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Kudzu root and maqui berry extract preclinical assessment in streptozotocin-induced nephropathy

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ABSTRACT:

Background and Objectives: A metabolic problem related to diabetes mellitus is hyperglycemia, which happens when the body doesn't make enough insulin. Nephropathy is a major capillary problem that can happen with diabetes. The purpose of this study is to find out how well Maqui berry and Kudzu root products can stop experimental mice from getting nephropathy caused by diabetes.

Methods: Streptozotocin (55 mg/kg) was given intraperitoneally to male Wistar rats that weighed 200–250 g to make them develop diabetic nephropathy. To check for nephritis biochemically, blood glucose, total protein, albumin, urea, uric acid, creatinine, and total bilirubin were measured in serum and urine. Along with membrane-bound ATPases, lipid peroxidation, reduced glutathione, and superoxide dismutase were used to measure signs of oxidative stress.

Results: Nephropathy rats were given extracts from kudzu roots and maqui berries by mouth for two weeks. The doses were 50 mg/kg orally for kudzu and 100 mg/kg orally for maqui. Rats with diabetic nephropathy had much higher levels of creatinine, albumin, total protein, total bile, uric acid, urea, and signs of oxidative stress like lipid peroxidation. On the other hand, their levels of superoxide dismutase and glutathione were much lower. Over the course of two weeks, treatment with 50 mg/kg and 100 mg/kg of Kudzu root extract and 50 mg/kg and 100 mg/kg of Maqui berry extract, either alone or together, changed the levels of oxidative stress markers, ATPases, and biomarkers of renal function, getting closer to normal levels.

Conclusion: Synergistic benefits in decreasing oxidative stress indicators and hyperglycemia, thereby alleviating renal injury, were shown when Kudzu root extract and Maqui berry extract were used together, according to current research.

Keywords: Streptozotocin, Kudzu root extract, Maqui berry, diabetic nephropathy.

INTRODUCTION:

The prevalence of diabetes among adults increased from 4.7% in 1980 to 8.5% in 2014, as reported in the World Health Report that was released on November 15, 2017. Nearly 1.6 million people lost their lives in 2015 as a direct result of the disease. The World Health Organization predicts that diabetes will rank as the sixth leading killer in 2011 [1-3]. Diabetes mellitus (DM) is projected to affect 693 million individuals globally by the year 2045. The most prevalent form of diabetes worldwide is type 2 diabetes mellitus (T2DM), which occurs when the body fails to effectively use insulin. According to reports, the most common major ailment in 2017 was chronic kidney failure [2-4].

The gradual deterioration of kidney function due to persistently elevated blood sugar levels is known as diabetic nephropathy (DN). Diabetic nephropathy is characterized by impaired kidney function [3-5]. With or without chronic renal insufficiency leading to end-stage renal disease (ESRD), these patients may experience early microalbuminuria, hyperfiltration, hyperperfusion, increased capillary permeability to macromolecules, and proteinuria [4-6].

One of the most prevalent complications of diabetes is diabetic nephropathy, which affects the blood vessels. Additionally, it is the primary driver of end-stage renal illness, which manifests itself in an imbalance of inflammation, mesangial development, renal basement membrane breakdown, oxidative damage, and so on [5-7].

The gradual decline in kidney function, elevated protein levels, interstitial fibrosis, and glomerular failure are the hallmarks of diabetic nephropathy. Diabetic nephropathy can result from a number of factors, including changes in metabolic processes, kidney hemodynamics, increased renin-angiotensin production, and inflammation. Issues with metabolism and blood circulation are likely the root causes of diabetic nephropathy (DN) [6-8]. Due to their numerous beneficial effects on health, flavonoids are an integral component of numerous nutraceutical, medicinal, cosmetic, and pharmaceutical products. Reason being, they eliminate free radicals, shield cells from harm, and decrease inflammation quite effectively [7-9].

The goal of this research is to determine whether or not extracts from the Kudzu root and the Maqui berry can prevent diabetic nephropathy in experimental mice.

MATERIALS AND METHODS:

Materials:

Drugs and chemicals:

Both the kudzu root extract and the maqui berry extract originated from the Indian state of Maharashtra. Streptozotocin (STZ) was obtained from Sigma Aldrich in Mumbai, India. All ingredients and diagnostic tests required conformed to established specifications.

Experimental animals:

Eight sets of six adult male Wistar rats, ranging in weight from 200 to 250 grams apiece, were utilized for the experiment. Separated from one another, the rats resided in polypropylene containers lined with rice husks. These animals were housed in standard laboratory settings in accordance with the guidelines established by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA). Water and regular lab food were readily available to the animals prior to the dietary modification [10-12].

Induction of DN using STZ:

To cause diabetic nephropathy, a single dose of streptozotocin (55 mg/kg) diluted in 0.2 ml of citrate buffer was given. An automated glucometer checked the blood glucose levels (BGL) 72 hours after STZ treatment, which proved the person had diabetes. The rats were watched for four weeks to see how the nephritis got worse [13-16].

