ORIGINAL ARTICLE

Effects of Biskhapra (*Trianthema portulacastrum* Linn.) leaves extract in adriamycin induced nephrotic syndrome

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Trianthema portulacastrum popularly known as Biskhapra, is a well documented drug, used for various kidney ailments, although no scientific evidence is available. The animals were divided into 7 groups of 10 animals each, i.e. plain, negative A and B, and two pre- and post-treated groups. Plain control treated with distilled water only and adriamycin (7.5 mg/kg) was administered to other groups. Negative A and B group were left untreated for 10 and 30 days, respectively, while pre- and post-treated groups were administered test drug in a dose of 450 and 900 mg/kg before and after the administration of adriamycin, respectively, for 20 days. Adriamycin produces proteinuria, increases the serum cholesterol, creatinine, blood urea nitrogen (BUN), and decreases the serum albumin and protein. Therefore, these parameters were taken into account along with histopathological changes in kidney. Test drug reduced the serum cholesterol, creatinine and BUN, and increased the serum albumin and protein levels. Histopathological examination revealed remarkable changes in negative control groups, which were corrected in all the test groups. Test drug has preventive as well as curative effect in adriamycin-induced nephrotic syndrome and is in consonance with the reports of Unani literature regarding its use in renal disorders.

Key words: Hydroalcoholic extract, minimal change nephropathy, preventive and curative effect, unani medicine, wistar rats

INTRODUCTION

Nephrotic syndrome is characterized by substantial loss of protein in urine (primarily albuminuria), leading to hypoproteinemia (hypoalbuminemia) and consequently edema. The overall prevalence of nephrotic syndrome in childhood is approximately 2-7 case per 100,000 children.[1,2] The disease occurs in the majority; more than 75% relapse frequently and almost half shows frequent relapse or steroid dependence.[3] Ill defined management of nephrotic syndrome and poor result of the present treatment of nephrotic syndrome with frequent relapse, steroid dependency, and various side effects of the conventional drugs were the key points, which exacerbate for selecting such type of challenging topic for research.

Nephrotic syndrome may develop in many mammalian species as a result of primary diseases such as minimal change disease in humans, inflammatory diseases such as membranous nephropathy or immune glomerulonephritis in humans or laboratory animals, or exposure to toxic substances such as adriamycin in rats.[4] Besides proteinuria, development of edema and ascites are permanent clinical symptoms in the majority of sufferers.[5] Biskhapra is a well documented and well-known drug in Unani system of medicine for its wide use in urinary system as diuretic, in ascites, anasarca, cystitis and in case of dribbling of urine. This drug was used by Diascorides for diuresis. Beside Diascorides, a lot of Unani classical literature as well as new literature from other discipline described its use as diuretic in ascites and anasarca.[6-9] Experimentally, it has been proved that the drug Biskhapra has nephroprotective,[10] hepato protective,[11-15] antioxidant,[14] and anti-inflammatory activities,[16] and it lowers high cholesterol, blood urea nitrogen and serum creatinine level.[10] But no experimental or clinical evidence is available to prove its effect in nephrotic syndrome. Therefore, the drug Biskhapra is taken to confirm its efficacy in experimentally induced nephrotic syndrome in rats.

Adriamycin is an anti-neoplastic agent,[17] causes nephrotic syndrome in rats that corresponds to minimal change nephropathy or focal segmental glomerulosclerosis in human,[18,19] and it characterized by proteinuria and high serum cholesterol, serum

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creatinine, blood urea nitrogen, and low level of serum protein and albumin.[20] Therefore, these parameters are taken as the biomarkers of the diseased condition of the animals. Apart from these biochemical parameters, histopathological examination by light microscopy of rat kidney was carried out to determine the degree of morphological damage caused by Adriamycin and any improvement by the test drug against toxicity.

MATERIALS AND METHODS

Preparation of the Test Drug

Plant material

The leaves of the plant Biskhapra (*Trianthema portulacastrum* Linn.) were procured from National Institute of Unani Medicine campus, Bangalore during the month of May – June, 2010. The authentication of drug was carried out by Dr. Siddamallayya N, botanist of National Ayurveda Dietetics Research Institute, Dept. of Ayush, Ministry of Health and Family Welfare, Govt. of India, Ashoka Pillar, Jaynagar, Bangalore. (Ref. No.-Drug Authentication/ SMPU/NADRI/BNG/2010-11/155, dated-28.05.2010) and the voucher specimen has been deposited there and in the Dept. of Ilmul Advia, NIUM, Bangalore for future reference.

