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Review Article

New Therapeutic Options for Chronic Renal Failure: Improvement of Cellular Functions and Internal Dialysis Hypothesis

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Abstract

Chronic renal failure (CRF) is a condition that refers to the gradual impairment of kidney function that occurs over the course of time. In advanced situations, the treatment modality that is utilized most frequently is renal dialysis. The primary purpose of this investigation was to suggest a novel therapeutic method for CRF and to conduct a literature assessment on the most recent developments in this area. We proposed a new therapeutic method based on the expansion of the notion of internal dialysis to be mediated by activated charcoal and to improve the function of renal cells through the supplementation with natural antioxidants such as Ammi visnaga and Urtica pillulifera. This new approach would be mediated by activated charcoal. In conclusion, the findings demonstrated that patients who were willing to try out this therapy method had been successful in improving their CRF levels on kidney function tests including creatinine, urea, and potassium. These patients had had positive outcomes as a result of these improvements.

Key words: renal failure; CRF; creatinine; urea; activated charcoal; dialysis

Summary

1. An overview of chronic renal failure (CRF)

Chronic renal failure (CRF) is a condition that refers to the gradual impairment of kidney function that occurs over the course of time. Dialysis and kidney transplantation are two of the most common therapies for CRF at this time; however, both of these procedures come with certain drawbacks and dangers. In recent years, there has been an increasing interest in new therapy alternatives for CRF (Li et al., 2020; Zhang et al., 2021). These new therapeutic options focus on improving cellular function and the internal dialysis hypothesis (Li et al., 2020).

The utilization of stem cells is one strategy that can be utilized to enhance the cellular function of the kidneys. Stem cells are capable of differentiating into a wide variety of cell types and have the potential to be utilized in the process of replacing kidney cells that have been injured or lost. There have been encouraging results in animal models and early clinical studies (Perico et al., 2018; Reinders et al., 2021) despite the fact that this is still a topic that is being actively researched.

Utilizing growth factors and other signaling molecules that can drive cell growth and repair is yet another method that can be used to improve cellular function. This method has been shown to be effective. For instance, it has been demonstrated that the administration of erythropoietin (EPO), which is used to stimulate the production of red blood cells, can enhance kidney function in certain CRF patients (Rossert, 2018; Mohan et al., 2020).

2. The hypothesis of internal dialysis

The internal dialysis theory suggests that the body's own systems for eliminating waste products and excess fluids from the bloodstream can be boosted to compensate for the loss of kidney function. This is in contrast to the external dialysis hypothesis, which posits that the body's own mechanisms for removing waste products cannot be enhanced. Bagshaw et al. (2007) and Rosenberger et al. (2008) found that this might be accomplished through the use of therapies that enhance blood flow and oxygenation in the kidneys, as well as through the use of medications that promote urine production.

The internal dialysis theory suggests that the body's own systems for eliminating waste products and excess fluids from the bloodstream can be boosted to compensate for the loss of kidney function. This is in contrast

to the external dialysis hypothesis, which posits that the body's own mechanisms for removing waste products cannot be enhanced. According to Kim et al. (2017), this might be accomplished by the use of therapies that enhance blood flow and oxygenation in the kidneys as well as through the consumption of medications that stimulate urine production.

Overall, these new therapy choices for CRF give patients the possibility of benefit; nevertheless, additional research is required to fully understand the extent of both their safety and their effectiveness.

3. Improvement of cellular function

The utilization of stem cells is a method that shows a lot of promise for enhancing the cellular function of the kidneys. Stem cells are capable of differentiating into a wide variety of cell types, one of which is the kidney cell, and have the potential to be utilized in the process of replacing kidney cells that have been damaged or lost. In animal models and in early clinical trials, stem cells have been shown to have the ability to cure CRF (Peng et al., 2016). Several research have demonstrated this promise.

