"The known is finite, the unknown is infinite; intellectually we stand on an islet in the midst of an illimitable ocean of inexplicability. Our duty in every generation is to reclaim a little more land"

- T.H. Huxley

Introduction
Diabetes Mellitus (DM) is a chronic metabolic disorder afflicting majority of population worldwide. According to WHO report the world wide prevalence of diabetes in adults is rising from 135 million (4%) in 1995 to 300 million (5.4%) by the year 2025. The WHO estimated that in India there were about 19.4 million persons suffering from diabetes in 1995 and may rise to 57.2 billion by 2025. Therefore, the India may become ‘Diabetic Capital of the World’ by the year 2025\(^1\). Therapeutic management involving antidiabetic drug therapy and lifestyle management, certainly are able to control progression of the disease. Despite the available therapy, certain group of population either do not respond or develop tolerance at later stage. Since therapy is for life time, the probability of development of complications is more likely.

The diagnosis as well as progression / remission of DM is usually based on evaluation of biochemical parameters namely blood glucose, serum insulin and C-peptide levels. Assessment of serum insulin level in freshly diagnosed DM is helpful in deciding about the type of oral hypoglycemic agent to be used\(^2\). In some patients C-peptide estimation is useful in determining the endocrine status of pancreas.

Among the diabetic complications, notable are retinopathy, nephropathy, cardiomyopathy, and gastrointestinal (GI) neuropathy. Complications involving the GI neuropathy cause considerable morbidity in the patients with long standing insulin-dependent diabetes with poor glucose control. About 76% of DM patients suffer from gastrointestinal symptoms\(^3\). These symptoms include, gastroparesis, abdominal pain, diarrhoea, fecal incontinence and constipation. They are chronic or recurrent in nature.

Transit disorders along the length of gastrointestinal tract is one of the predisposing factors for unstable metabolic condition in diabetic patients\(^4\). In addition, the small intestine (SI) is generally considered as the main site of drug absorption and fluid exchange. Patients with diabetic diarrhoea will have less time for absorption of drugs taken orally.
Disturbances of small bowel motor function with glycemic alterations are increasingly recognized in subjects suffering from diabetes that may affect the neurohormonal control of the gut motility. Motility studies of small intestine in diabetes with glycemic or insulinemic alterations are not extensive and available reports are contradictory to one another.\(^5,16-18\).

Insulin is the drug of choice in controlling hyperglycemic state in type 1 and sometimes for type 2 DM. In addition to established action of clearing the glucose from blood, it is reported to act as a neurotransmitter in CNS and as a mild analgesic. There is a clinical evidence that normal subjects with higher insulin levels showing an elevated threshold for thermal nociceptive stimuli.\(^6\) In addition, insulin administration effectively blocks diabetic pain.\(^7\) The mild analgesic property of insulin may also be responsible for its clinical benefit in relieving neuropathic pain. An inherent antinociceptive response for insulin when administered i.c.v., in mice, has been demonstrated.\(^8\) Their study also show that the antinociceptive response is independent of hypoglycemic action of insulin. An important area of exploring the inherent effect of insulin on intestinal motility remains un-explored. The possibility of an effect for insulin in this smooth muscle, like antinociceptive response deserves attention. Insulin was reported to increase the gastric emptying through hypoglycemic effect.\(^9\) However, a systematic study of insulin effect on small intestinal motility is not available.

Chemically-induced experimental diabetes (streptozotocin or alloxan) is considered as a prototype animal model for screening of various agents that could be useful in the management of diabetes. However, the experiments with streptozotocin (STZ)-induced diabetic rats demonstrated gross abnormalities of small intestinal motor function.\(^10,11\).
In addition, Fox et al (1999) reported that measurement of nociceptive stimuli in this chemically-induced DM model do not reflect the true response as STZ has been documented to destroy the neuronal function in this model. The choice of the model should not become a variable itself. Therefore, the problems associated with STZ-induced diabetes in animals may be overcome by employing healthy animals and bringing about alterations of glycemic state by physiological and pharmacological means.

The evidence cited above led us to hypothesize that whether (1) any relationship exists between the changes in the blood glucose and peripheral insulin levels and small intestinal transit under physiological conditions and during pharmacological interventions (2) any inherent effect of insulin on small intestinal transit exists.