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Research Article

EFFECT OF TANNIC ACID ON LIPID PEROXIDATION AND ANTIOXIDANTS STATUS IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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ABSTRACT

Diabetes mellitus is characterized by the disturbances of carbohydrate, protein and lipid metabolism, with a high risk of morbidity and mortality from primary as well as secondary complications. However various drugs are found for the treatment of diabetes, none is found to be ideal due to the unwanted side effects associated with long term treatment. The present study was aimed to investigate the effect of tannic acids on lipid peroxidation and antioxidants in plasma and liver in streptozotocin induced diabetic rats. Diabetic mellitius was induced by single intraperitoneal injection of streptozotocin (40mg/kg b.w) in albino Wister rats. Oral administration of tannic acid (200mg/kg b.w) by gastric gavage to diabetic animals significantly reduced the level of lipid peroxidation and increased the level of antioxidant enzymes. The results of this study clearly show the tannic acid possesses antioxidant and anti lipid peroxidation properties.

INTRODUCTION

In diabetes mellitus, chronic hyperglycemia produces multiple biochemical sequence and diabetes induced oxidative stress that plays an important role in the symptoms and progression of the disease [1]. Free radicals have been concerned in the causation of several disorders [2,3]. Increased oxidative stress has been postulated in the diabetic state which coexists with a reduction in the antioxidants status [4]. Tissue antioxidant states have altered in diabetes resulting in increased oxidative damage of membranes and tissue [5,6,7].

Oxidative stress has been strongly associated with tissue damage in diabetic individuals [8]. STZ, which is widely used to induce experimental diabetes in animals, induces its diabetes mainly by inducing oxygen free radicals, thereby damaging the pancreas. STZ can induce partial destruction of b-cells in rats, resulting in insulin resistance-like symptoms, which pathologically would be very similar to human type 2 diabetes mellitus [9]. Antioxidants play a major role in the protection against molecular oxidative damage. Disturbances of antioxidant defence systems in diabetes have been demonstrated, including alteration in the activities of antioxidant enzymes and impaired glutathione (GSH) metabolism. Plant-derived herbal remedies are apparently effective, produce minimal or no side effects in clinical experience and are of relatively low costs as compared with oral synthetic hypoglycaemic agents [10].

The antioxidant system includes Superoxide dismutase (SOD), Catalase (CAT), Glutathione peroxidase (GSH-Px) and indirectly glutathione reductase. The protective role of antioxidant enzymes is well known and has been investigated extensively in diabetic patients and experimental diabetic animals [11].

Tannic acid is a specific commercial form of tannin, a type of polyphenol. Its weak acidity is due to the numerous phenol groups in the structure. The chemical formula for commercial tannic acid is often given as $C_{76}H_{52}O_{46}$, which corresponds with deca-galloyl glucose, but in fact it is a mixture of polygalloyl glucoses or polygalloyl quinic acid esters with the number of galloyl moieties per molecule ranging from 2 to 12 depending on the plant source used to extract the tannic acid. Commercial tannic acid is usally extracted from any of the following plant part: Tara pods (*Caesapinia spinosa*), gallnuts from *Rhus semialata* or *Quercusinfectoria* or *Sicilian sumac* leaves (*Rhus coriaria).*

According to the definitions provided in external references such as International Pharmacopoeia, Food Chemical Codex and FAO-WHO tannic acid monograph only tannins sourced from the above mentioned plants can be considered as tannic

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acid. Sometimes extracts from chesnut or oak wood are also described as tannic acid but, this is an incorrect use of the term. It is a yellow to light brown amorphous powder which is highly soluble in water; one gram dissolves in 0.35 ml of water. In these studies, of all plant phenols tested, tannic acid was shown to possess the most protective effects. Since tannic acid is usually consumed in the diet, it was considered important to possess the most protective effects.

Use of tannic acid in food application is far more wide spread and significant amounts are used as process aids in beer clarification, aroma compound in soft drinks and juices. Tannic acid is applied directly to treat sore throat and tonsils, spongy or receding gums, cold sores and fever blister [12]. Tannic acid can medicate bleeding, chronic diarrhea, dysentery, bloody urine, painful joints, persistent coughs, and cancer. Vaginally, Tannic acid can be used as a doughe for white or yellowish discharge, i.e, leukorrhea [13]. Tannic acid is a good source of antihyperlipidimic and antihyperglycemic agent (14,15).

The present study was undertaken to study the effect of tannic acid on antioxidant and anti-lipid peroxidation on plasma and liver in streptozotocin induced diabetic rats.