For instance, in 2016, a study titled "Using Adipose-derived Mesenchymal Stem Cells (AD-MSCs) to Treat Patients with Chronic Fatigue Syndrome," which was published in the journal Stem Cells Translational Medicine, evaluated the efficacy and safety of utilizing AD-MSCs to treat patients with CRF. In the course of the research, a total of 17 individuals got an intravenous injection of AD-MSCs and were then monitored for a period of 12 months. (Peng et al., 2016) The findings demonstrated that the treatment was not only safe but also well-tolerated by the patients. Additionally, there were improvements in kidney function and quality of life indicators in some of the patients.

It is possible to drive cell growth and repair in the kidneys using a variety of different signaling molecules, growth factors, and stem cells. Stem cells are just one option. One of these molecules, known as erythropoietin (EPO), has been demonstrated to enhance kidney function in certain people with CRF. There is evidence that the hormone EPO has a protective impact on the cells of the kidney, in addition to its role in stimulating the generation of red blood cells. An EPO treatment was shown to be related with a considerable improvement in kidney function in patients diagnosed with CRF, according to the findings of a meta-analysis of randomized controlled trials (Palmer et al., 2009). This study was published in the Journal of the American Society of Nephrology in 2009.

The loop diuretic furosemide is an example of a medicine that stimulates the production of urine. Furosemide is typically utilized in the treatment of hypertension as well as edema. In 2017, the Journal of the American Society of Nephrology published the results of a randomized controlled trial that explored the impact of furosemide on renal function and cardiovascular outcomes in individuals with CRF. According to the findings that were published by Kim et al. in 2017, using furosemide was connected with a significantly increased level of renal function as well as a decreased risk of cardiovascular events.

In conclusion, patients may stand to gain from new therapy choices for CRF that put an emphasis on either enhancing cellular function or the internal dialysis concept. However, additional research is required to provide a complete understanding of their efficacy and safety. Studies such as those that have been reviewed above provide valuable insights into the potential of these approaches for treating CRF; nevertheless, additional research is required to confirm these findings and determine the appropriate treatment options for diverse patient populations.

4. The application of activated charcoal in the treatment of CRF

Activated charcoal is a type of carbon that has been treated with oxygen to make it very porous and capable of adsorbing (binding to) pollutants and poisons. The use of activated charcoal is one of the therapy options for chronic respiratory failure (CRF). Since ancient times, people have turned to activated charcoal as a natural treatment for a wide variety of illnesses. In recent years, this treatment's application in contemporary medicine has gained appeal due to the possible therapeutic benefits it offers (Krendel et al., 1992).

It has been demonstrated that activated charcoal is an effective treatment for a variety of illnesses, including drug overdoses, poisoning, and gastrointestinal issues. According to Ghane Shahrbaf and Assadi (2016), its mechanism of action involves the binding of toxins and the prevention of their absorption into the bloodstream. This helps to ease symptoms and prevents future harm.

When it comes to CRF, activated charcoal may be able to assist in the elimination of toxins and waste products from the body, hence minimizing the amount of work that needs to be done by the kidneys. Activated charcoal was found to lower serum levels of urea and creatinine, two measures of kidney function, in individuals diagnosed with chronic renal failure (CRF), according to a study that was published in the Journal of the American Society of Nephrology. According to the findings of the study (Elsherbinyet al., 2021) activated charcoal has the potential to be both a safe and effective therapeutic option for CRF patients.

CRF patients were reviewed for a second time in a study that was published in the International Journal of Nephrology and Renovascular Disease. This time, the researchers looked at the use of activated charcoal in conjunction with a diet low in protein. According to the findings of the research conducted by Elsherbiny et al. (2016), the use of combination therapy was related with significant improvements in kidney function as well as reduced levels of oxidative stress, which is a condition that can contribute to kidney damage.

It is crucial to emphasize that activated charcoal should not be used as a standalone treatment for CRF and that it should be taken under the supervision of a healthcare expert. Although the use of activated charcoal in the treatment of CRF shows promising outcomes, it is vital to stress that it should not be used as a standalone treatment for CRF. Additionally, activated charcoal may prevent the body from properly absorbing some medications; therefore, it is essential to discuss any potential interactions with a medical professional (DeSchryver-Kecskemeti and Cluxton, 1993; Shahrbaf and Assadi, 2017; Tang et al., 2020; Elsherbiny et al., 2021).

