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Protective Effect of *Dodonaea viscosa* (L) Against Lead Acetate Induced Altered Glycoprotein Profiles in Rats

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Abstract: The present study was undertaken to examine the inhibitory effect of crude leaves of *Dodonaea viscosa* (L) on lead acetate induced synthesis of glycoproteins and sialic acid in liver and plasma. Enhanced synthesis of glycoproteins (protein - bound hexose and protein - bound hexosamine) and sialic acid levels were found in liver and plasma of the lead acetate poisoned rats. Administration of crude leaves of *D.viscosa* (100 mg/100 g body weight P.O.) effectively suppressed the synthesis of glycoproteins and sialic acid in liver and thereby controlling the concentration in plasma. The results suggest that *D.viscosa* may exert its membrane protection effect by inhibiting the synthesis of glycoproteins and sialic acid induced by lead acetate.

Keywords: *Dodonaea viscosa,* Flavonoids, Glycoproteins, Sialic acid

Introduction

Lead is well known for its involvement in various biochemical and metabolic process. Absorption of inorganic lead can lead to certain biochemical and metabolic toxicities[1]. Lead is known to inhibit many enzyme[2-4] activities and it may interfere with the synthesis of protein or RNA or both[4]. An earlier report shows that, the lead induces cell proliferation in mouse kidney[5]. Factors like tuberculosis, malignancy, renal disorders and inflammatory conditions can stimulate production of proteins in the liver, so called acute phase proteins[6,8] which contain high amount of carbohydrate. Changes in their plasma concentration are regarded as sensitive tests for diagnostic and prognostic assessments[7].

Membrane glycoproteins are responsible for cell recognition and various immunological phenomena like autoimmune diseases and cancer. Sialic acid, a membrane constituent involved in cell contact phenomena, growth control and cellular invasiveness has been demonstrated to be increased at the surface of cancer cells in humans[9].

Xenobiotics are known to cause profound alterations in the cell membrane. The current focus of chemo prevention is on intermediate biomarkers capable of detecting early subtle changes that can be correlated with inhibition of the carcinogenic process. Flavonoids are diphenyl propanoids that occur ubiquitously in plant foods and form important constituents of the human diet[10]. Although flavonoids are generally considered to be non-nutritive, interest in flavonoids has risen because of their potential antioxidant, free radical-scavenging and pharmacological activities[11-13].

Dodonaea viscosa, Linn is a small tree belonging to the family sapindaceae. It is widely used by the tribal as a traditional medicine for bone fracture and others inflammation conditions[14]. An investigation of *D.viscosa* afforded nearly eight flavonoids[15]. Hence, in the present study the chemoprotection potential of the flavonoid rich *D.viscosa* leaves was studied against the alterations in plasma and membrane glycoprotein's and sialic acid contents in lead acetate intoxicated rats.

Experimental

Animals

Wistar male rats weighing 100-120 g were housed in poly propylene cages in a temperature and humidity controlled environment, with a 12 h light/dark cycle in the Animal House of J.J. College of Arts and Science, Pudukkottai, Tamilnadu, India. All the animal experiments were carried out according to the guidelines of the Institutional Animal Ethics Committee. Standard pellets were obtained from Amrut feed Ltd. The animals had free access to food and deionised water.

Chemicals

Lead acetate was obtained from Himedia chemicals Mumbai, India. All others reagents and chemicals used were of analytical grade with high purity.

Drug

The leaves of *D.viscosa* were collected from Kunnandar Koil village located in Pudukkottai District, Tamil Nadu and dried under shade. The dried material was powdered sieved through muslin cloth and the fine powder suspended in deionised water was used as drug in the present study.

The animals were divided into four groups of six animals each. Animals in group 1 had free access to 200 ppm lead acetate in drinking water for 30 days. Group 2 animals were allowed to lead acetate exposure as in group 1. In addition, the animals were administered *D.viscosa* leaf suspended in deionised water at a dose of 100 mg/100 g body weight orally throughout the study. Animals in group 3 received only the *D.viscosa* leaf as in group 2. Group 4 served as control animals received neither lead acetate nor *D.viscosa* leaf. The experiment was terminated at the end of 30 days and all the animals were sacrificed by cervical dislocation after an over night fast. Blood was collected in heparinised tubes. The plasma was separated after centrifugation at 1000 x g for 15 min. The liver of the animals were perfused with physiological saline and made in to a 10% homogenate with phosphate buffered saline. Protein-bound hexose[16], protein-bound hexosamine[17] and sialic acid[18] were estimated from the plasma and liver homogenate.

