DOI: 10.22270/jmpas.V10I6.1658 ISSN NO. 2320–7418

International peer reviewed open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com CODEN: JMPACO

Case report

Investigation of enalapril and quercetin on chronic renal failure

Anushika Singh, Arvind Kumar Srivastava*, Alok Mukerjee, Sunil kumar Singh, Abhishek Kumar Tripathi, Vandana Yadav

United Institute of Pharmacy, Naini Prayagraj, Uttar Pradesh India

ABSTRACT

Kidneys have a capability to filter waste from our blood, when this capacity of kidney is compromised several disturbances in our body arise. Acute kidney injury is a reversible disorder characterized by a rapid loss of renal function shown by an increase in Serum creatinine, urea nitrogen on an hourly, daily, weekly basis. According to the WHO Kidney disease causes over 850,000 deaths every year. Chronic kidney disease being greatest cause of mortality and largest cause of disability. Chronic renal failure is irreversible but precaution may prevent further damage of nephrons. Quercetin is a flavonol present in a number of plant parts that belongs to the category of polyphenols. Enalapril is an ACE inhibitor that is extensively used now days to treat chronic renal failure. In this study adenine is used to induce chronic renal failure and enalapril in conjunction with a natural compound quercetin is applied for the suppression of chronic renal failure. Water intake, urine output, food intake, biochemical analysis of blood and urine with kidneys histopathological markers were investigated for all five treatment groups were compared with control group. Quercetin with enalapril treated animals recovered significantly when compared with the control and standard groups. Quercetin shows free radical scavenging and anti-inflammatory response on kidney and reduces the stress on kidneys, on the other hand Enalapril, due to its diuretic action expels the waste materials from the blood circulation.

Keywords: Quercetin, Enalapril, Captopril, Chronic renal failure

Received - 13-08-2021, Reviewed - 11/09/2021, Revised/ Accepted- 16/10/2021

Correspondence: Dr. Arvind Kumar Srivastava* ✉ arvind.org@live.com

United Institute of Pharmacy, Naini Prayagraj, Uttar Pradesh India

INTRODUCTION

Renal Failure

Kidney failure happens when kidneys' capability to filter waste from your blood is compromised. Nephro health and functionality can be harmed by a variety of circumstances, including hazardous exposed to external toxins or certain medications, pathological disease, extreme dehydration, and organ damage. There are two types of renal failure one is acute kidney damage while other is chronic renal failure

Acute Renal Failure

Acute kidney injury has taken the place of acute renal failure. Acute kidney failure is a reversible disorder characterized by a rapid loss of renal function shown by an increase in serum creatinine and Blood urea Nitrogen on an hourly/daily/weekly basis. Nitrogen is a nutrient that is found In developing and developed countries the global incidence of this disease in the community is 2,147 and 4,085 per million persons per year, respectively[1,2].According to recent estimates from affluent nations, death rate is reported in 4.3-8.5% patients while hospitalization treatment cures 20% to 60% patients. Renal replacement treatment shows a low range of patients with 30 percent hospital mortality rate [3]. Every year, it is estimated that almost 2 million individuals die from this disease around the world [4].The treatment of disease is primarily effective but in severe cases need of renal replacement is required [5].

Chronic Renal failure

Chronic renal failure is now referred to as chronic kidney disease is a long-term, gradual, and irreversible decrease of renal function. Chronic kidney disease (CKD), Kidney damage or a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m constantly sustaining for more than three months is considered CKD. Pathologic abnormalities or indications of damage, such as abnormalities in blood or urine tests or imaging investigations, are the markers of kidney injury [6].

Incidence of CKD According to the World Health Organization, kidney disease causes over 850,000 deaths each year, with CKD being the 12th greatest cause of mortality and the 17th largest cause of disability [7]. Approximately 800 million people are

affected globally with this disease and annual incidence of CKD is between 150 and 200 million in India [8].

