ABSTRACT

Diabetes is a life-severe disease all over the universe and causes abnormal glucose level and it also leads number of complication, such as neurodegenerative and cardiovascular diseases. Valproate is widely used as an anti-epileptic globally. Valproate has been shown to inhibit inflammatory cytokines, prevent fibrosis and reduce oxidative stress in various experimental models. Some studies reported anti-inflammatory and histone deacetylase 1 (HDA1) inhibitory properties for sodium valproate. Further, it improves glycemic control in diabetics. Pioglitazone is known to improve insulin sensitivity, glycemic control, dyslipidemia, hypertension, and micro-albumin urea with T2DM. Pioglitazone decreases fasting and postprandial plasma glucose levels by improving the sensitivity of hepatic and peripheral (muscle) tissue to insulin.

The objective of the present study was to assess the action of VPA and Pioglitazone on alloxan induced diabetic mice. Herein, forty eight male albino mice were used for experimental design. Diabetes was induced by injection of alloxan (250 mg/kg). After diabetes induction mice were given the drug treatment intraperitoneal at different doses of VPA (25, 75 and 200 mg/kg) and PIO (5, 10 and 20 mg/kg) daily for 21 days. The body weights and blood glucose levels of all mice were recorded daily before treatment with VPA and Pioglitazone. The mice underwent cardiac puncture after drugs treatment and organ (brain, liver, kidney and pancreas) were removed and weighted. Blood samples were collected for assay of serum biochemical parameters and tissues of all organs were analyzed for histological study. In diabetic mice, VPA (75 mg/kg) and PIO (10 mg/kg)caused significant reduction ($P < 0.001$) in blood glucose level on day 21 with 102.33 ± 1.8 and 105.6 ± 5.87mg/dl reduction respectively and all treated groups shown a significant ($P < 0.001$) increase in body weights of mice. Moreover, the serum liver enzyme such as alkaline phosphate (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin and urea showed significant ($P < 0.001$) difference between VPA and PIO treated groups.

The histopathological effect appeared in the liver tissue include leukocyte infiltrations, cytoplasmic vacuolization of the hepatocytes, fatty degeneration and congestion of blood vessels. Some unwanted effects on the kidney cortex which

histologically observed as degeneration in renal tubules, atrophy of glomeruli and edema.

In addition, the disorganization of acinar cells, infiltration, congestion, fat droplets and irregular shape of islets in pancreas section of mice were observed in diabetic group. There were also morphological changes in islets, congestion, fat droplets and disorganization acinar cells were examined in different VPA and Pioglitazone dosages treatments. In brain there were no significant changes in hippocampal level, pyramidal cells lose their shapes, inter-neurons cells damage and less apoptotic cells were present in diabetic induced VPA and Pioglitazone treated mice. Therefore, it is concluded that VPA and Pioglitazone treatments possess beneficial antidiabetic effects which showed control hyperglycaemia .