SUMMARY
Diabetes mellitus is a state in which homeostasis of carbohydrate and lipid metabolism is improperly regulated by insulin. This results primarily in elevated fasting and postprandial blood glucose levels. If this imbalanced homeostasis does not return to normal and continue for a retracted period of time, it leads to hyperglycemia that in due course turns into a syndrome called diabetes mellitus. In the present experimental study, one group of rabbits was made diabetic by intraperitoneal administration of alloxan (@ 80 mg/kg b.w.) and the other group of rabbits was kept as control (normal healthy) which received normal saline. The establishment of diabetes mellitus in alloxanized rabbits was confirmed by periodical elevated levels of fasting blood glucose, blood urea and serum creatinine. The alloxan-induced diabetic rabbits showed a decline in body weight throughout the experimental period. Further, the diabetic rabbits showed a change in behaviour such as dullness, lethargy, decreased physical activity, a tendency to lie down, polyuria and polydipsia. The subsequent effect of hyperglycemia on tissue morphology of diabetic rabbits revealed degenerative changes in most of the organs. The pancreatic sections showed necrosis, vacuolations, increased eosinophilia, islet congestion, nuclear changes, karyolysis, disappearing of nucleus and rarefaction of nuclear contents. However, in five month old alloxan-induced diabetic rabbits chronic pancreatitis, haemorrhage, proliferation of fibroblasts and disorganization of
pancreatic acini were observed. Using special stains (Halmi, 1952 and Scott, 1952), the number of beta cells in pancreatic islets were found to be highly reduced in contrast to control rabbits. The kidney sections of alloxan induced rabbits showed nephrosis, occlusion of tubules, proliferation of polygonal cells, lower nephron nephrosis and degenerative changes in cortex, subcapsular region, collecting tubules and tubular epithelium. Further, chronic nephritis, interstitial nephritis, tubular nephrosis and chronic changes in medullary sties were observed in five month old diabetic rabbits. The liver sections showed hepatosis (degeneration of hepatocytes), biliary hyperplasia, chronic hepatitis in prolonged diabetic rabbits. Heart sections revealed degenerative changes such as edema, haemorrhage and histocyte proliferation. Myocarditis as also observed in prolonged diabetic rabbits. The brain sections showed degeneration of neurons and edema in cerebellum. The lung sections showed haemorrhage, bronchial hyperplasia and emphysema in prolonged diabetic rabbits. Furthermore, alimentary canal showed intestinal congestion and gastritis. All these histomorphological changes were observed in alloxan-induced diabetic rabbits in comparison to saline-treated (control) rabbits. The pathological changes in tissues were found to be aggravated with the progression of disease.

In another set of experiment, one group of rabbits were made diabetic by intravenous administration of streptozotocin (@ 65 mg/kg b.w.) and the second group of rabbits were kept as control that received normal saline. The onset of diabetes in streptozotocin-induced group of rabbits was checked by raised levels of blood glucose (F), blood urea and serum creatinine. Further, behavioural changes were also observed in streptozotocin-induced rabbits like alloxan diabetic rabbits. However, a decline in body weight was observed initially which latter on, showed an increased trend throughout the experimental period. The subsequent effects of streptozotocin-induced diabetes in different organs of rabbits showed histomorphological changes. Pancreatic sections
showed slight congestion and mild degenerative changes in the acini. The acinar epithelium showed swelling and the cells within islets were fusiform and diminished in number. Using special stains (Halmi, 1952 and Scott, 1952) for quantitative study of islet cells, the number of beta cells were found to be reduced in comparison to saline-treated normal rabbits. The lung sections showed congestion and haemorrhage in alveoli and bronchioles. Further, congestion in kidneys, degeneration and congestion in liver, haemorrhage and myopathy in heart, and mild neuronal damage were observed in the streptozotocin-induced diabetic rabbits. However, no histopathological findings were observed in the alimentary canal but stomach sections showed proliferation of yeasts.

The experimental study was further extended to elucidate the therapeutic efficacy of antidiabetic drugs on biochemical, behavioural and histomorphological parameters of rabbits. For this purpose, rabbits were made diabetic by intraperitoneal administration of alloxan (80 mg/kg b.w.). When diabetes mellitus was well established which was confirmed by periodical estimation of blood glucose, blood urea and serum creatinine, the rabbits with a blood sugar (F) level above 250 mg/dl were selected for therapeutic study. The diabetic rabbits were divided into four groups viz., group II, group III, group IV and group VI excluding control (group I) rabbits. Group I served as normal control and received normal saline orally. Group II were untreated alloxanized diabetic rabbits and received normal saline orally. Group III alloxanized diabetic rabbits received water extract of Abroma augusta @ 2 ml daily. Group IV alloxanized diabetic rabbits received aqueous extract of Syzygium jambolanum @ 2 ml daily. Group V alloxanized diabetic rabbits received glimepiride @ 2mg/kg b.w. The assessment of treatment was checked on biochemical, behavioural and histomorphological ameliorations. The drug treated diabetic rabbits showed a significant improvement in behaviour in
contrast to saline-treated diabetic rabbits. The biochemical changes with regard to fasting blood sugar, blood urea and serum creatinine of all the drug treated diabetic rabbits showed a significant improvement comparable to the normal levels. However, glimepiride treated diabetic rabbits showed highly significant improvement in biochemical values followed by *Syzygium jambolanum* treated and *Abroma augusta* treated diabetic rabbits. Furthermore, a significant amelioration of diabetic organs were observed. The quantitative study of beta cells using special stains showed a high regeneration of beta cells in all the treated groups of diabetic rabbits. The highest number of regenerated beta cells were observed in glimepiride treated diabetic rabbits followed by *Syzygium jambolanum* treated and *Abroma augusta* treated diabetic rabbits respectively.

The therapeutic study for the management of diabetes mellitus in rabbits indicates that the drugs contain a variety of herbal/non-herbal ingredients that seem to act on a variety of targets by various modes and mechanisms. The entire experiment presents an overview of diabetic pathogenesis, particularly impaired carbohydrate metabolism leading to hyperglycemia. It analyses how herbal/allopathic medicines and their ingredients correct/manipulate the vitiated homeostasis of carbohydrate metabolism and other related complications particularly biochemical and histomorphological changes.