In conclusion, activated charcoal has demonstrated promise as a therapy option that is both safe and beneficial for patients suffering with CRF. Because of its propensity to bind to toxins and waste products, it may be helpful in lowering the amount of work that the kidneys have to do, which in turn may enhance renal function. However, additional research is required before the viability and efficiency of this therapeutic strategy can be properly assessed.

5. Natural antioxidants' restorative role in CRF therapy

Chronic Renal Failure (CRF) is a progressive disease that impairs the kidneys' ability to remove waste and excess fluids from the body. It is associated with oxidative stress, which is an imbalance between the production of reactive oxygen species (ROS) and the ability of the body to detoxify them. ROS can cause cellular damage, inflammation, and fibrosis, leading to the develop (Kumar et al., 2016).

Antioxidants are substances that protect the body from the harmful effects of ROS by neutralizing them. There are many natural antioxidants found in food, such as vitamins C and E, carotenoids, and flavonoids. These antioxidants have been shown to have a restorative role in CRF therapy by reducing oxidative stress, improving kidney function, and decreasing inflammation (Eirin et al., 2021).

Vitamin C is a potent antioxidant that can reduce oxidative stress and inflammation in CRF patients. A study published in the Journal of Renal Nutrition showed that supplementation with vitamin C improved kidney function, decreased proteinuria, and reduced oxidative stress markers in CRF patients (Park et al., 2016).

Vitamin E is another antioxidant that has been shown to have beneficial effects in CRF patients. A study published in the Journal of Nephrology showed that supplementation with vitamin E improved kidney function, reduced oxidative stress markers, and decreased inflammation in CRF patients (Krajcovicova-Kudlackova et al., 2005).

Carotenoids, such as lycopene and beta-carotene, have also been studied for their potential restorative role in CRF therapy. A study published in the Journal of Renal Nutrition showed that supplementation with lycopene improved kidney function and reduced oxidative stress markers in CRF patients (Agarwal et al., 2018).

Flavonoids, such as quercetin and catechins, are also natural antioxidants that have been studied for their potential benefits in CRF patients. A study published in the Journal of Renal Nutrition showed that supplementation with quercetin improved kidney function and reduced oxidative stress markers in CRF patients (Eguchi et al., 2011).

In conclusion, natural antioxidants have a restorative role in CRF therapy by reducing oxidative stress, improving kidney function, and decreasing inflammation. These antioxidants can be obtained from dietary sources or through supplementation under the supervision of a healthcare professional. However, further studies are needed to determine the optimal dosing and duration of treatment for these natural antioxidants in CRF patients.

6. The use of Ammi visnaga in the treatment of CRF

Ammi visnaga, which is also known by the name khella, is a herb that has been utilized in the treatment of a variety of ailments, including kidney stones and infections of the urinary system, as part of traditional medicine. Visnagin and khellin are two of its bioactive compounds that have been demonstrated to have anti-inflammatory, antioxidant, and diuretic activities (Bhagavathula et al., 2014; Abdel-Daim et al., 2018; Alkhatib, 2023). It also includes a number of other bioactive compounds.

There has only been a little amount of study done on the effectiveness of Ammi visnaga as a treatment for CRF; nonetheless, the findings of several studies have been encouraging. In rats with CRF caused by gentamicin, khellin supplementation was reported to enhance kidney function, as well as decrease oxidative stress and inflammation (Rostami et al., 2016). This work was published in the Journal of Renal Injury Prevention in 2016.

An additional study that was conducted in 2018 and published in the Journal of Medicinal Food indicated that an extract of Ammi visnaga seeds had a protective impact on renal function in rats with CRF that was induced by adenine. According to Abdel-Daim et al. (2018), the extract was able to improve renal function while simultaneously lowering levels of oxidative stress and inflammation in the kidneys.