Experimental design:

The rats were put into eight groups, with six rats in each group. Here are the names of the groups: Group I: a treatment that only used a vehicle on the control rat Group II: STZ was given to rats. 11 Rats in Group III were given kudzu root extract that had been diluted in pure water. Rats in Group IV were given kudzu root extract that had not been diluted. 11 In Group V, rats were given distilled water that had Maqui berry extract added to it. In Group VI, rats also got distilled water that had Maqui berry extract added to it [17-20].

Serum and urine biochemical estimation:

After the second week of treatment, each rat was kept in its own metabolic box for one day, during which time a urine sample was taken. Microcapillaries were used to take blood from the retroorbital nerve while the person was anesthetized with ether. High-speed centrifugation was then used to separate the serum. For different biochemical analyses, serum and pee samples were kept at -20°C. A glucometer was used to measure the blood glucose levels. To check for total protein, albumin, urea, uric acid, creatinine, and total bilirubin in blood and urine samples, commercial diagnostic tools were used [21-25].

Tissue homogenization:

At the end of the treatment, the rats were killed by cutting off their heads. The kidneys were washed in cold physiological saline after they were cut out. The amount of antioxidant enzymes in the kidney was measured. The kidney was carefully cut into small pieces that were then put in a 0.25M sugar solution that was kept cold. To make the kidney cells more uniform, a 10% w/v tris-hydrochloride buffer was used. One that cools down was used to spin the mixture at 0°C and 10,000 rpm for 15 minutes.The amounts of lipid peroxidation (LPO), superoxide dismutase (SOD), and reduced glutathione (GSH) were measured in the supernatant. To test Na+/K+ ATPase, a sedimentation-based method was used [26-29].

Assessing oxidative stress signals:

Assessment of lipid peroxidation (LPO):

After 2.0 ml of freshly made 10% w/TCA was added to the kidney homogenate liquid, the mixture was put in an ice bath for 15 minutes. Centrifugation was used to separate the residue. Two milliliters of freshly made TBA were mixed with two milliliters of the clear leftover solution. The solution that was made was heated in a bath of hot water for ten minutes. After that, it was quickly cooled for five minutes in ice. A 532 nm reading was used to compare the pink color that formed when TBA and MDA reacted with the blank. Malondialdehyde that is standard was used in different amounts. The numbers were shown as MDA in nanomoles per mg of protein [30-35].

Assessment of reduced glutathione (GSH):

The kidney purée was centrifuged after being deproteinized with a 20% TCA solution. The next step was to combine 0.25 mL of the supernatant with 2 mL of the DTNB solution. Using phosphate buffer, the remaining portion was reduced to 3 ml. It was at 412 nm that the subsequent golden hue became visible. Standard glutathione was prepared in varying concentrations. Magnesium per gram of protein was used to measure the quantity of GSH [34-40].

RESULTS:

Effect of KRE, MBE, and combination on BGL:

Blood glucose levels were significantly greater in diabetic nephropathy rats compared to normal rats that had not been administered STZ after 72 hours. This role remained unchanged throughout week four. Table 1 shows that blood glucose levels in DN rats decreased more after KRE treatment than after no treatment at all, although the decreases were less pronounced with MBE alone treatment [41-44].

Table 1: Combined BGL effects of Kudzu root and Maqui berry extract

Sr. No.	Groups	Blood glucose level (mg/dl)		
		72hr after STZ injection	Final at week 4	Final after 6th week
1.	I	84.12±3.147	85.55±3.784	80.11±3.142
2.	II	255.6±8.36	332.4±8.641	254.7±3.34
3.	III	256.2±5.48	340.8±6.458	255.1±5.42
4.	IV	256.3±3.78	481.9±3.147	255.2±3.45
5.	V	256.8±3.47	443.7±3.254	258.3±3.25
6.	VI	242.7±6.89	440.3±8.456	243.6±5.56
7.	VII	266.8±8.46	302.4±6.148	267.1±7.25

8.	VIII	445.4±18.22	443.8±5.143	426.3±11.33

The effects of kudzu root and maqui berry on hypertrophy index, kidney weight, and urine volume:
By the end of the sixth week, we had measured the hypertrophy index, renal weight, and urine volume. After 24 hours, the urine volume (ml) of DN rats was noticeably higher than that of control rats. But because their kidneys weren't functioning as well, there was a marked shift in their hypertrophy index and kidney weight. In comparison to the DN group, the rats administered Kudzu root extract, Maqui berry extract, or a combination of the two showed a marked decrease in pee volume. Both their hypertrophy index and excessive kidney weight went back to normal (Table 2).

