

DPP-IV Inhibitory Potential of Methanolic Extract of *Pueraria tuberosa* DC in Liver of Alloxan Induced Diabetic Model

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DPP-IV is usually found to be over expressed in many pathological conditions of Liver via disturbing immune system, lipid accumulation, ECM degradation etc. The main objective of this work was to explore the effect of methanolic extract of *Pueraria tuberosa* (PTME) against Alloxan induced liver damage with respect to its potential of inhibiting DPP-IV activity. PTME was prepared through continuous soxhlet extractor. Alloxan injections were given to the same age group with weight range of 80-100 g *Charles foster albino* male rats at the dosage of 120mg/kg bw. Rats were divided into five groups. Group 1 was given with PTME dose of 20mg/100 g bw for 7 days, Group 2 for 14 days, Group 3 for 30 days, Group 4 for 40 days and Group 5 taken as an Alloxan control. Animals were sacrificed at their respective time along with the normal rats. DPP-IV activity in liver homogenates were done through the kit based on fluorescence ELISA. After treatment with PTME (20 mg/100 g bw) at different time intervals, the alloxan induced stress enhanced DPP-IV activity in liver significantly decreased in a time dependent manner. This short study provides an idea, how PTME protects liver via its potential role as DPP-IV inhibitor. But it needs further deep study to reveal the overall mechanism at pathological, clinical and molecular basis in different models of liver diseases.

Keywords: Alloxan, DPP-IV, Liver, PTME.

Patients with liver diseases like NASH, NAFLD, cirrhosis etc. leading from obesity and diabetes are found to be increased day by day, because of having bad lifestyles with consumption of junk foods and living in polluted environment (Yasutake *et al.*, 2014). Liver is the largest gland of our body and most of the important blood proteins and other proteins, are synthesized in this organ showing its important role in human metabolism (Burra, 2013). Due to sedentary and junk food

consumption, liver is overburdened alongwith stressful conditions. It is an accessory digestive organ involving the various role of digestive hormones. Recently, the use of DPP-IV inhibitor has been found to be a very potential approach in order to treat the above mentioned disorders and diseases, and also having pleiotrophic effect on various organs simultaneously (Aroor *et al.*, 2014) (Itou *et al.*, 2013). Overexpression of DPP-IV, leads to imbalance in immunity, lipid accumulation,

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extracellular matrix (ECM) degradation, resistance to anti-cancer agents etc (Itou *et al.*, 2013). In our previous laboratory papers, we have already reported the findings that *Pueraria tuberosa* has the ability to inhibit DPP-IV enzyme activity (Srivastava *et al.*, 2015)(Srivastava *et al.*, 2017). In addition to its DPP-IV inhibitory potential, it also have properties like anti-inflammatory (Pandey *et al.*, 2013), antioxidant (Pandey and Tripathi, 2010) and as hypoglycemic drug (Srivastava *et al.*, 2018). Here, we have hypothesized that, its potential as DPP-IV inhibitor could be helpful in reducing the alloxan induced stress condition in rats liver liver

METHODS

Sample preparations

Pueraria tuberosa DC tubers were purchased from Ayurvedic pharmacy, Banaras Hindu University. Its coarse powder was extracted with a mixture of water-methanol through continuous soxhlet extractor and then distillation was done in order to get solvent-free extract (Yadav *et al.*, 2016).

Animal Design

Charles foster albino male rats nearly of same age group with weight range of 80-100 g were acclimatized in our laboratory conditions for seven days with free access to normal standard chow diet and tap water. The animal protocol was approved by the Institute's Ethical committee, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India with Letter No Dean/2015/CAEC/1266. Before administering Alloxan dose, they were kept in fasting for 8 hours and then injection was given at the dose of 120mg/kg bw. Rats were then divided into five groups (n=6). *viz.* Group 1 for Alloxan control, Group 2, 3, 4 and 5 for PTME treatment at the dose of 20 mg/100 g bw for 7, 14, 30 and 40 days. The animals were sacrificed at their respective days along with normal rats. Organ liver was taken out after sacrificing the rats for further study. Liver was crushed in liquid nitrogen and kept in -20°C and 10% homogenate was prepared in needed buffer as per requirement.

DPP-IV activity in liver homogenate

DPP-IV activity in liver homogenates were measured by fluorometric based ELISA assay kit (Sigma MAK088).