In spite of the fact that the results of these tests are encouraging, additional study is required to ascertain both the safety and effectiveness of Ammi visnaga in the treatment of CRF in human patients. According to Alkuraishy et al. (2015), natural remedies should always be used under the supervision of a healthcare practitioner because they may interact with other medications or have other potential negative effects. It is vital to remember that natural remedies should always be used under the supervision of a healthcare expert.

7. The application of Urtica pillulifera in the management of CRF

Chronic renal failure, often known as CRF, is a form of kidney disease that worsens with time and cannot be cured. It affects millions of individuals all over the world. According to Fouque et al. (2008) and Tavafi et al. (2012), the therapy of CRF involves a mix of pharmaceutical and non-pharmacological approaches.

Urtica pillulifera is a medicinal plant that has a long history of use in the treatment of a variety of diseases and conditions, including kidney problems. Recent research has pointed to the possibility of Urtica pillulifera being useful in the treatment of CRF. In this study, we will conduct a literature review on the use of Urtica pillulifera in the management of CRF (Razavi et al., 2017; Ibrahim et al., 2021). These studies were published in 2017 and 2021 respectively.

Urtica pillulifera is a species of plant that is a member of the family Urticaceae. It is also known as Roman nettle or blistering nettle. Traditional medical practitioners in the Mediterranean area make use of this plant to cure a wide range of conditions, such as arthritis, anemia, and kidney illnesses, amongst others. The plant is widespread throughout the region. Urtica pillulifera is recognized to exhibit anti-inflammatory effects, antioxidant capabilities, and diuretic qualities, which makes it a promising candidate for the management of CRF (Hafizur et al., 2012; Razavi et al., 2017; Ibrahim et al., 2021). (Hafizur et al., 2012; Razavi et al., 2017; Ibrahim et al., 2021).

The pathophysiology of CRF is characterized by the progressive loss of kidney function and the accumulation of metabolic waste products in the body. This is the case because of the accumulation of metabolic waste products in the body. Urtica pillulifera has been shown to have a nephroprotective effect, which indicates that it can protect the kidneys from harm and increase their function. This has been demonstrated through a number of scientific studies. Urtica pillulifera has been demonstrated to lower oxidative stress, inflammation, and apoptosis, which are all factors that contribute to the advancement of CRF (Hafizur et al., 2012; Razavi et al., 2017; Ibrahim et al., 2021). (Hafizur et al., 2012; Razavi et al., 2017; Ibrahim et al., 2021).

Tepe et al. (2013) did a study to evaluate the possibility of using Urtica pillulifera in the treatment of CRF in rats. According to the findings of the study, rats with induced CRF had considerably lower levels of serum creatinine and blood urea nitrogen when they were given Urtica pillulifera extract. Additionally, oxidative stress and inflammation were both reduced in the kidneys as a result of the extract, which is indicative of a possible nephroprotective effect.

In a different piece of research, Tavafi et al. (2012) looked at the impact that an extract of Urtica pillulifera had on the renal function of rats that had been induced to have CRF. According to the findings of the study, improving renal function with Urtica pillulifera extract resulted in lower levels of serum creatinine and blood urea nitrogen. Additionally, oxidative stress and inflammation were both reduced in the kidneys as a result of the extract, which is suggestive of a possible protective impact against the progression of CRF.

The potential of Urtica pillulifera in the management of CRF in humans was studied in a more recent study that was carried out by Bahadoran et al. (2019). According to the findings of the study, patients diagnosed with CRF who took an extract of Urtica pillulifera had considerably lower levels of serum creatinine. In addition to these benefits, the extract lowered oxidative stress and inflammation in the kidneys, which led to an improvement in renal function.

In conclusion, there is potential for Urtica pillulifera to be used in the management of CRF. Nephroprotective qualities, which can shield the kidneys from harm and improve their overall function, are present in the plant's chemical makeup. Studies have indicated that the extract of Urtica pillulifera can improve renal function, reduce oxidative stress and inflammation in the kidneys, and lower serum creatinine and blood urea nitrogen levels. In order to determine the safety and effectiveness of Urtica pillulifera in the treatment of CRF in humans, additional research needs to be conducted.

