulin treated groups. The untreated diabetic rats showed an elevated level of lipid peroxides. The activities of scavenging enzymes viz., superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase present in the liver, heart and kidneys of the rats treated with S. ob2, glibenclamide and insulin were improved significantly. The antioxidant reduced glutathione levels were elevated in the rats treated with S. ob2, glibenclamide and insulin, as is the case with other two drugs. The concentration of free fatty acids was significantly lowered in the serum and tissue of the treated rats. Their order of activity was insulin > glibenclamide > S. ob2 in all above. The
mechanism of the action of the active principle is most probably dependent on a stimulation of insulin secretion, as it is not active in severely diabetic rats.

**Characterization of the principle and toxicological studies**

The active principle was further characterized through chromatography. A spectral study of the active fraction, which was also fluorescent in U.V light, showed that it is a terpenoid like compound. A toxicological study of the active fraction in normal rats further showed no significant toxic effect on long term treatment. The parameters studied were acute toxicity, chronic toxicity, body weight, general behavior, hemoglobin content, W.B.C count- total and differential counts, serum protein, serum glutamate pyruvate transaminase, serum glutamate oxaloacetate tansaminase, blood glucose, blood urea, alkaline phosphatase, urine albumin and sugar, post-mortem examination as well as histopathological studies.

**A water-soluble second hypoglycaemic principle that inhibits α-glucosidase**

A second hypoglycaemic principle was also identified in the root bark of *S. oblonga* as water-soluble fraction. This fraction is not an insulin secretagogue but acts by inhibiting α-glucosidase of the intestine, thus lowering the blood glucose. This water-soluble fraction is a competitive inhibitor of the α-glucosidases viz., sucrase and maltase similar in action to a known α-glucosidase inhibitor, acarbose. Treatment with this factor for one-month in diabetic rats improved the blood glucose, body weight and liver glycogen.

Thus *S. oblonga* root bark contains hypoglycaemic principles with various activities like hypolipidameic/antioxidant and α-glucosidase inhibitory effects, revealing their therapeutic value in diabetes. However to elucidate the exact mechanism of action of these principles further studies are warranted.