# Contents

1. **ABSTRACT**

2. **INTRODUCTION**

3. **AIM AND OBJECTIVES**

4. **REVIEW OF LITERATURE**

5. **MATERIALS AND METHODS**

6. **RESULTS**

7. **DISCUSSION**

8. **SUMMARY**

9. **CONCLUSION**

10. **REFERENCES**

11. **PUBLICATIONS**
List of Figures

Figure 1: Prevalence of diabetes mellitus worldwide

Figure 2: Mechanism of hyperglycemia-induced superoxide overproduction and activation of metabolic pathways

Figure 3: Glucose Homeostasis

Figure 4: Stimulation of insulin secretion by glucose in pancreas

Figure 5: Chrysin Structure

Figure 6: Dose determination study for chrysin (Blood glucose)

Figure 7: Effect of chrysin on food and water intake in experimental rats

Figure 8: Effect of chrysin on OGTT in experimental rats

Figure 9: Effect of chrysin on hemoglobin and glycosylated hemoglobin in experimental rats after 28 days

Figure 10: Photomicrographs of hematoxylin–eosin staining of pancreatic tissues in control and experimental groups of rats

Figure 11: Photomicrographs of hematoxylin–eosin staining of hepatic tissues in control and experimental rats

Figure 12: Photomicrographs of hematoxylin–eosin staining of renal tissues in control and experimental rats

Figure 13: Effect of chrysin on renal biomarkers in experimental rats

Figure 14: Effect of chrysin on hexokinase and pyruvate kinase enzymes in hepatic tissue of experimental rats

Figure 15: Effect of chrysin on G6PDH enzyme and LDH enzyme in liver tissue of experimental rats

Figure 16: Effect of chrysin on glucose-6-phosphatase and fructose-1, 6-bisphosphatase enzyme in liver tissue of experimental rats
**Figure 17:** Effect of chrysin on glycogen synthase and glycogen phosphorylase enzyme in liver tissue of experimental rats

**Figure 18:** Effect of chrysin on glycogen content in liver and skeletal muscle of experimental rats

**Figure 19:** Effect of chrysin on hexokinase and pyruvate kinase enzymes in renal tissue of experimental rats

**Figure 20:** Effect of chrysin on G6PDH enzyme and LDH enzyme in renal tissue of experimental rats

**Figure 21:** Effect of chrysin on glucose-6-phosphatase and fructose-1, 6-bisphosphatase enzyme in renal tissue of experimental rats

**Figure 22(a):** Immunoblot analysis of IRS-1, IRS-2 and GLUT-2 in liver tissue

**Figure 22(b):** Histogram of IRS-1, IRS-2 and GLUT-2 relative intensity of protein expression in liver

**Figure 23(a):** Immunoblot analysis of GLUT-4 in skeletal muscle

**Figure 23(b):** Histogram of GLUT-4 relative intensity of protein expression in skeletal muscle

**Figure 23(c):** Immunoblot analysis of GLUT-4 in adipose tissue

**Figure 23(d):** Histogram of GLUT-4 relative intensity of protein expression in adipose tissue

**Figure 24(a):** Reverse transcription-PCR analysis of TNF-α, IL-6, IL-1β, NF-κB and iNOS mRNA expression in pancreatic tissue samples

**Figure 24(b):** Histogram of mRNA transcript levels of TNF-α, IL-6, IL-1β, NF-κB and iNOS in pancreatic tissue samples

**Figure 25(a):** Reverse transcription-PCR analysis of TNF-α, IL-6, IL-1β, NF-κB and iNOS mRNA expression in hepatic tissue samples

**Figure 25(b):** Histogram of mRNA transcript levels of TNF-α, IL-6, IL-1β, NF-κB and iNOS in hepatic tissue samples
List of Tables

| Table 1:   | Comparison of IDDM and NIDDM                     |
| Table 2:  | Insulin therapy changes at a glance              |
| Table 3:  | Primer sequences and expected product size of the genes amplified |
| Table 4:  | Effect of chrysin on body weight in experimental rats |
| Table 5:  | Effect of chrysin on the levels of blood glucose and plasma insulin in experimental rats |
| Table 6:  | Effect of chrysin on serum hepatic biomarker enzymes in experimental rats |
| Table 7:  | Effect of chrysin on serum lipid profile in experimental rats |
| Table 8:  | Effect of chrysin on enzymatic antioxidants in pancreatic tissue of experimental rats |
| Table 9:  | Effect of chrysin on non-enzymatic antioxidants and LPO in pancreatic tissue of experimental rats |
| Table 10: | Effect of chrysin on enzymatic antioxidants in liver tissue of experimental rats |
| Table 11: | Effect of chrysin on non-enzymatic antioxidants and LPO in liver tissue of experimental rats |
| Table 12: | Effect of chrysin on the activities of mitochondrial enzymes and respiratory chain enzyme in liver tissue of experimental rats |
| Table 13: | Effect of chrysin on PCC, NO and ROS in pancreatic tissue of experimental rats |
| Table 14: | Effect of chrysin on PCC, NO and ROS in liver tissue of experimental rats |
Abstract

Diabetes mellitus (DM) is a metabolic disease, characterized by hyperglycemia resulting from defects in insulin secretion or insulin action or both. In type 2 diabetes (T2DM), insulin insufficiency or insulin resistance and a relative β-cell defect are the underlying pathological problems leading to hyperglycemia. Oral hypoglycemic agents that improve insulin sensitivity are used for the treatment of T2DM which have restricted efficacy and adverse effects such as hypoglycemia, liver toxicity etc. In recent years, phytochemicals from natural resources open new avenues for the treatment of various diseases including diabetes. Many conventional drugs have been derived from prototypic molecules in plants. Flavonoids are nowadays regarded as promising and extensively natural substances to enrich the current therapy against diabetes. Chrysin (5, 7- Dihydroxyflavone) is a natural flavonoid with diverse pharmacological actions.

In this context, the present study has been designed with an overall objective to understand the antidiabetic mechanism of chrysin on streptozotocin-nicotinamide (STZ-NA) induced T2DM in albino rats. Also, it is an attempt to unravel the molecular mechanism of action of chrysin in insulin resistance and glucose homeostasis. The results of the study concludes that chrysin attenuated STZ-NA induced metabolic alterations by regeneration of pancreas, maintaining biochemical indices in hepatic and renal tissues, increasing insulin sensitivity and down regulating the mRNA expression of inflammatory genes. Altogether, these findings reinforce that chrysin may have therapeutic potential for the management of T2DM.