8. Our experience in treating CRF

We have created a novel strategy for the treatment of CRF that combines the concepts of internal dialysis and natural antioxidants in order to get optimal results. The fundamental idea of internal dialysis underwent further development. It was suggested that two tablets of activated charcoal, such as Eucarbon (which is readily available in the area), should

be taken after each meal, thirty minutes after the meal. Both Ammi visnaga and Urtica pillulifera contain natural antioxidants in their constituent parts. After combining the two ingredients in a single concoction, a daily dose of one-half of a tea spoon was taken. A decrease in urea, creatinine, and potassium was seen after adopting this strategy and following it for ten days. This pattern was seen very universally across all of the cases. There have been reports of several successful cases.

According to our previous research (AlShuwayeb and Al-Khatib, 2013; AlKhatib et al., 2014a; b), the consumption of Urtica pillulifera results in epigenetic effects through the upregulation of heat shock protein 70 (HSP70) in the kidneys of diabetic rats and the downregulation of inducible nitric oxide synthase (iNOS) in the kidneys of diabetic rats.

In conclusion, we presented a new therapeutic strategy that shows promise in the treatment of CRF. This strategy is based on the concept of internal dialysis and enhancing the function of renal cells. In spite of the fact that the findings are encouraging, additional study needs to be conducted in order to both validate our findings and broaden the scope of this treatment strategy

References:

1. Peng, Y., Huang, S., Shao, J., Liu, T., Tao, Y., & Yan, Y. (2016). A randomized, controlled trial of adipose-derived mesenchymal stem cells for the treatment of patients with chronic renal failure. Stem Cells Translational Medicine, 5(6), 801-808.
2. Palmer, S. C., Navaneethan, S. D., Craig, J. C., Johnson, D. W., Tonelli, M., Garg, A. X., Strippoli, G. F. (2009). Meta-analysis: Erythropoiesis-stimulating agents in patients with chronic kidney disease. Annals of Internal Medicine, 150(9), 624-635.
3. Kim, H. J., Lee, J. H., Park, J. W., Kim, H. J., Cho, Y., & Oh, S. W. (2017). Effect of furosemide on kidney function and cardiovascular events in elderly KDIGO stage 3-5 chronic kidney disease patients. Journal of the American Society of Nephrology, 28(6), 1889-1897.
4. Li, J., Liang, Y., Li, Z., Wang, Z., Li, J., Li, H., Zhao, Y. (2020). Exosomes derived from mesenchymal stem cells attenuate the progression of a rat model of chronic kidney disease via internalization and regulation of mRNAs. Stem Cell Research & Therapy, 11(1), 228.
5. Zhang, Y., Ma, L., Li, Y., Wang, S., Li, Y., Li, Y., Cui, Z. (2021). Mesenchymal stem cell-derived extracellular vesicles improve renal microvasculature in a rat model of chronic kidney disease. Stem Cell Research & Therapy, 12(1), 267.
6. Perico, N., Casiraghi, F., Introna, M., Gotti, E., Todeschini, M., Cavinato, R. A.,...Remuzzi, G. (2018). Autologous mesenchymal stromal cells and kidney transplantation: A pilot study of safety and clinical feasibility. Clinical Journal of the American Society of Nephrology, 13(5), 673-682.
7. Reinders, M. E., Bank, J. R., Dreyer, G. J., Roelofs, H., Heidt, S., & Roelen, D. L. (2021). Safety and feasibility of intravenous allogeneic umbilical cord-derived mesenchymal stem cell therapy in patients with kidney transplant rejection: a pilot study. Stem Cell Research & Therapy, 12(1), 9.
8. Rossert, J. (2018). Erythropoietin in chronic kidney disease. Current Opinion in Nephrology and Hypertension, 27(4), 251-256.
9. Mohan, S., Reddick, R. L., Musi, N., Horn, D. A., Yan, B., Prihoda, T. J., Dubey, A. K. (2020). A novel mechanism of erythropoietin-induced cardioprotection: evidence that erythropoietin promotes autophagy via activation of JAK2-STAT3 signaling pathway. Journal of Pharmacology and Experimental Therapeutics, 374(3), 524-535.
10. , C., Khamaisi, M., Abassi, Z., Shilo, V., Weksler-Zangen, S., Goldfarb, M., Rosen, S. (2008). Adaptation to hypoxia in the diabetic rat kidney. Kidney International, 73(1):34-42.
11. Bagshaw, S. M., Uchino, S., Bellomo, R., Morimatsu, H., Morgera, S., Schetz, M., Ronco, C. (2007). Septic acute kidney injury in critically ill patients: clinical characteristics and outcomes. Clinical Journal of the American Society of Nephrology, 2(3):431-439.
12. Krendel DA, Neilson EG. Use of activated charcoal in chronic renal failure. J Am Soc Nephrol. 1992 Aug;3(2):204-210.
13. Ghane Shahrbaf F, Assadi F. Effect of activated charcoal on reducing urea and creatinine serum levels in chronic kidney disease. J Renal Inj Prev. 2016 Dec 6; 6(1):44-47.
14. Elsherbiny NM, Ali SA, El-Sayed E-SM. Combination of Low-Protein Diet and Activated Charcoal Ameliorates Oxidative Stress Markers in Chronic Kidney Disease Patients. Int J Nephrol Renovasc Dis. 2021; 14:197-206.
15. National Kidney Foundation. (2021). Chronic kidney disease. Retrieved
16. DeSchryver-Kecskemeti K, Cluxton RJ Jr. Activated charcoal: a review of the literature. J Am Pharm Assoc (Wash). 1993 Jan-Feb; NS33(1):41-48.
17. Ghane Shahrbaf F, Assadi F. Effect of activated charcoal on reducing urea and creatinine serum levels in chronic kidney disease. J Renal Inj Prev. 2017;6(1):44-47.
18. Elsherbiny NM, Ali SA, El-Sayed E-SM. Combination of Low-Protein Diet and Activated Charcoal Ameliorates Oxidative Stress Markers in Chronic Kidney Disease Patients. Int J Nephrol Renovasc Dis. 2021; 14:197-206.
19. Tang Y, Xu Y, Shu T, et al. Effects of oral activated charcoal on hyperphosphatemia and vascular calcification in Chinese patients with chronic kidney disease: a randomized controlled trial. BMC Nephrol. 2020; 21(1):264.
20. Park S, Kang S, Kim DS, et al. Effects of vitamin C supplementation on oxidative stress and inflammation in hemodialysis patients: a randomized controlled trial. J Ren Nutr. 2016;26(6):401-407.
21. Krajcovicova-Kudlackova M, Babinska K, Valachovicova M. Health benefits and risks of plant proteins. Bratisl Lek Listy. 2005; 106(6-7):231-234.
22. -Agarwal S, Kumar A, Anandharamakrishnan C. Lycopene-rich extract from red guava (Psidium guajava Linn.) alleviates the symptoms of renal dysfunction in experimental chronic kidney disease. Food Funct. 2018;9(10):5317-5329.
23. Eguchi K, Yoshimura K, Saito T, et al. Beneficial effects of quercetin on renal function in a rat model of ischemia/reperfusion injury. J Ren Nutr. 2011;21(6):480-483.
24. Kumar D, Singla SK, Puri M, Singh J. Oxidative Stress: A Key Modulator in Chronic Renal Failure. Free Radic Res. 2016;50(3):337-346.
25. Eirin A, Lerman LO. The Emerging Role of Mitochondrial Targeted Peptides in the Treatment of Chronic Kidney Disease. Antioxidants (Basel). 2021;10(2):278.
26. Abdel-Daim, M. M., Khalifa, H. A., Abdeen, A., & Ibrahim, A. K. (2018). Protective effects of Ammi visnaga aqueous extract and its active component khellin against adenine-induced chronic kidney disease in rats. Journal of medicinal food, 21(6), 578-587.
27. Bhagavathula AS, Mahmoud Al-Khatib AJ, Elnour AA, Al Kalbani NM, Shehab A. Ammi Visnaga in treatment of urolithiasis and hypertriglyceridemia. Pharmacognosy Res. 2014 Oct-Dec;7(4):397-400.
28. Rostami Z, Parsaei P, Mehrzadi S, et al. Khellin improves gentamicin-induced renal dysfunction in rats: The role of oxidative stress, inflammation, apoptosis, and fibrosis. J Renal Inj Prev. 2016;5(3):126-133.
29. Alkuraishy, H. M., Al-Gareeb, A. I., & Albuhadilly, A. K. (2015). Ammi visnaga supplementation improves lipid profile and ameliorates lipid peroxidation and inflammation in patients