Management of chronic renal failure

The CRF is irreversible but initial precautions are useful to stabilize the CRF condition and stop damaging the new nephrons. Withdrawal of CKD-causing drugs, Protein restriction in the diet, elctrolyte and fluid balance, diuresis, dialysis, or at last replacement therapy for the kidneys is the treatment regimen of CKD.

Quercetin

Quercetin is a plant pigment flavonol present falls to the polyphenolic compounds of polyphenols[9]. Many fruits, vegetables, leaves, seeds, and grains contain large amounts of querectin. Red onions are a typical item that contains significant amounts of querectin. Querectin is a miserable substance that is utilized in herbal remedies, liquids, and meals [10].

Enalapril

Enalapril is an ACE inhibitor that is extensively was using to treat acute and chronic renal failure. Enalapril has been linked to a low incidence of transient serum aminotransferase elevations and is used to help diagnose pathological changes in rare cases.

MATERIALS AND METHODS

All chemicals used in the study are of analytical grade. Quercetin, enalapril and other reagents were purchased from Sigma-Aldrich. 36 Wister albino rats of either sex were purchased from M/S Chakraborty Enterprise Kolkata India and transported in temperature controlled vehicle. The animals were acclimatized for 21 days in animal house of united Institute of Pharmacy. Naini, Prayagraj. Animal study was approved by institutional animal ethical committee (IAEC), approval UIP/ IAEC/ Nov-2020/01-A.

Initiation of renal failure

CRF is initiated by administration of powdered adenine mixed with animal food pellets for adenine-induced chronic renal failure. However, in this experiment, adenine was dissolved in water and given once a day for four weeks using an oral feeding tube [11].

Experimental design for chronic renal failure

Animals were divided into six respective groups into which six rat are placed in each group [12].

Table 1 Effect of quercetin with enalapril on adenine induced CRF

Groups	Treatment	Doses
Groups-1	Control	Normal saline (10ml/kg
Groups-2	(Negative Control) Adenine	0.75%
Groups-3	Adenine+Quercetin	0.75% + 50 mg/kg /d
Groups-4	Adenine+Enalapril	0.75% + 20mg/kg/d
Groups-5	Adenine+Quercetin+Enalapril	0.75% + 50mg/kg/d+20mg/kg/d
Groups-6	Adenine+Captopril	0.75% + 20mg/kg/d

Animal groups were prepared as 6 animals in each group as categorized in table no.1.Quercetin and enalapril were administered 60 minutes before adenine administration, this dosing was continued for 28 days. Food intake (g), water intake (ml), body weight (g), urine output (ml) in 24 hrs) serum creatinine (mg/dl) blood urea nitrogen (mg/dl), erum total proteins (g/dl),serum albumin (g/dl), antioxidant enzymes lipid peroxidase, superoxide dismutase, catalase and histopathological changes were investigated to justify the study [13,14,15,16,17,18,19,20,21,22].

RESULTS

Body weight

The body weight of different groups was monitored on weekly basis, and the data changes in body weight are mentioned below and compare with normal group. The finding of the experiment is decrease in body weight in non-treated group and groups which has been treated with standard drug (captopril) was recover the body weight Upto the normal. Other groups has been also maintance their body weight as compare to non-treated group data are represented in table no 2

Food intake

On the basis of analysis, results suggested that food intake in group 2 is reduced by adenine as compared by group 1 and group 6. Whereas other treated groups intake less than normal but more than group 2. Data are represented in table no 3

Water intake

Group 2 animal who was treated with adenine has shown less water consumption as compare with group 1 and group 6. Drinking capability in group 3, 4 and 5 was more than group 2. The data of drinking estimation is mentioned in table 4

Urine output

The Urine output of different groups was measured in weekly basis. The finding of the experiment is total urine collection for 24hr in control group was upto normal. Whereas adenine administered groups found less urine out in initial days, after the treatment with respective drug urine output comes to normal as shown in table no 5

BIOCHEMICAL ANALYSIS

The biochemical estimation of different groups was analyzed and the finding of our result is decsibed as follow-