Preparation of extract

The leaves of the plant were plucked from fresh plant of Biskhapra and dried in hot air oven below 40°C and powdered in electrical grinder. The powder thus obtained was extracted in 50% hydro alcoholic solvent (ethanol and distilled water 1:1) in the ratio of 1:6 (drug: solvent) by Soxhlet's apparatus for 8 hours at fixed temperature of 80°C. The extract was filtered by filter paper and evaporated on water bath till it dried completely. The yield percentage was calculated with reference to the weight of crude drug and was found to be 30% w/w.

Dosage of the drug

The human therapeutic dose of test drug, mentioned in Unani classical literature is 12 gm.[21] The dose for Wistar rat was calculated by multiplying the human therapeutic dose by the conversion factor of 7[22] and found to be 1.5 gm/kg. The dose of the extract was determined with reference to the dose of crude drug and found to be 450 mg/kg. Another higher dose was calculated that is just double of the first dose (900 mg/kg), to evaluate the efficacy of test drug in a dose-dependent manner.

Animals

The study was carried out on healthy Wistar rats of either sex weighing about 150-200 gm. The animals were obtained from the Central Animal Research Facility, National Institute of Mental Health and Neuro Sciences (NIMHANS), Bangalore. They were acclimatized to the laboratory condition for 5 days before the experimental studies. The animals were housed in polypropylene cages and kept under standard environmental condition of 12 hrs light and dark cycle, temperature (23°± 2°C) and humidity (55±15%). They were fed with standard food pellets and water *ad libitum*. Study was conducted after obtaining the ethical clearance by the Institutional Animal Ethics Committee of National Institute of Unani Medicine, Bangalore. (Reg. No. - 953/C/CPCSEA/2006.)

Drugs and chemicals

Adriamycin (Batch No-NI9201) was procured from Intas Biopharmaceuticals Ltd. Moraiya- 382210, Ta: Sanand, Ahmadabad, India. Urine protein (Lot No-GP-1001) was procured from Lab-Care Diagnostics (India) Pvt. Ltd. Srigam, Dist-Vasad, Gujrat, India. Blood urea and serum creatinine kits (Lot No-B110935 and B031060 respectively) were purchased from Transasia Bio-Medicals Ltd., Nalagarh Road, Village Malpur, Baddi, Dist. Solan, HP. Serum protein, serum albumin and serum cholesterol kits (Product No- 11013100, 11001100 and 11403102, respectively) were obtained from Agappe Diagnostics Ltd., Agappe Hills, Dist. Ernakulum, Kerala, India. Thiopentone sodium (Batch No-173141) was procured from Neon Laboratories Limited, 28 Mahal Ind. Est, Andheri (East), Mumbai. The auto analyser used for the analysis, was from B.S.S. Co. Ltd. Model Star 21 Plus, No. E12046 marketed by Aspen Laboratories.

Experimental design for adriamycin induced nephrotic syndrome

This test was carried out by the method of Bertani *et al.*,[20] with some modification in treatment schedule. The rats were divided into seven groups of 10 animals each. The animals in group I was administered with 1 ml of distilled water orally, once daily for 20 days and served as plain control. Other than plain control group all the groups were administered with single i.v. injection of adriamycin in the dose of 7.5 mg/kg. The animals of group II were left for 10 days, while group III was left for 30 days after adriamycin injection and served as negative control group A and B respectively. In group IV and V, treatment was started 10 days before the administration of adriamycin. Then were treated with hydroalcoholic extract of test drug in a dose of 450 mg/kg and 900 mg/kg (suspended in 1 ml distilled water) once, orally, per day for 20 days, and served as pre-treated test group A and B, respectively. While the animals of group VI and VII were treated with hydroalcoholic extract of test drug in the dose of 450 and 900 mg/kg, once daily for 20 days after 10 day of administration of adriamycin and served as post treated group A and B, respectively.

Analytical Procedures

At the end of the experiment, all the animals of each group were kept in metabolic cages for 24 hrs urine collection for the estimation of urine protein, with free access of water but

deprived of food. Thereafter, animals were sacrificed under thiopentone anaesthesia (60 mg/kg i.p). Blood was collected by cardiac puncture for the estimation of serum creatinine, serum protein, serum albumin, serum cholesterol and blood urea nitrogen (BUN). These parameters were assessed by using auto analyzer and specific kits. One kidney from one animal of each group was dissected out, washed with tap water and preserved in 10% formalin solution for the histopathological studies.

Statistical Analysis

The results among different groups were analysed by using one way ANOVA with post hoc. Tukey Kramer multiple comparison test and urine protein by Kruskal Wallis test with post Dunn: Comparison test. Statistical difference was considered significant at $P<0.05$.

RESULTS

Both the negative groups were compared with plain control, pre-treated A and B groups were compared with negative control group A, and post-treated groups A and B were compared with negative control group B.