Statistical analysis

One-way ANOVA test followed by post hoc analysis with Dunnett's test was done. All the results were expressed as means \pm SD. Statistical significance was considered at a p-value less than or equal to 0.05

RESULTS

As compared to normal, the DPP-IV activity enhances prominently in the liver of alloxan model. PTME (20 mg/100 g bw) was found to be effective in reducing the raised DPP-IV activity significantly in a time dependent manner. Thus, as a DPP-IV inhibitor, PTME can be used in the treatment of diseases like NASH, NAFLD, liver cirrhosis or steatosis, leading from diabetic metabolic disorders because of its ability to ameliorate DPP-IV activity.

DISCUSSIONS

DPP-IV, the pleotropic enzyme generally enhanced during the stress induced diseases of many organs like intestine, heart, liver etc. Liver diseases like NASH, NAFLD, cirrhosis etc. are continuously expanding in this area due to changes in the life styles. Many allopathic drugs have been developed in this area in order to treat these diseases. Many animal models have been developed to mimic the human diseased condition for drug development (Liu *et al.*, 2013; Muriel and Rivera-Espinoza, 2008). Due to high economic costs and many side effects provided by allopathic medicines, many scientists are doing researches on herbal plants and their products to find out the drugs with negligible side effects with low cost (Govind, 2011). Here, in our results PTME proved to be an effective inhibitor of liver DPP-IV activity in a time dependent manner. As discussed above, DPP-IV has the potential role in the development of liver diseases; this herbal preparation could be taken as a treatment against the same. This very important short and crisp study should be expanded in future at cellular, clinical and molecular level in order to track the signalling pathways through which PTME protects liver by inhibiting the activity of DPP-IV. Since DPP-IV is an important enzyme which controls our digestive secretions and thus acting as

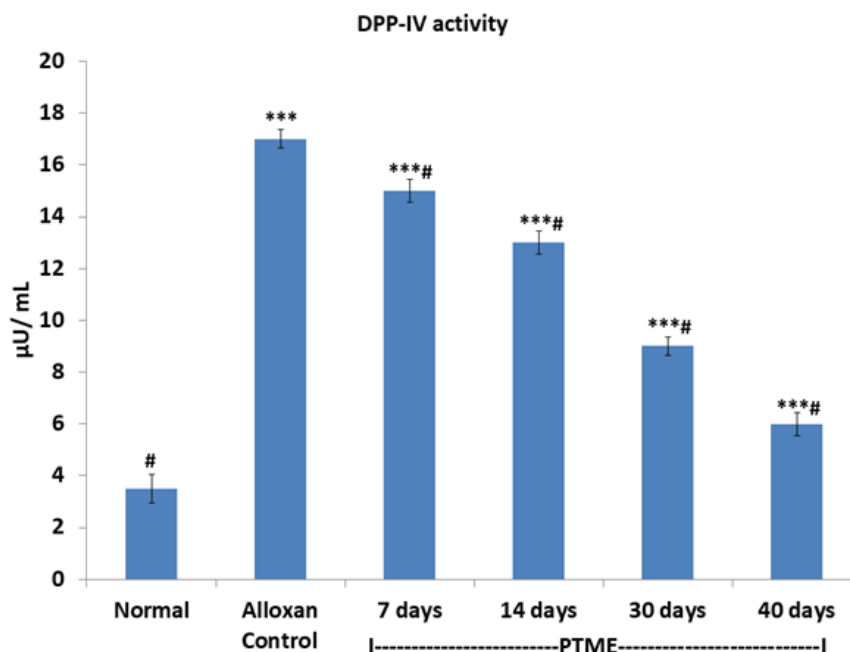


Fig. 1. DPP-IV activity in liver homogenates of alloxan induced diabetic rats treated with PTME, alloxan control and normal rats. DPP-IV activity was decreased significantly in a time dependent manner. *** $p < 0.05$ compared with normal group. # $p < 0.05$ compared with alloxan control

an important part of the second brain of our body i.e., digestive system.(Dworken *et al.*, 2010).

CONCLUSION

PTME downregulates liver DPP-IV activity in Alloxan induced diabetic rats., thus can be taken as an important line of treatment against various liver diseases like NASH, NAFLD, cirrhosis etc.

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