S.protein has been decresed in group 2 due to renal failure. In other groups that were treated with drugs shown regular amount of protein in blood. S. Creatinine has been increased in group 2 due to renal failure. In other groups that were treated with drugs shown regular amount of creatinine in blood. BUN Similar to creatinine the BUN level increased progressively in group-2.S. Albumin in all the groups was about normal but Albumin level was grossly reduced in group-2 due to renal failure. Group 4 animals had increased albumin, in other groups that was treated with drugs shown regular amount of albumin in blood [23].results are shown in figure 5-8 and table no 6

Antioxidant levels of homogenized kidney in CRF

The increased level of Lipid peroxidation in group 2 demonstrates that adenine causes toxic effects [24].

Values articulated as Mean ± SD, n=6, group 2 was compared with group 1, 3, 4, 5 and 6. The p value had shown <0.0001.

Table. 2. Effect on body weight in CRF treated animal groups

Group name	0th day	7th day	14th	21st day	28th day
Group 1	116.16±3.97	123.5±4.23	127±4.81	130.33±5.60	135.66±4.76
Group 2	124.16±2.63	121.5±2.16	117.33±2.87	113.5±2.07	106±3.52
Group 3	126.5±3.27	123.16±2.85	126±3.16	131±3.52	136±2.96
Group 4	128.33±2.73	126±3.63	129.66±3.32	134.83±1.94	138.5±2.07
Group 5	129±2.52	126±3.63	130.33±4.17	134.83±1.94	138.5±2.07
Group 6	127.5±4.32	134.66±4.67	138.83±2.99	142.16±3.60	147±3.09

Table. 3 Food Intake in various CRF treated animal groups

Group name	1st week	2nd week	3rd week	4th week
Group 1	87±3.28	86.83±5.74	87.16±2.78	86.16±3.86
Group 2	77±1.26	74.83±3.48	73.5±2.50	73.66±2.73
Group 3	87.66±3.20	86.5±2.16	86.83±1.94	83.33±2.80
Group 4	84.66±2.16	83.5±6.22	86.5±1.64	87.16±2.48
Group 5	82.16±3.12	82±2.28	83.5±1.37	84±1.26
Group 6	84.33±1.75	86.83±2.13	86.5±.57	87.83±3.12

Values articulated as Mean ± SD, n=6, group 2 was compared with group 1, 3, 4, 5 and 6. The p value had shown <0.0001.

Table 4. Water intake in CRF treated animals

Group name	1st week	4th week
Group 1	37.4±1.89	37.6±2.07
Group 2	28±1.78	25.4±2.25
Group 3	28.4±2.63	30.8±1.78
Group 4	33±1.72	35.6±2.58
Group 5	37±2.50	39.2±1.75
Group 6	38.6±2.92	39.2±1.36

Values articulated as Mean ± SD, n=6. The p value had shown <0.0001.

Table. 5. 24 hour urine output in CRF treated animals

Group name	0th day	7th day	14th	21st day	28th day
Group 1	7.32±0.17	7.04±0.45	7.18±0.14	7.36±0.10	7.32±0.08
Group 2	7.3±0.08	5.48±0.44	5.04±0.52	4.64±0.36	3.48±0.21
Group 3	7.18±0.31	6.82±0.38	6.4±0.19	5.78±0.31	5.72±0.33
Group 4	7.16±0.53	6.56±0.56	7.4±0.16	6.72±0.52	6.9±043
Group 5	7.26±0.28	7.08±0.27	7.38±0.21	6.8±0.38	6.96±0.30
Group 6	7.28±0.34	6.7±0.38	7.34±0.30	7.04±0.37	7.02±0.33

Values articulated as Mean ± SD, n=6, group 2 was compared with group 1, 3, 4, 5 and 6. The p value had shown <0.0001.