Assessment of Urine Protein

The median urine protein in plain control group was observed to be 1(0, 3), while it was increased to 4 (2, 4) in negative control groups A and B. In pre-treated groups A and B, it was found 3 (2, 4) and 3 (0, 4), while in post-treated groups A and B, 4 (4, 4). The results showed no significant alteration in urine protein when compared with negative control groups [Tables 1 and 2].

Assessment of Biochemical Parameters

The mean serum cholesterol in plain control was observed as 50.05±6.64 mg/dl, it increased to 104.8±6.53 mg/dl ($P<0.01$) in negative control group A, while 139±23.62 mg/dl ($P<0.01$) in negative control group B. In pre-treated group A, it was decreased to 69.11±9.66 mg/dl ($P<0.05$) and in B, 59.73±3.13 mg/dl ($P<0.01$). In post-treated A and B groups, serum cholesterol level decreased significantly to 77.28±8.14 mg/dl ($P<0.01$) and 73.16±5.13 mg/dl ($P<0.01$) respectively, in comparison to negative control B [Tables 1 and 2].

The mean serum creatinine in plain control was observed to be 0.81±0.021 mg/dl, which increased in negative control group A and was found to be 1.05±0.08 mg/dl ($P<0.05$), while it increased to 1.06±0.072 mg/dl ($P<0.05$) in negative control group B. In pre-treated group A, it decreased up to 0.87±0.035 mg/dl and in pre-treated group B, to 0.84±0.033 mg/dl ($P<0.05$). In post-treated A and B groups, serum creatinine level decreased significantly to 0.85±0.054 mg/dl ($P<0.05$) and 0.80±0.033 mg/dl ($P<0.01$), respectively [Tables 1 and 2].

Table 1: Effect of hydro alcoholic extract of Biskhapra (*Trianthema portulacastrum* Linn.) leaves in adriamycin-induced nephrotic syndrome in preventive regimen groups

Parameters	Groups			
	Plain control (Distilled water 1 ml/kg)	Negative control group A (Adriamycin 7.5 mg/kg)	Pre treated group A (Biskhapra 450 mg/kg + Adriamycin 7.5 mg/kg)	Pre treated group B (Biskhapra 900 mg/kg + Adriamycin 7.5 mg/kg)
Urine protein (median with range)	1 (0, 3)	4 (2, 4) a^{ns}	3 (2, 4) b^{ns}	3 (0, 4) b^{ns}
S. cholesterol (mg/dl)	50.05±6.64	104.8±6.53 a**	69.11±9.66 b*	59.73±3.13 b**
S. creatinine (mg/dl)	0.81±0.021	1.05±0.08 a*	0.87±0.035 b^{ns}	0.84±0.033 b*
Blood urea nitrogen (mg/dl)	48.85±0.44	69.60±4.41 a*	54±3.91 b^{ns}	52.2±3.42 b*
S. protein (gm/dl)	7.36±0.313	5.92±0.351 a*	6.25±0.311 b^{ns}	6.29±0.182 b^{ns}
S. albumin (gm/dl)	4.63±0.140	3.5±0.234 a*	4.26±0.264 b^{ns}	4.38±0.126 b*

Values expressed in Mean±SEM, ns - non significant, *$P<0.05$, **$P<0.01$, $n=10$ in each group, test used ANOVA one-way followed by Tukey Kramer comparison test and urine protein was analysed by Kruskal Wallis test with post Dunn: Comparison test. a - Vs Plain control and b - Negative control A

Table 2: Effect of hydro alcoholic extract of Biskhapra (*Trianthema portulacastrum* Linn.) leaves in adriamycin-induced nephrotic syndrome in curative regimen groups

Parameters	Groups			
	Plain control (Distilled water 1 ml/kg)	Negative control group B (Adriamycin 7.5 mg/kg)	Post-treated group A (Adriamycin 7.5 mg/kg + Biskhapra 450 mg/kg)	Post-treated group B (Adriamycin 7.5 mg/kg + Biskhapra 900 mg/kg)
Urine protein (median with range)	1 (0, 3)	4 (2, 4) a^{ns}	4 (4, 4) b^{ns}	4 (4, 4) b^{ns}
S. cholesterol (mg/dl)	50.05±6.64	139±23.62 a**	77.28±8.14 b**	73.16±5.13b**
S. creatinine (mg/dl)	0.81±0.021	1.06±0.072 a*	0.85±0.054 b*	0.80±0.033 b**
Blood urea nitrogen (mg/dl)	48.85±0.448	73.54±6.08 a**	65.57±3.670 b^{ns}	56.66±2.99 b*
S. protein (gm/dl)	7.36±0.313	5.05±0.397 a*	6.65±0.306 b^{ns}	6.43±0.709 b^{ns}
S. albumin (gm/dl)	4.63±0.140	2.96±0.399 a*	4.15±0.372 b^{ns}	4.64±0.388 b*