Statistical analysis

Values are mean±SD for 6 rats in the each group and statistical significant differences between mean values were determined by one way analysis of variance (ANOVA) followed by the Tukey's test for multiple comparison, values of $P<0.05$ was considered to be significant. Statistical Package for Social Studies (SPSS) 7.5 version was used for the statistical analysis.

Results and Discussion

Table 1 shows the levels of protein - bound hexose, hexosamine and sialic acid in liver and plasma of control and experimental rats. Liver and plasma glycoproteins and sialic and were found to be significantly increased in group 1 rats intoxicated with lead acetate compared with control group 4 rats. Groups 2 and 3 showed a significant decrease in the levels of the glycoprotein and sialic acid of liver and plasma compared to group 1 rats.

Table 1. Levels of protein-bound hexose, protein-bound hexosamine and sialic acid in experimental and control animals (mean ± SD; n=6)

Parameters	Lead acetate	Lead acetate + *D.viscosa*	*D.viscosa*	Control
Liver (mg/g of defatted tissue)				
Protein-bound Hexose	31.66±3.41*	26.31±3.10*	20.65±1.4NS	21.78±2.79
Protein-bound Hexosamine	11.36±0.81*	6.85±0.43*	4.12±0.11NS	4.71±0.38
Sialic acid.	8.06±0.18*	6.11±0.11*	5.10±0.27NS	4.92±0.28
Plasma (mg/dL)				
Protein-bound Hexose	335.89±7.67*	248.62±5.82*	196.98±5.98NS	205.7±5.2
Protein-bound Hexosamine	64.22±1.16*	56.04±1.65*	53.95±1.21NS	49.70±2.57
Sialic acid	104.39±4.26*	95.21±2.88*	82.83±1.34NS	84.39±2.06

*Statistical significance: Group I and III Vs Groups IV, Group II Vs Group I.P values *<0.01; **<0.05; NS-not significant.*

Many reports are available on the existence of significant correlation between protein bound hexose in the plasma and level of typical acute phase reactants like hepatoglobulin, fibrinogen or seromucoid fraction[19,20]. Heavy metals were reported to affect the serum glycoprotein levels[21,22]. Hexoses are one of the basic constituents of glycoprotein's and elevation in serum protein-bound hexose levels have shown to be indicative of dissemination of malignant disease[23]. Accumulation of metal in liver may lead to liberation of lysosomal enzymes resulting in the increased production of various glycoproteins by liver, which liberated to the blood[24]. Various animal tissues are composed of neutral glycoproteins with the same carbohydrate constituents as that of plasma. Hence, an increase in hepatic level of these glycoproteins may increase the level of glycoproteins in circulation. Alterations in the levels of plasma glycoproteins of lead intoxicated group of rats observed in the present study can be explained in relation to changes observed in hepatic cells. Macbeth *et al*., postulated that, presence of tumour induces hepatic cells to synthesis glycoproteins which subsequently apear in circulation.

Cell peroxisome proliferators are reported to increase the levels of protein-bound hexose, hexosamine and sialic acid[25]. Lead acetate (a hepatic and renal cell proliferator) poisoned group of rats showed an increased sialic acid content of plasma and liver in the present study is probably a reflection of cell surface changes. Sialic acid residues are responsible for the net negative charge on the surface of membrane. Alterations in the content of sialic acid may alter the rigidity of the cell membrane.

In the present study, treatment with the flavonoidal drug, *D.viscosa* to lead poisoned rats resulted a significant decrease in the levels of glycoproteins and sialic acid contents in liver and plasma. Previous reports showed that plant flavonoids are natural antioxidants, which act as effective protective agents against membrane damages during hepatic[26] and renal[27] toxicity. Taken together, these results suggest that the flavonoids rich *D.viscosa* leaves attenuated the lead acetate induced alterations in the membrane and plasma glycoproteins and sialic acid contents and offer promise as potential chemoprotective agent against lead poison in rats.

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