Table. 6. Biochemical analysis of CRF treated animal groups

Group name	S. protein	S. Creatinine	BUN	S. albumin
Group 1	5.26±0.11	0.7±0.02	17.08±3.90	4.16±0.21
Group 2	3.58±0.26	3.38±0.24	25.84±0.71	2.78±0.32
Group 3	5.14±0.32	1.78±0.24	20.5±0.49	4.06±0.29
Group 4	4.92±0.26	0.81±0.02	21.5±0.71	4.02±0.52
Group 5	5.52±0.13	0.69±0.03	18.96±1.05	3.36±0.14
Group 6	5.74±0.25	0.66±0.05	19.86±1.30	4.24±0.16

Evaluation of biochemical analysis data represents the mean ± standard deviation for six rat per group. The p value had shown <0.0001.

Table7 Antioxidant levels of CRF treated animal Groups

Parameters	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
LPO	2.34 ± 0.30	7.32 ± 0.25	4.38 ± 0.29	3.34 ± 0.21	4.48 ±0.231	5.42 ±0.26
SOD	0.42 ± 0.23	0.4 ± 0.27	1.44 ± 0.22	1.56 ±0.25	2.54 ± 0.16	3.44 ±0.27
CAT	22.56 ±0.21	17.4 ± 0.18	19.32 ±0.16	20.38 ±0.35	23.58 ± 0.29	34.54 ±0.29

Values expressed as Mean ± SEM, n = 6, group was compared with group 1, 3,4, 5 and 6. The p value had shown<0.0001.