Value expressed in Mean±SEM, ns - non significant, *$P<0.05$, **$P<0.01$, $n = 10$ in each group, test used ANOVA one way followed by Tukey Kramer comparison test and urine protein was analysed by Kruskal Wallis test with post Dunn: Comparison test. a - Vs Plain control and b - Vs Negative control B. Histopathological findings of rat kidney by light microscopy

In plain control group mean BUN level was observed 48.85±0.44 mg/dl, it increased to 69.60±4.41 mg/dl (P<0.05) in negative control group A and 73.54±6.08 mg/dl (P<0.01) in negative control group B. In pre-treated group A, it decreased up to 54±3.91 mg/dl treated with low dose of test drug and in pre-treated group B treated with high dose of test drug, 52.2±3.42 mg/dl (P<0.05). In post-treated A and B groups, blood urea nitrogen level decreased significantly to 65.57±3.67 mg/dl and 56.66±2.99 mg/dl (P<0.05), respectively [Tables 1 and 2].

The mean serum protein in plain control was observed to be 7.36±0.313 gm/dl, which decreased to 5.92±0.351 gm/dl (P<0.05), and 5.05±0.397 gm/dl (P<0.05) in negative control groups A and B. In pre-treated group A, it was increased to 6.25±0.311 gm/dl and in pre-treated group B, 6.29±0.182 gm/dl. In post-treated A and B groups, serum protein level was observed as 6.65±0.306 gm/dl and 6.43±0.709 gm/dl, respectively [Tables 1 and 2].

The mean serum albumin in plain control was found to be 4.63±0.140 gm/dl, which decreased in negative control group A and B up to 3.5±0.234 gm/dl (P<0.05), and 2.96±0.399 gm/dl (P<0.05). In pre-treated group A, serum albumin level was increased up to 4.26±0.264 gm/dl and in pre-treated group B, 4.38±0.126 gm/dl (P<0.05). Similarly, in post-treated A and B groups, serum albumin level increased to 4.15±0.372 gm/dl and 4.64±0.388 gm/dl (P<0.05), respectively [Tables 1 and 2].

Histopathological Examination of Rat Kidney

Histopathological examination of rat kidney by light microscopy revealed mesengial cell proliferation, glomerular inflammation, atrophy, and interstitial congestion, ischemic changes, tubular changes and vacuolation with mild degree in negative control group A, while same parameter with more severity along with glomerular sclerosis and interstitial fibrosis were observed in negative control group B. All the parameters were remarkably reduced in pre-treated groups and much profoundly reduced in post-treated groups and no pathological changes were observed in plain control [Figures 1-7].

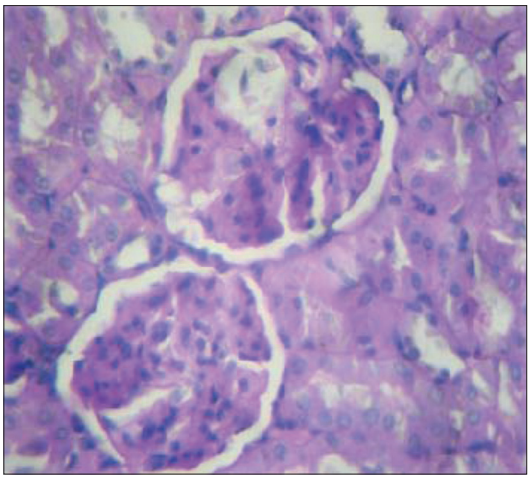

Figure 1: Plain control group showing normal structure of the kidney

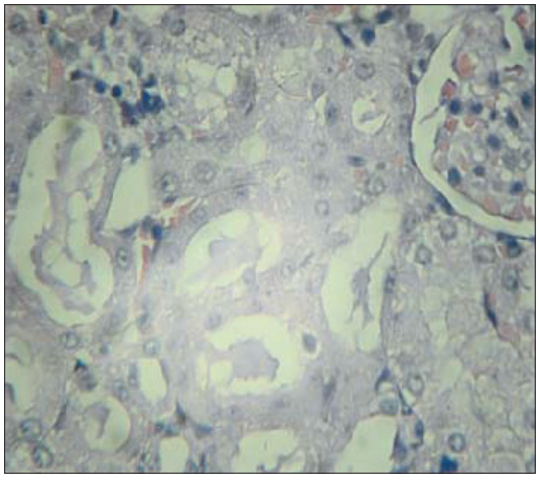

Figure 2: Negative control group A showing moderate ischemic changes in proximal convoluted tubule

