

TITLE OF THE PROJECT: AN ELABORATE STUDY OF PANCREATIC AND EXTRAPANCREATIC INFLUENCES ON FENUGREEK- INDUCED HYPOGLYCEMIA IN DIABETES WITH SPECIAL REFERENCE TO GESTATIONAL DIABETES

SPONSORING ORGANISATION: UGC (Sanction No. F NO. 42-526/2013(SR) Dt. 22/03/2013)

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SUMMARY OF THE PROJECT

Diabetes mellitus (diabetes) is a complex, heterogeneous group of metabolic disorders, the prevalence of which is rapidly rising all over the globe at an alarming rate. According to the reports of International Diabetes Federation, the number of diabetes people in India currently around 40.9 million and is expected to rise to 69.9 million by 2025. Globally, an estimated 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. However, because of inadequate access to insulin in many countries, unwanted side effects of commonly used hypoglycemic medicines, etc., WHO recommended phytotherapy for diabetes management. Thereafter, plant-derived hypoglycaemic agents are nowadays getting significant importance for the treatment of diabetes. Fenugreek (*Trigonella foenum-graecum*) is one of such commonly used medicinal herb whose seed-extract exerts both hypoglycaemic and anti-hyperglycaemic effects in diabetic subjects. In addition to pancreatic hormones (insulin and glucagon), other counter regulatory hormones secreted from thyroid and adrenal glands also have important influences on glucose homeostasis. In this context the current project entitled "AN ELABORATE STUDY OF PANCREATIC AND EXTRAPANCREATIC INFLUENCES ON FENUGREEK- INDUCED HYPOGLYCEMIA IN DIABETES WITH SPECIAL REFERENCE TO GESTATIONAL DIABETES" was undertaken to investigate the role of thyroid-and adrenal-hormones in addition to pancreatic hormones in fenugreek-induced hypoglycemic diabetic and normal subjects. Additionally, role of fenugreek seed extract on pancreatic beta cell growth, GLP-1 and leptin secretion and gestational diabetes were also emphasised.

Beyond fulfilling all aims and objectives embodied in the project, the overall findings provided some significant messages regarding the therapeutic use of FSE. Present results showed that amongst different bioactive compounds present in fenugreek seed extract, trigonelline is the most potent hypoglycaemic or antihyperglycaemic fraction that significantly increased insulin and GLP-1 secretion in both normal and diabetic rats. It also increased the number of β cells in the pancreatic islets and the expression of GLP-1R mRNA in β cells through which it consequently stimulated insulin release and exerted FSE-induced antihyperglycaemic effects in normal as well as diabetic rats. FSE impaired HPT (Hypothalamo-Pituitary- Thyroid) axis with a rise in insulin secretion in diabetic rats, indicating insulin-independent central hypothyroidism. Results also suggested that low leptin level resulting from decreased adiposity index

following FSE feeding was dominant signal for suppressed HPT axis. Finally, fenugreek being hypoglycaemic and hypothyroidal in action, raises questions whether it can safely be used to treat diabetes and/or hyperthyroidism as was suggested by many workers. FSE significantly impaired HPA (Hypothalamo-Pituitary-Adrenal) axis in both normal and diabetic rats with a fall in glucocorticoid secretion. In experimentally induced diabetic pregnant rats, FSE might have acted as teratogen, causing both loss of pups and decrease in live pup's body weight. In essence, continuous usage of fenugreek seed either by diabetic or non diabetic normal subjects can result in severe hypoglycemia and other life threatening problems related to the functions controlled by thyroid and adrenal glands. So dose of FSE for curing hypoglycemia cannot be formulated without verifying functional conditions of other important endocrine glands.

PUBLICATION FROM THE PROJECT WORK (till date):

1. Jayjeet Majumdar, Pratip Chakraborty, Analava Mitra, Nirmal kumar Sarkar, Supriti Sarkar.(2017). *Fenugreek, A Potent Hypoglycaemic Herb Can Cause Central Hypothyroidism Via Leptin – A Threat To Diabetes Phytotherapy*. **Exp Clin Endocrinol Diabetes**; 125: 441-448.
2. Jayjeet Majumdar, Sumitra Chakraborty, Supriti Sarkar.(2016). Fenugreek has GLP-1 and GLP-1r Secretagogue Activities-a Novel Approach Towards Diabetes Phytotherapy. Proceedings of International Conference on Diabetes and Metabolism. OP7-3, pg 145, ICDM-2016, Seoul, South Korea (Paper was presented by Mr Jayjeet Majumdar at ICDM, 2016).
3. Supriti Sarkar, Jayjeet Majumdar, Sumitra Chakraborty. (2016). Fenugreek, A Potent Hypoglycaemic Herb Can Cause Central Hypothyroidism– A Threat To Diabetes Phytotherapy. Proceedings of International Conference on Diabetes and Metabolism. PE-129, pg181, ICDM-2016, Seoul, South Korea (Paper was presented by Dr Supriti Sarkar at ICDM, 2016).

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