Figure 1. Body weight in CRF treated animal Groups

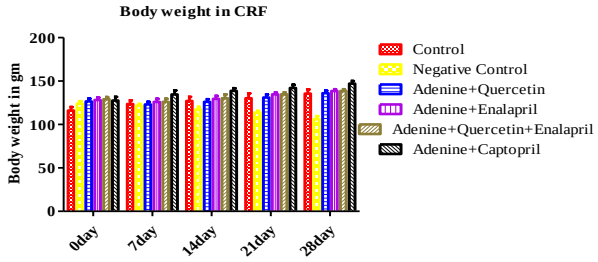


Figure 2. Food intake in CRF treated animal groups

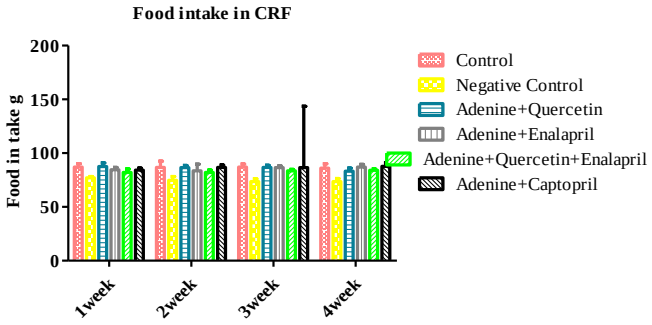


Figure 3. Water intake in CRF treated animal groups

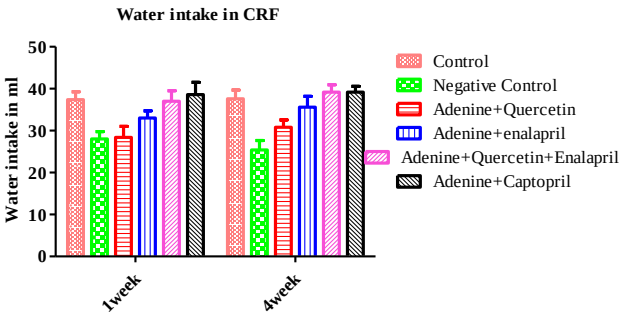


Figure 4. Urine output in CRF treated animal groups

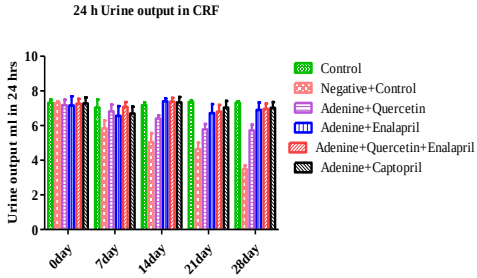


Figure 5. Biochemical analysis in CRF treated animal groups

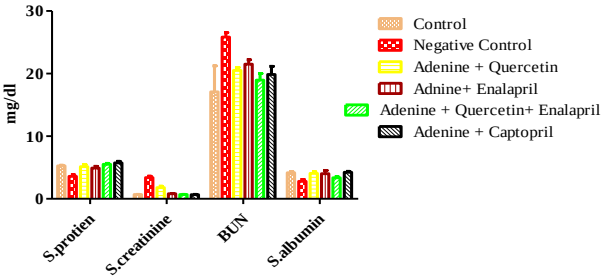


Figure 6. Lipid peroxide levels in CRF treated animal groups

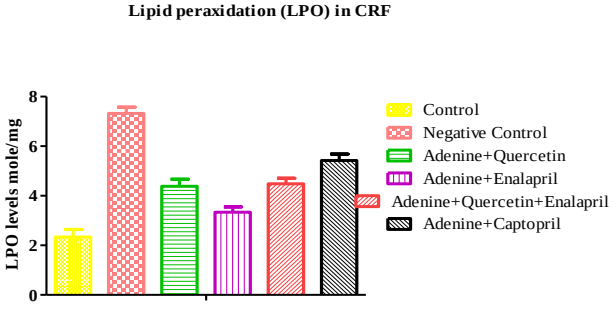


Figure 7. Super oxide dismutas in CRF treated animal groups

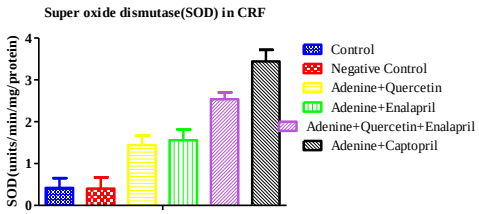


Figure 8. Catalase (CAT) in CRF treated animal groups

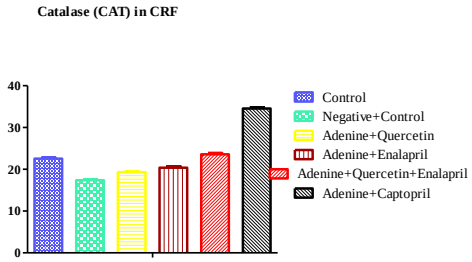
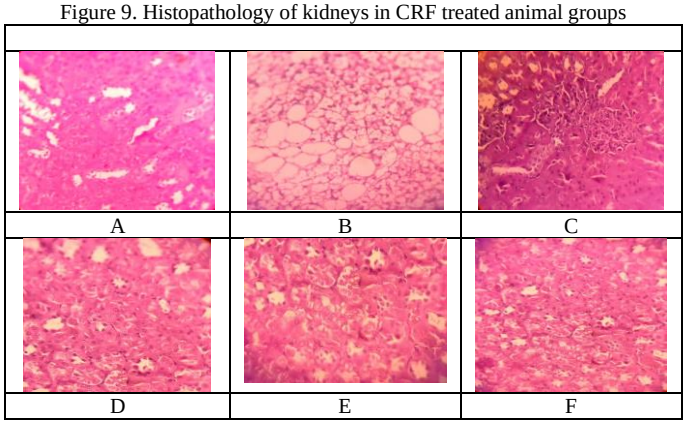


Figure 9. Histopathology of kidneys in CRF treated animal groups



A) Normal kidney had shown normal glomeruli, PCT and DCT. (B) Adenine treated group had shown several ruptured tubules. (C) Adenine + Quercetin treated group had shown minimal interfacial injury.(D) Adenine +Enalapril treated group had shown capillary lesions are well protected. (E) Adenine + Quercetin + Enalapril treated had group minimal interstitial loss. (F) Adenine + Captopril treated had group capillary are well protected.