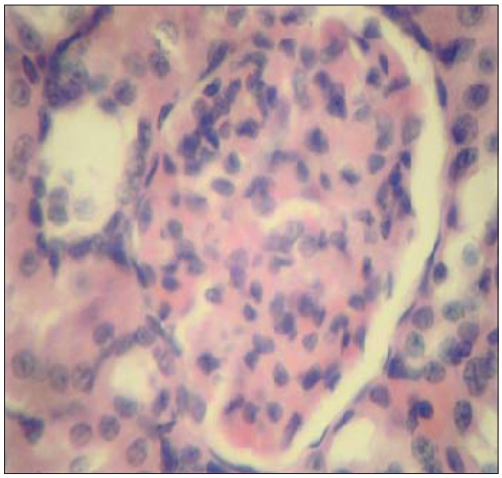

Figure 3: Negative control group B showing severe mesengial proliferation

DISCUSSION AND CONCLUSION

In this study urine protein, BUN, serum cholesterol and serum creatinine were increased while serum protein and albumin were found to be decreased significantly in both the negative groups treated with adriamycin. The result clearly indicates the toxic effect of adriamycin. In the groups receiving test drug, these markers were decreased and protein and albumin were found to be increased and renal function was also ameliorated.

Normally, protein is not found in urine, but in plain control group some urine protein was observed further in pre- and post-treated group A and B no significant reduction in urine protein was observed in comparison to negative control groups. It indicates that there is no effect of test drug to check the urinary protein of nephrotic rats. But the presence

