Adiponectin is an adipocyte-specific secretary protein of 244 amino acids that is produced by the adipQ gene in rats. It appears to be involved in the regulation of glucose homeostasis and lipid metabolism. Adiponectin has now been added on the list as a new and a very exciting player in the field of obesity-related insulin resistance and atherosclerosis. Rhazya stricta is commonly used in folk medicine of the Arabian Peninsula for the treatment of many diseases such as diabetes mellitus. In many studies, relatively large doses of the plant extract were used to determine the pharmacological and toxicological actions. Therefore, it was necessary to study the biochemical effects of this plant using low doses, almost near the dose that is used by humans in the folk medicine. In the present study, rat serum was used for the determination of the concentrations of adiponectin, insulin, glucose, lipid profile including total cholesterol, high density lipoprotein (HDL-c), low density lipoprotein (LDL-c) and Triglycerides (TG), and also for the activities of aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP), as well as the determination of the concentrations of uric acid, urea and creatinine. In addition, rat blood was used to study the molecular effects of aqueous extracts of Rhazya stricta on exon 3 of adiponectin gene. To our knowledge, this work is the first to study the effects of treatment with Rhazya stricta leaves on adipQ gene and its protein (adiponectin). This study clearly shows that oral administration of Rhazya stricta leaves for eighteen weeks produced highly significant increases in adiponectin concentrations in treated rats. In addition, aqueous extracts of Rhazya stricta leaves produced significant effects on lipid profile concentrations including HDL-c, LDL-c, cholesterol and triglycerides as well as insulin, glucose and insulin resistance levels. These results suggest that Rhazya stricta might play an important role in the regulation of lipid and carbohydrate metabolism. Therefore, it may prevent cardiovascular diseases. Urea, uric acid and creatinine concentrations were also significant. Rhazya stricta extracts did not show any significant effects on the activity of liver enzymes. In addition, the molecular analysis of exon 3 of adipQ gene indicated that Rhazya stricta extracts showed no mutagenic potential and are not toxic to rats. However, more work is needed to investigate possible mechanisms of action of Rhazya stricta leaves on the biochemical variables, using the same method of extraction that have been used by humans in the folk medicine.