DISCUSSION

The main features of chronic renal failure are increased plasma creatinine, blood urea nitrogen and reduced total proteins, albumin and urine output. The ultimate aim in producing the animal model for CRF is to reduce the renal function progressively and reducing the blood supply to kidney by causing renal artery occlusion, reducing the urine output by ureteric obstruction. The model reported has been widely used at present to study CKD. In this model renal failure is induced by oral administration of adenine, on high dose causes renal toxicity and reduces renal function. Among these models adenine induced CRF model was selected for this study. Mechanism of nephroprotective activity as oxidative stress and inflammatory damage have been attributed to the development of chronic kidney injury, any compound or drug having antioxidant & anti-inflammatory activity will have a protective action against renal damage. The importance of protecting the antioxidants pool in preventing renal damage. The quercetin had shown antioxidant activity in vivo assays [25]. Adenine treatment has reduced the levels of these antioxidants. Co-administration of quercetin has reduced the oxidative damage evidenced by the dose dependent increase in the level of the antioxidants. The anti-inflammatory activity could be explained by the presence of flavonoids which are well known for their anti-inflammatory action. Flavonoids inhibit enzymes involved in inflammatory pathway [26].

CONCLUSION

Adenine was used to successfully produce CRF in Wister albino rats. Adenine was given by direct oral administration to induce CRF for the first time in this study. It did not cause death ,but it cause renal failure earlier than dietary adenine Renal failure was confirmed by decrease in urine output , alteration of renal biochemical parameter , decrease in food ,water intake and body weight .In vivo tests revealed quercetin to have antioxidant activity. In CRF quercetin + enalapril pre-treatment and standard drug had a protective effect. Treatments lowered SCr and BUN while increasing urine production. The levels of total proteins and albumins in the blood were like wise elevated There was a significant reduction in kidney damage in group treated with quercetin + enalapril and standard captopril in adenine – induced model .In addition to protecting the kidneys from adenine induced tissue damage quercetin was found to have significant nephro-protective effect. This study gives a clue to the scientists to focus their study on combination of synthetic and natural compounds for treatment of various chronic diseses

REFERENCES

1. Cerda J, Bagga A, Kher V, Chakravarthi R, 2008. The contrasting characteristics of acute kidney injury in developed and developing countries, Nature Clinical Practice Nephrology 4 (3):138-153.
2. Ali T, Khan I, Simpson W, Prescott G, Townend J, 2007. Smith W et al. Incidence and outcomes in acute kidney injury: A comprehensive population-based study, Journal of the American Society of Nephrology 18(4):1292-1298.
3. Fang Y, Ding X, Zhong Y, Zou J, Teng J, Tang Y, 2010. Acute kidney injury in a Chinese hospitalized population, Blood Purification 30(2):120-126.
4. Uchino S, Bellomo R, Morimatsu H, Morgera S, Schetz M, Tan I, 2007. Continuous renal replacement therapy: A worldwide practice survey, Intensive Care Medicine 33(9):1563-1570.
5. Ftouh S, Thomas M, 2013. Acute kidney injury guideline development group, acute kidney injury: summary of NICE guidance. British Medical Journal 28 ;(8)347:930.
6. Kramer H, Berns J, Nally J, Choi M, Rocco M, 2012. A Decade after the KDOQI CKD Guidelines: Impact on NKF-KDOQI, American Journal of Kidney Diseases 60(5):694-696.