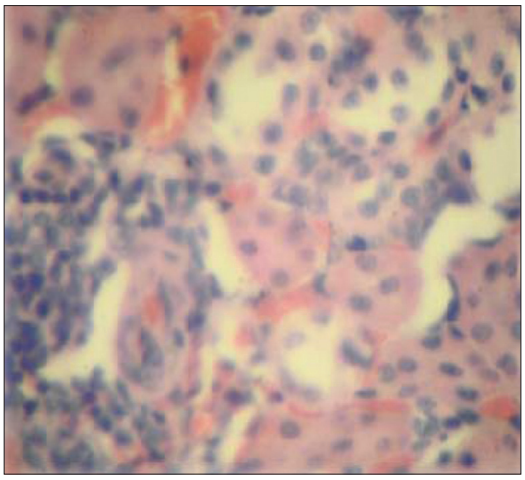

Figure 4: Pre-treated group A showing mild mesengial proliferation

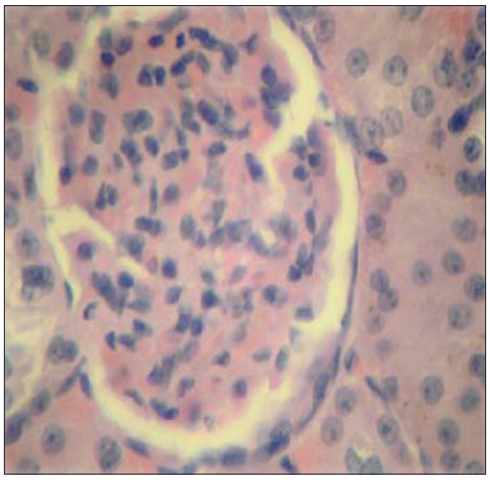

Figure 5: Pre-treated group B showing mild glomerular congestion

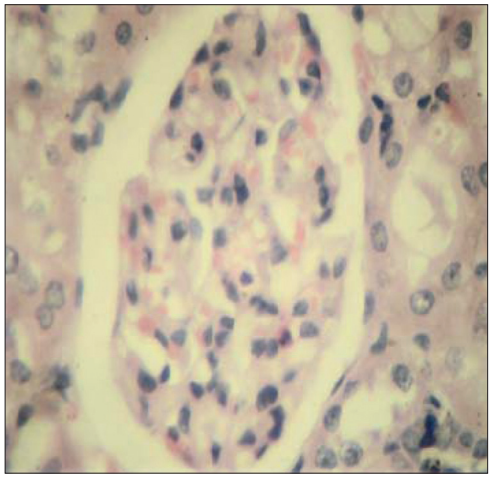

Figure 6: Post-treated group A showing mild degree of glomerular congestion

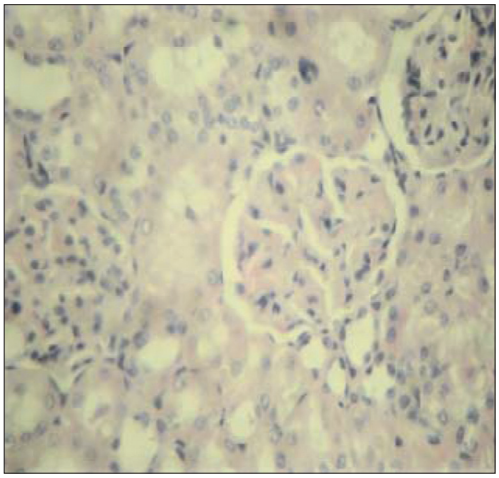

Figure 7: Post-treated group B showing almost normal glomeruli

of protein in plain control indicates that there is some other factor which is responsible for proteinuria and hindered the efficacy of test drug. Similar results were found in case of serum protein and albumin. Though the test drug in low dose did not show any significant elevation of serum protein and albumin but values were found to be nearly similar to the plain control. Further, in high dose serum albumin in pre-treated and post-treated B groups was found to be significantly (P<0.05) increased. Since proteinuria did not relieve by the test drug, there may be the possibility that the drug was not able to reconstruct the fusion of foot processes, due to which protein leaked. Further, proteinuria leads to hypoproteinemia and hypoalbuminemia, therefore in this study, test drug failed to correct the hypoproteinemia and hypoalbuminemia, significantly. Although the test drug increased the serum albumin level in higher dose in both the groups of pre-treated as well as post-treated animals. It means that the test drug may help to some extent in synthesis of protein in the liver, which compensates the excessive loss of urinary protein. As it has been reported by Sengottuvelu,[23] that, one of the species of Trianthema (*Trianthema decandra*) is able to synthesise protein in liver. The findings of the present study further support the study of Sengottuvelu.

Serum cholesterol and serum creatinine level decreased significantly in pre and post treated groups in dose dependent manner. These results demonstrate that the drug has both preventive and curative effect. This result is akin to the result observed by Saunder *et al*.[10] He reported that methanolic extract of *Trianthema portulacastrum* Linn. (100 and 200 mg/kg) cause significant reduction in the level of serum cholesterol (P<0.001) and serum creatinine (P<0.01) in atherosclerotic diet-fed male Wistar rats.

Moreover, the test drug also has significant diuretic activity.[24] Diuretics increase the Glomerular filtration rate (GFR) and stimulate diuresis, which cause excessive excretion of creatinine and urea from kidney due to increase in urine output. Therefore, it can be concluded that the diuretic property of Biskhapra has a supportive action in the significant reduction of BUN and serum creatinine in test groups.

Adriamycin, an anticancerous drug, forms a complex with DNA, inhibiting synthesis of both Deoxyribonucleic acid (DNA) and Ribonucleic acid (RNA).[25] Kidney injury induced by adriamycin in a range of laboratory animals is an analogue of nephrotic syndrome in humans, the appearance of which is minimal change nephropathy, focal and segmental glomerulosclerosis.[26] Our histopathological findings showed tubulointerstitial changes with cellular infiltration and vacuolar degeneration in untreated groups. Interstitial inflammation is considered to be an important determinant of the outcome of glomerular inflammation. Several studies suggested that myofibroblasts of the interstitium may play a crucial role in the pathogenesis of fibrosis in glomerular diseases. [27,28] Thus, the tubulointerstitial cellular response and vacuolar degeneration seen in negative groups emphasizes the severity of nephrotic syndrome. On the other hand, attenuation of interstitial inflammation and other renal injuries are secondary to inhibition of proteinuria by test drug. The metabolism of adriamycin results in reactive oxygen species (ROS) formation.[29] This ROS is responsible for these types of pathological changes in the kidney.[30] The test drug has antioxidant property,[14] which may be one of the factors by which amelioration of toxicity, which was insulted by the adriamycin, took place. This property of the test drug scavenges the ROS and protects the normal architecture of the kidney.

Inflammatory mediators like interleukin-1 (cytokine) could also be important for structural and functional disturbances occurring in glomerulus.[31] The test drug Biskhapra, as described that it has anti-inflammatory property,[16,32] which may ameliorate the inflammatory changes of the kidney and prevent the kidney from the chronic progressive diseased conditions like glomerulosclerosis and interstitial fibrosis, as seen in negative control. Further, the test drug has astringent property,[9] which may treat or check the mesengial proliferation and infiltration of other inflammatory mediators like Interleukin (IL), cytokine, Tumor necrosing factor (TNF)-α and Platelet activating factor (PAF) and reverse the kidney to its normal state. Studies reported that hyperlipidemia may induce mesengial cell proliferation.[33] The test drug has been proved that it lowers the total cholesterol and triglyceride level.[10] Similar effect was observed in the present study. This property of the drug may be an important mechanism to protect the kidney from mesengial cell proliferation.