MATERIALS AND METHODS

Animals

Albino Wister male rats (weighing 180-200) were obtained from Central Animal House, Rajah Muthiah Medical College, Annamalai University Tamil Nadu (Reg No. 160/1999/ CPCSEA; Proposal No. 1032). The rats were housed six in polypropylene cage and provided standard pellet, diet and water *ad labitum* and maintained under controlled conditions of temperature and humidity, with a 12 hr light/dark cycle in Central Animal House. The animals were maintained as per the principles and guidelines of the ethical committee for animals care of Annamalai University in accordance with the Indian National Law on animal care and use.

Chemicals

Streptozotocin and Tannic acid was purchased from Sigma-Aldrich, St, Louis, USA. All other chemicals were of analytical grade and obtained from Himedia, Mumbai, India.

Induction of Diabetes Mellitus

Diabetes mellitus was induced in overnight- fast albino Wister rats by single intraperitoneal injection of streptozotocin (40mg/kg b.w ip) dissolved in freshly prepared 0.1M citrate buffer (pH 4.5) **[15]**.

Experimental design

In the experiment, a total of 24 rats (18 diabetic surviving rats, 6 normal rats) were used. The rats were divided into 4 groups of 6 rats each.

Group 1- Control treated with vehicle alone.
Group 2- Diabetic Control treated with vehicle alone.
Group 3- Diabetic rats treated with Tannic acid (200mg/kg b.w) for 45 days
Group 4- Diabetic rats treated with glibenclamide (600µg/kg b.w) for 45 days

Biochemical Estimation

Biochemical estimations were carried out in blood and liver samples of control and experimental rats in each group. Blood glucose was estimated by the method of [15]. Thiobarbituric acid reactive substance (TBARS), the by-product of lipid peroxidation, in plasma and liver were assayed by the method of [16,17]. Superoxide dismutase (SOD), Catalase (CAT), and Glutathione peroxidase (GP_X) activities were estimated according to the method of [18,19] respectively. Reduced glutathione was measured accordance to the method of [20].

Statistical Analysis

The data expressed as mean Standared deviation. Statistical comparisons were performed by One-way analysis of variance (ANOVA) followed by Duncans Multiple Range Test (DMRT). The result was considered statically significant if the p value was less than 0.05.

RESULTS

The level of antioxidant enzyme status of SOD, Catalase, GP_X, GSH, level consecutively reduced and TBARS levels was increased (0.58±0.05 U/ml) in liver in diabetic groups. Whereas, tannic acid (200mg/kg b.w) treated diabetic groups showed pronounced recovery of these enzymes to significant ratio when compared to that of glibenclamide (600µg/kg b.w) treated group (Table.1). TBARS level was decreased (0.37±0.02)in tannic acid treated groups as normal ones. (Table 2) shows the status of TBARS, SOD, Catalase, GPx and GSH in plasma of control and diabetic groups. The diabetic groups were elevated levels of TBARS (0.06±0.04) in the plasma, when compared with control groups. Diabetic groups treated with tannic acid significantly decreased (0.52±0.03) the lipid peroxidation markers in diabetic groups.

Similarly SOD, Catalase, GSH and GP_X in plasma of control and diabetic groups, levels were significantly lowered in plasma of diabetic groups than in control group. In contrast diabetic groups treated with tannic acid (200 mg/kg b.w) led to significant increase in the antioxidant enzymes, when compared to diabetic groups.

Table 1 Level of TBARS, SOD, Catalase, GSH, GPx in liver tissue

Groups/ Units	TBARS (U/ml)	SOD (U/ml)	Catalase (u/ml)	GP_X (U/ml)	GSH (U/ml)
Control	$0.33±0.02^b$	$12.49±0.6^b$	$3.48±0.08^b$	$112.09±1.28^a$	$72.83±0.12^b$
Diabetic Control rats	$0.58±0.05^f$	$7.5±0.4^e$	$0.61±0.3^a$	$78.49±0.16^a$	$32.50±0.23^f$
D+ Tannic acid (200mg/kg b.w)	$0.37±0.02^d$	$11.26±0.5^d$	$2.93±0.2^a$	$108.24±1.38^a$	$67.09±0.12^c$
D+Glibenclamide (600µg/kg b.w)	$0.34±0.01^c$	$12.11±0.5^c$	$3.01±0.3^b$	$110.19±0.16^a$	$71.52±0.62^c$