7. Tunstall-Pedoe H, Preventing Chronic Diseases, 2005. A Vital Investment: WHO Global Report, Geneva: World Health Organization pp 200.
8. Acharya VN, 2011. Diabetic and hypertensive nephropathy in India, J Assoc Physicians India (3) 59:143.
9. Srivastava AK, Mukerjee A, Tripathi A, 2020. Antidiabetic and antihyperlipidemic activities of Cucumis melo var. momordica fruit extract on experimental animals, Future Journal of Pharmaceutical Sciences 6(1) 1-9.
10. Agrawal AD, 2011. Pharmacological activities of flavonoids: A Review, International Journal of Pharmaceutical Sciences and Nanotechnology (4) 2, 1394-97.
11. Bing P, Maode L, Li F, Sheng H, 2006. Expression of renal transforming growth factor beta and its receptors in a rat model of chronic cyclosporine-induced nephropathy, Transplant Proc 38(7): 2176-9
12. Yokozawa T, Zheng PD, Oura H, Koizumi F, 1986. Animal model of adenine induced chronic renal failure in rats, Nephron 44(3), 230–234.
13. Kurien BT, Everds NE, Scofield RH, 2004. Experimental animal urine collection: a review, Laboratory Animals 38, 333-361.
14. Chromy V, Rozkosna K, Sedlak P, 2008. Determination of serum creatinine by Jaffe method and how to calibrate to eliminate matrix interferenceproblems, Clin Chem Lab Med 46: 1127–1133.
15. Kabeya T, Ohkura Y, 1972. A New Colorimetric Method for the Determination of Urea Nitrogen in Blood with Diacetyl Monoxime-Glucuronolactone Glucosaccharodilactone Reagent, Chem Pharm Bull 20(4):837-839.
16. Domumas BT, Bayse DD, Carter RJ, Peters TJr, Schaffer RA, 1981. Candidate reference method for determination of total protein in serum I. Development and validation. Clin Chem. 27(10):1642-50.
17. Affonso A, Lasky F, 1985. Bromocresol purple dye-binding method for the estimation of serum albumin adapted to the SMA 12/60, Clinical Biochemistry 18 (5):285-289.
18. Ohkawa H, Ohishi N, Yagi K, 1979. Assay for lipid peroxidation in animal tissues by thiobarbituric acid reaction, Anal. Biochem 95, 351-358.
19. Marklund S, Marklund G, 1974. Involvement of the superoxide anion radical in the autoxidation of pyrogallol and a convenient assay for superoxide dismutase, Eur J Biochem 47(3):469-74. Epub 1974/09/16.
20. Sinha AK, 1972. Colorimetric assay of catalase, Anal Biochem 47(2), 389-94. Epub 1972/06/01.
21. Gowrisri M, Kotagiri S, Swamy BM, Swamy P, Vishwanath KM, 2012. Anti-oxidant and nephroprotective activities of Cassia occidentalis leaf extract against paracetamol induced nephrotoxicity in rats, Research Journal of Pharmaceutical, Biological and Chemical Sciences 3, 572-586.
22. Hoult JR, Moroney MA, Paya M, 1994. Actions of flavonoids and coumarins on lipoxygenase and cyclooxygenase, Methods Enzymol 234, 443-454.
23. Srivastava AK, Mukerjee A, Ramteke PW, Pandey H, Mishra SB, 2018. Evaluation of wound healing activity of ethanolic extract and its fraction from Cucumis melo var momordica Duthie and Fuller 6(1)225-228
24. Brady HR, Brenner BM: Acute Renal Failure. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, 2016. eds. Harrison's Principles of Internal Medicine, 16th ed, New York, NY: McGraw-Hill 11, 1644-1653.
25. Srivastava AK, Mukerjee A, Ramteke PW, Pandey H, Mishra SB, 2017. Antiulcer potential of Cucumis melo Var, momordica (Roxb), Duthie & Fuller fruits in experimental animal. Journal of Pharmaceutical Research 16, 218-223.
26. Samman S, Wall PML, Cook NC, Evans CA, Packer L, 1998. Flavonoids and coronary heart disease, Dietary perspectives. In: Rice- eds. Flavonoids in Health and Disease, New York: Marcel Dekker Inc 469-481.

How to cite this article

Anushika Singh, Arvind Kumar Srivastava, Alok Mukerjee, Sunil kumar Singh, Abhishek Kumar Tripathi, Vandana Yadav, 2021. Investigation of enalapril and quercetin on chronic renal failure. Jour. of Med. P'ceutical & Allied. Sci. V 10 - I 6, 1658, P- 3889-3893. doi: 10.22270/jmpas.V10I6.1658