Diabetes mellitus is a disease that occurs as a result of the lack of insulin and/or insulin resistance and characterized by the defects in carbohydrate, fat and protein metabolism. Metabolic disorders in diabetes is observed due to insulin is a significant anabolic hormone. Lack of insulin or insulin resistance is responsible from abnormalities that occur on insulin receptors, signal transduction, effector enzyme and genes especially in fat and muscle tissues (1). It might be chromosomal changes, DNA strand breaks, DNA replication-transcription-repair defects in diabetes through affecting DNA by advanced glycosylation products. Comet assay which is a simple, rapid and sensitive technique for analyzing and quantifying DNA damage in individual cells (2). Silibinin is a flavonoid which has anti-inflammatory, anticarcinogenic, antioxidant and cytoprotective effects and derived from a plant called Silybum marianum (3,4). Purpose of current study was to investigate protective effect of silibinin against diabetic DNA damage in streptozotocin (STZ) induced diabetic rat lymphocytes via comet assay. There were four groups including control group, diabetic group (STZ, 65 mg/kg as intraperitoneal and single dose), silibinin treatment group (STZ+100 mg/kg silibinin) and silibinin group (100 mg/kg silibinin). In conclusion, results indicate that there is a statistically significant increase in the DNA damage in lymphocytes of diabetic group compared to the control group and this damage is significantly reduced in silibinin treatment group. There is no statistically significant damage in silibinin group compared to the control group. In this case it can be interpreted as silibinin can prevent or reduce diabetes induced DNA damage.