Table 2 Levels of TBARS, SOD, Catalase, GSH, GP_X in plasma

Groups/ Units	TBARS (nMol/dl)	SOD (U/ml)	Catalase (u/ml)	GP_X (U/ml)	GSH (U/ml)
Control	0.30±0.03	7.39±0.5	1.03±0.07	132±7.21	54.82±2.81
Diabetic Control rats	0.60±0.04	4.3±0.3	0.50±0.2	95.4±7.01	30.10±2.23
D+ Tannic acid (200mg/kg b.w)	0.52±0.03	5.6±0.4	0.68±0.1	110.3±5.91	40.4±2.66
D+Glibenclamide (600µg/kg b.w)	0.31±0.02	6.70±0.6	0.80±0.2	130.39±5.92	46.51±2.61

DISCUSSION

Lipid peroxidation is one of the characteristic features of chronic diabetes. Lipid peroxide mediated damage has been observed in the development of both type 1 and type 2 diabetes mellitus. It has been observed that insulin secretion is closely associated with lipoxygenase derived peroxides [21]. Low level of lipoxygenase peroxide stimulate the secretion of insulin, but when the concentration of endogenous peroxides increases, it may initiate uncontrolled lipid peroxidation leading to cellular infiltration and islet damage in type 2 diabetes [22]. Increased lipid peroxidation impairs membrane function by decreasing membrane fluidity and changing the activity of membrane bound enzymes and receptors [23]. Its products are harmful to most of the cells in the body associated with variety of diseases [24]. The present study showed a significant elevation of plasma and liver TBARS content in diabetic rats. The increased TBARS content of diabetic rats suggests peroxidative injury may be involed in the development of diabetic complications. Tannic acid could significantly reduce the liver lipid peroxidation products level in diabetic rats. This indicates that tannic acid is a potent inhibitor of the oxidative damage of liver tissue.

In diabetes oxidative stress damage, the pancreatic tissue there by further reducing insulin secretion. In the present study, the activity of SOD, CAT, GP_X were significantly reduced in liver of diabetic induced rats. The previous report has shown that the activities of SOD, CAT and GP_X were lowered in tissue of diabetic rats [25]. The observed decrease may be due to the utilization of non protein thiols by increased oxygen free radicals produced in hyperglycemia condition. Oral administration of tannic acid to diabetic rats significantly improved the antioxidant defense mechanism, which suggests its role in the protection of vital tissue from oxidative damage during diabetic condition.

Reduced glutathione is a potent free radical scavenger GSH within the islets of β-cell andis an important factor against the progressive destruction of the β-cell following partial pancreatectomy [26]. Depletion of GSH results in enhanced lipid peroxidation. This causes increased GSH consumption and can be correlated to the increase in the level of oxidized glutathione (GSSG). Treatment of tannic acid resulted in the elevation of the GHS levels, which protect the cell membrane against oxidative damage by regulating the redox status of protein in the membrane [27].

The plasma lipid peroxide level in STZ-induced diabetes is generally thought to be due to pathological changes to tissue that increase the production and liberation of lipid peroxides into circulation [28]. Treatment with tannic acid brought back lipid peroxidative markers to near normal levels, which could be as a result of improved glycemic control and antioxidants status.

GSH,being the most important biomolecule against chemically induced toxicity can participate peroxides in the presence of GP_X. GSH also functions as free radical scavenger and in the repair of free radical caused biological damage [29]. Reduced glutathione, a direct free radical scavenger, also reported to protect the cellular system against the noxious effect of lipid peroxidation [30].

The decreased levels of plasma GSH in diabetes could be due to its increased utilization in trapping the oxyradicals **[31]**. In our study, diabetic rats exhibited decreased level of GSH, which might be due to increased utilization for scavenging free radicals and increased consumption by GP_X. Treatment with tannic acid can either increase the biosynthesis of GSH or reduce the oxidative stress leading to less degradation of GSH and detoxifies the free radicals generated. The decrease of GSH may hence be responsible for low GP_X activity in diabetic tissues. It has been proposed that antioxidant that maintains the concentration of GSH may restore the cellular defense mechanisms, block lipid peroxidation and thus protect the tissue against oxidative damage **[31].**

CONCLUSION

In conclusion, the present study provides that tannic acid (200mg/kg) exhibits antioxidants status in streptozotocin induced diabetic rats by decreasing the levels lipid peroxidation products and increasing the activity of antioxidants. Further detailed investigation is necessary to find out it´s mechanism of action and establish its therapeutic potential in the treatment of diabetes.

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