On the basis of the above findings, it can be concluded that the preventive and curative effect of the test drug may be through its anti inflammatory,[14,16] and hypolipidemic activities.[10] Leaves of the plant contain various phyto constituents like steroids, alkaloids, terpenoids, flavonoids, phenolic compounds, saponins and carbohydrates.[34,35] One of the alkaloids found in the test drug is punarnavine, which is used to promote urination and useful in dropsy and kidney disease.[36] Flavonoids have free radical scavenging and antioxidation properties.[37] Some saponins have also been found to have anti-oxidative or reductive activity.[38] This further demonstrates that the test drug produced effect through diverse mechanisms complementing each other and the collective response actually translated into nephroprotection.

In the light of the above findings and discussion, it can be concluded that the test drug possessed significant nephroprotective effect. Thus, the study validated the claim of Unani system of medicine that Biskhapra is a drug that can be used in kidney ailments.

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1. Not presented anywhere
2. It is not a clinical trial

REFERENCES

1. Niaudet P. Steroid sensitive idiopathic nephrotic syndrome. In: Anver ED, Harmon WE, Niaudet P, editors. Pediatric nephrology. 5th ed. Philadelphia: Lippincott Williams and Wikkins; 2004. p. 545-73.
2. Behrman RE, Kligman RM, Jenson HB. Nelson Text Book of Pediatrics. 17th ed. New Delhi: Elsevier India Private Limited; 2004. p. 1753-7.
3. Constantinescu AR, Shah HB, Foote EF, Weiss LS. Predicting first-year relapses in children with nephrotic syndrome. Pediatrics 2000;105:492-5.
4. Bos H, Laverman GD, Henning RH, Tiebosch AT, de Jong PE, de Zeeuw D, *et al*. Involvement of renal ACE activity in proteinuria associated renal damage in untreated and treated adriamycin nephrotic rats. J Renin Angiotensin Aldosterone Syst 2003;4: 106-12.
5. Vogt B, Dick B, Marti HP, Frey FJ, Frey BM. Reduced 11 β-hydroxysteroid-dehydrogenase activity in experimental nephritic syndrome. Nephrol Dial Transplant 2002;17:753-8.
6. Ibn Baitar, Jameul Mufradat al Advia wal Aghzia (Urdu translation by CCRUM). Vol 2. 2nd ed. New Delhi: CCRUM, Ministry of Health and Family Welfare; 2000. p. 82.
7. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal Plant. 1st ed. New Delhi: National Institute of Science Communication and Information Resources; 2002. p. 246.
8. Prajapati ND, Kumar U, Agro's Dictionary of Medicinal Plants. 1st ed. Jodhpur, India: Dr. Updesh Purohit for Agrobios; 2003. p. 352.
9. Ibn Sina, Al Qanoon Fil Tibb (Urdu translation by Kantoori GH). Vol 2, Part 1. New Delhi: Idara Kitabus Shifa; 2007. p. 105.
10. Saunder AS, Reddy AR, Rajeshwar Y, Kiran G, Prasad DK, Baburao B, *et al*. Protective effect of methanolic extract of *Trianthema*

