6 Summary and conclusions

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. Long term hyperglycemia leads to the micro and macro vascular complications. The increasing prevalence of diabetes is alarming around the globe. Diabetes pandemic reaches each and every part of India with the highest prevalence. However till date, no study has been carried out on the prevalence of diabetes in Gwalior- Chambal region of Central India. The present study reports the prevalence of diabetes and prediabetes in rural and urban populations of this region and also its relation with gender, age, physical activity, occupation, family history, personal habits and food habits. The study covered a population of 7422 subjects including males (N=3467) and females (N=3955). Of these, 5456 subjects were from urban areas (males =2429, females =3027) and 1966 from rural areas (males =1038, females =928). Fasting blood glucose was measured in these subjects by glucometer and categorized into normal, diabetes and prediabetes based on the WHO criteria. The prevalence of T2DM and prediabetes was found to be 7.7% and 7.9% in rural area, whereas in urban areas it was 12.7% & 4.9%. The males recorded relatively higher rate of diabetes (14.3%) than female counterparts (8.9%) and no such gender variation was recorded in case of prediabetes irrespective of their domicile.

The diabetes prevalence was found significantly high in older age groups. Those with family history of diabetes coupled with sedentary life style are at high risk of developing diabetes. Thus, the factors predisposing to diabetes include sedentary life style, professional stress and prior family history. This study underlines the importance of diabetic education to vulnerable groups of the society particularly to prediabetics and diabetics in order to protect them from serious complications associated with diabetes mellitus.

Metabolic syndrome (MetS) refers to clustering of metabolic risk factors including central obesity, glucose intolerance, hyperinsulinemia, low HDL-cholesterol, high triglycerides and hypertension. Metabolic syndrome is increasingly being
recognized as a risk factor for cardiovascular disease and cardiovascular mortality. Harmonized criteria were used to check the prevalence of MetS. The prevalence of MetS was observed to be about 72.7%. There were about 71.1% of males and 76.3% of females presented with MetS. Prevalence of MetS was seen to increase with age. Based on the diabetes status, the prevalence of MetS was found to be 83.5%, 80.5% and 39.6% in diabetic, pre-diabetic and normal subjects respectively.

Prevalence of MetS in the normal subjects predisposes the individual to developing diabetes and CVD in near future. In this population, almost all (99%) people had at least one abnormal biochemical or anthropometric parameter leading to MetS. The highest prevalence of (20.7%) MetS was seen in the combination of central obesity, high blood pressure and low HDL cholesterol. While only 12.8% of MetS subjects exhibited all five abnormalities. The prevalence rate was higher than the earlier reported in this area. This variation may be due to the criteria used and/or time of the study.

This study evaluated the therapeutic potential of GSAE and GSEE in T2DM subjects with MetS. GSAE and GSEE were given to 40 subjects (20 subjects each group) selected from the epidemiological study for 3 months. The markers of T2DM and MetS were monitored before and after the therapy. *G. sylvestre* treatments resulted in restoration of all major physiological variables of MetS. The reduction in fasting blood glucose was seen to be 12.2% with GSAE and 17.5% with GSEE after three months of therapy while decrease in postprandial blood glucose was found to be 13.9% and 15.6% in GSAE and GSEE therapy respectively. C-peptide levels were increased by 20.8% in GSAE and 21.05% in GSEE administered subjects.

Total cholesterol (about 10 -12%), triglyceride (about 14 - 16%) levels were reduced and HDL cholesterol (8 – 8.5 %) levels increased significantly in both therapies. The antioxidant markers like GSH (about 39 - 40 %), SOD (14 -17 %), catalase (about 27 - 31 %) were increased and TBARS levels reduced by about 15 - 17 %. *G. sylvestre* therapies did not shown any toxic properties on liver and kidney. Both aqueous as well as ethanolic extracts of *G. sylvestre* were found effective in addressing the metabolic abnormalities associated with T2DM and MetS, there was no significant difference between the (GSAE vs. GSEE) two drug forms.

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Molecular docking using PatchDock and FireDock for known bioactive principle of *G. sylvestre* showed that, *G. sylvestre* molecule binds with the inhibitory sites of PTP1B, GSK3-β and it also has allosteric binding with Akt /PKB.

The *in silico* observations were supported by studies on L6 skeletal muscle cell line. This study revealed, increased phosphorylation of IRS, Akt and GSK3-β by *G. sylvestre*. *G. sylvestre* was also found to increase membrane translocation of GLUT4 molecule even in the insulin resistance condition (with palmitate) through PI3K dependent pathway. It was also found that, *G. sylvestre* molecules reduce the low-grade inflammation by reducing the pro-inflammatory markers like IL-6, MCP-1, TNF-α and increasing the IL-10 in palmitate treated cells.

Thus, early interventions particularly with proper monitoring, medication, lifestyle changes could delay the onset of advanced forms of T2DM and MetS. *G. sylvestre* therapies have multiple metabolic targets and would serve a better therapeutic option in dealing with T2DM and MetS. The *G. sylvestre* may be considered as safe therapy for a long term and effective management of T2DM as well as MetS.