Table 2: Volume, weight, and hypertrophy index of the kidneys as affected by extracts from Kudzu root and Maqui berries

Sr. No.	Groups	Urine Volume			Kidney weight
		0 Day	4th week	6th week	
1.	I	15.2±0.81	16.3±0.82	15.3±0.89	0.11±0.02
2.	II	19.2±0.64	20.3±0.65	20.1±0.25	1.81±0.04
3.	III	20.3±0.82	21.5±0.89	21.2±0.46	1.12±0.02
4.	IV	17.3±0.38	18.5±0.42	18.2±0.43	1.23±0.05
5.	V	19.2±0.89	20.4±0.90	20.1±0.90	1.34±0.05
6.	VI	18.5±0.82	19.6±0.91	19.6±0.78	1.66±0.06
7.	VII	19.2±0.14	20.3±0.23	20.4±0.26	1.18±0.05
8.	VIII	20.4±0.65	21.6±0.70	19.5±0.55	1.37±0.01

Hormonal and biochemical effects of Kudzu root and Maqui berry extracts on urine:
At the six-week mark, we re-analyzed the urine for albumin, urea, and total protein levels. Significant alterations occurred in the concentrations of albumin, urea, and total protein within the bodies of diabetic nephropathy rats. When compared to non-DN rats, DN rats' albumin, urea, and total protein levels were significantly greater. Kidney biomarker levels decreased significantly in DN rats treated with Kudzu root extract, Maqui berry extract, or a combination of the two. Serum creatinine, total bilirubin, and uric acid levels were assessed six hours later. Diabetic nephropathy rats' urine contained significantly greater concentrations of creatinine, total bilirubin, and uric acid compared to normal rats' urine. Rats' uric acid, creatinine, and total bilirubin levels were dramatically altered after administration of Kudzu root extract, Maqui berry extract, or a combination of the two. Table 3 shows that after the second week of therapy, all treatment groups had significantly lower biomarker levels than the DN group.

Table 3: Hormonal and biochemical effects of Kudzu root and Maqui berry extracts on urine

Sr. No.	Groups	Total Protein	Albumin	Urea	Creatinine	Bilirubin
1.	I	4.35±0.06	1.23±0.03	16.3±0.14	1.23±0.01	0.87±0.03
2.	II	8.29±0.08	4.29±0.02	21.1±0.26	3.29±0.03	6.45±0.05
3.	III	6.31±0.06	3.31±0.05	22.2±0.47	4.31±0.04	2.12±0.01
4.	IV	8.56±0.08	4.56±0.07	35.2±0.45	5.56±0.06	3.23±0.04
5.	V	6.21±0.09	4.21±0.08	35.1±0.84	3.21±0.07	2.34±0.06
6.	VI	5.58±0.06	3.58±0.04	35.6±0.80	2.58±0.05	2.66±0.04
7.	VII	5.46±0.04	4.46±0.05	23.4±0.30	4.46±0.04	2.18±0.06
8.	VIII	5.75±0.05	2.75±0.06	23.5±0.61	3.75±0.05	3.37±0.02

Metabolic and enzymatic effects of Kudzu root and Maqui berry extracts on blood samples:
Blood samples were taken after six weeks to measure albumin, urea, and total protein levels. Rats suffering from diabetic nephropathy showed substantial changes in albumin, urea, and total protein concentrations. The levels of creatinine, total bilirubin, and uric acid were noticeably greater ($p<0.001$) in the urine of rats with diabetic nephropathy compared to normal rats. After six weeks, there were notable variations in the blood levels of uric acid, creatinine, and total bilirubin among rats that were administered Kudzu root extract, Maqui berry extract, or a combination of the two. Rats with

diabetic nephropathy had significantly higher concentrations of creatinine, total bilirubin, and uric acid in their urine compared to rats without the condition. Rats' uric acid, creatinine, and total bilirubin levels were dramatically altered after administration of Kudzu root extract, Maqui berry extract, or a combination of the two [45-48]. Table 4 shows that after two weeks of treatment, all treatment groups had significantly lower biomarker levels than the DN group.

Table 4: The impact on serum biochemical parameters of extracts from Kudzu root and Maqui berries, as well as their combination

Sr. No.	Groups	Total Protein	Albumin	Urea	Creatinine	Bilirubin
1.	I	5.35±0.05	2.23±0.03	20.3±0.14	1.23±0.01	0.88±0.06
2.	II	13.29±0.08	5.29±0.02	52.1±0.26	3.29±0.03	4.45±0.04
3.	III	4.31±0.04	4.31±0.05	33.2±0.47	4.31±0.04	3.12±0.02
4.	IV	5.56±0.07	3.56±0.07	36.2±0.45	5.56±0.06	4.23±0.03
5.	V	4.21±0.08	6.21±0.08	38.1±0.84	3.21±0.07	1.34±0.04
6.	VI	3.58±0.05	2.58±0.04	31.6±0.80	2.58±0.05	3.66±0.03
7.	VII	4.46±0.04	3.46±0.05	29.4±0.30	4.46±0.04	4.18±0.04
8.	VIII	3.75±0.08	1.75±0.06	31.5±0.61	3.75±0.05	2.37±0.03

CONCLUSION:

Natural antioxidants like maqui berry and kudzu root extract may help manage high blood sugar and the oxidative damage that comes with diabetes, according to a recent study. The kidneys were strongly protected from damage when treated with kudzu root extract and maqui berry extract, which enhanced the efficiency of the antioxidant system and corrected morphological alterations. Compared to using just one of the antioxidants, the combined effect was much stronger when all three were employed. The study found that diabetic nephropathy was able to be prevented from worsening by combining the strong antioxidant properties of kudzu root extract with those of maqui berry extract.

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Conflict of Interest:
None

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