portulacastrum in atherosclerotic diet induced renal and hepatic changes in rats, Scholars Research Library 2010;2:540-5.
11. Mandal A, Karmakar R, Bandyopadhyay S, Chatterjee M. Antihepatotoxic potential of *Trianthema portulacastrum* in carbon tetrachloride induced chronic hepatocellular injury in mice: Reflection in haematological, histological and biochemical characteristics. Arch Pharm Res 1998;21:223-30.
12. Sarkar A, Pradhan S, Mukhopadhyay I, Bose SK, Roy S, Chatterjee M. Inhibition of early DNA-damage and chromosomal abberations by *Trianthema portulacastrum* L. In carbon tetrachloride-induced mouse liver damage. Cell Biol Int 1999;23:703-8.
13. Kumar G, Banu GS, Pappa PV, Sundararajan M, Pandian MR. Hepatoprotective activity of *Trianthema portulacastrum* L. against paracetamol and thioacetamide intoxication in albino rats. J Ethnopharmacol 2004;92:37-40.
14. Kumar G, Banu GS, Pandian MR. Evaluation of Antioxidant activity of *Trianthema portulacastrum* Linn. Indian J Pharmacol 2005;37:331-3.
15. Banu GS, Kumar G, Murugesan AG. Ethanolic leaves extract of *Trianthema portulacastrum* Linn. ameliorates Aflatoxin B1 induced hepatic damage in rats. Indian J Clin Biochem 2009;24:250-6.
16. Vohora SB, Shah SA, Naqvi SA, Ahmad S, Khan MS. Studies on *Trianthema portulacastrum*. Planta Med 1983;47:106-8.
17. Bertazzoli C, Chieli T, Ferni G, Ricevuti G, Solcia E. Chronic toxicity of adriamycin: A new antineoplastic antibiotic. Toxicol Appl Pharmacol 1972;21:287-301.
18. Remuzzi G, Zoja C, Remuzzi A, Rossini M, Battaglia C, Broggini M, *et al*. Low protein diet prevents glomerular damage in adriamycin-treated rats. Kidney Int 1985;28:21-7.
19. Deschenes G, Doucet A. Collecting duct (Na+/K+)-ATPase activity is correlated with urinary sodium excretion in rat nephrotic syndromes. J Am Soc Nephrol 2000;11:604-15.
20. Bertani T, Poggi A, Pozzoni R, Delaini F, Sacchi G, Thoua Y, *et al*. Adriamycin induced nephrotic syndrome in rats: Sequence of pathologic events. Lab Invest 1982;46:16-23.
21. Ghani N, Khazainul Advia. 1st ed. New Delhi: Idara Kitabus Shifa; 1929. p. 371.
22. Freireich EJ, Gehan EA, Rall DP, Schmidt LH, Skipper HE. Quantitative comparision of toxicity of anticancer agents in mouse, rat, hamster, dog, monkey and man. Cancer Chemother Rep 1966;50:219-44.
23. Sengottuvelu S, Srinivasan D, Duraisami R, Nandhakumar J, Vasudevan M, Sivakumar T. Hepatoprotective activity of *Trianthema decandra* on carbon tetrachloride-induced hepatotoxicity in rats. Int J Green Pharm 2008;2:122-5.
24. Shafat MK, Kalam MA, Jahan N, Ahmad G, Jafri MA. Evaluation of diuretic activity of hydro alcoholic extract of Biskhapra (*Trianthema portulacastrum* Linn.) leaves in rats, Hippocratic Journal of Unani Medicine. Vol. 6. New Delhi: CCRUM; 2011. p. 81-8.
25. Tesar V, Zima T, Jirsa M Jr, Crkovská J, Stípek S, Vernerová Z, *et al*., Influence of losartan and enalapril on urinary excretion of 8-isoprostane in experimental nephritic syndrome. Med Sci Monit 2002;8:BR69-74.
26. Comporti M. Lipid peroxidation. Biopathological significance. Mol Aspects Med 1993;14:199-207.
27. Krag S, Danielsen CC, Carmeliet P, Nyengaard J, Wogensen L. Plasminogen activator inhibitor-1 gene deficiency attenuates TGF-beta1-induced kidney disease. Kidney Int 2005;68:2651-66.
28. Crean JK, Finlay D, Murphy M, Moss C, Godson C, Martin F, *et al*. The role of p42/p44 MAPK and protein kinase B in connective tissue growth factor induced extracellular matrix protein production, cell migration and actin cytoskeletal rearrangement in human mesengial cells. J Biol Chem 2002;277:44187-94.
29. Zima T, Tesar V, Crkovská J, Stejskalová A, Pláteník J, Temínová J, *et al*. ICRF-187 (dexrazoxan) protects from adriamycin-induced nephrotic syndrome in rats. Nephrol Dial Transplant 1998;13:1975-9.
30. Myers CE, McGuire WP, Liss RH, Ifrim I, Grotzinger K, Young RC. Adriamycin: The role of lipid peroxidation in cardiac toxicity and tumour response. Science 1977;197:165-97.
31. Bricio T, Molina A, Egido J, Gonzalez E, Mampaso F. IL-1-like production in adriamycin-induced nephrotic syndrome in the rat. Clin Exp Immunol 1992;87:117-21.
32. Kabeeruddin AM, Makhzanul Mufradaat. 1st ed. New Delhi: Idara Kitabus Shifa; 2007. p. 110.
33. Thomas WA, Kim DN, Lee KT, Reiner JM, Schmee J. Population dynamics of arterial cells during atherogenesis. XIII. Mitogenic and cytotoxic effects of a hyperlipidemic (HL) diet on cells in advanced lesions in the abdominal aortas of swine fed an HL diet for 270-345 days. Exp Mol Pathol 1983;39;257-70.
34. Shafat K, Nasreen J, Jafri MA. Physico-chemical studies of Biskhapra (*Trianthema portulacastrum* Linn.) leaves. Indian J Unani Res 2011;11:52-60.
35. Kokate CK. Practical pharmacognosy. 1st ed. New Delhi: Vallabh Prakashan; 1994. p. 107.
36. Bhattacharjee SK. Handbook of Medicinal Plants. 4th ed. Jaipur: Pointer Publishers; 2004. p. 353.
37. Sharma DK. Pharmacological properties of flavonoids including flavonolignans integration of petrocrops with drug development from plants. J Sci Ind Res 2006;65:477-84.
38. Francis G, Kerem Z, Makkar HP, Becker K. The biological action of saponins in animal systems: A review. Br J Nutr 2002;88:587-605.

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