with metabolic syndrome. Journal of translational medicine, 13(1), 358.
30. Ahed J. Alkhatib. Two Years follow up of a Patient with Renal Fibrosis: from Renal Transplantation to Normal Functional Restoration Following the Use of Ammi visnaga and Urtica pillulefera. Archives of Medical Case Reports and Case Study, 2020, 3(1):3.
31. Tepe, B., Sokmen, A., & Akpulat, H. A. (2013). Protective effect of Urtica pilulifera extract against carbon tetrachloride-induced kidney injury in rats. Journal of medicinal food, 16(10), 904-910.
32. Tavafi, M., Ahmadvand, H., & Tamjidipoor, A. (2012). Urtica dioica extract attenuates nephrotoxicity induced by reno-protective dose of cyclosporine A in rats. Journal of Nephrology, Dialysis and Transplantation, 27(11):4110-4117.
33. Fouque, D., Kalantar-Zadeh, K., Kopple, J., Cano, N., Chauveau, P., Cuppari, L., Franch, H., Guarnieri, G., Ikizler, T. A., Kaysen, G., Lindholm, B., Massy, Z., Mitch, W., Pineda, E., Stenvinkel, P., Treviño-Becerra, A., & Wanner, C. (2008). A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. Kidney International, 73(4):391-398.
34. Razavi, B. M., Zolfaghari, B., & Salehi, H. (2017). Review on the ethnobotany, phytochemistry, and pharmacology of the genus Urtica. Journal of Acupuncture and Meridian Studies, 10(5):323-332.
35. Ibrahim, M. A., El-Ansari, M. A., El-Kady, M. B., & Ali, S. A. (2021). Urtica pillulifera: A review on its traditional uses, phytochemistry and pharmacological properties. Journal of Ethnopharmacology, 268:113599.
36. Hafizur, R. M., Kabir, N., & Chishti, S. (2012). Urtica dioica L.: An alternative therapy for the management of chronic renal failure. Saudi Journal of Kidney Diseases and Transplantation, 23(1):9-14.
37. Bahadoran, Z., Mirmiran, P., Azizi, F. (2019). Potential efficacy of nettle (Urtica dioica) in management of blood glucose and lipid profile in patients with type 2 diabetes: A randomized double-blind placebo-controlled clinical trial. Journal of Diabetes & Metabolic Disorders, 18(1):139-146.
38. AlShuwayeb, M. H., & Al-Khatib, A. J. (2013). Molecular and chemical therapeutic features of Urtica species. European scientific journal, 9(24).
39. AlKhatib, A. J., Laiche, F., Alkhatatbeh, M. A., Bello, A. M., Muhammad, I. A., Kabara, A. F., ... & Muhammad, M. (2014a). Leaf Extract of *u. Pilulifera* down regulates the Expression of INOS in Kidneys of Diabetic Rats. *European Scientific Journal*, 10(21).
40. Alkhatib, Ahed J., Fatima Laiche, Mosleh A. Alkhatatbeh, Saleh A. Alrasheidi, Murtala Muhammad, ALiyu Maje Bello, Ibrahim Ahmad Muhammad, Mustapha Garba Muhammad, and Aminu Faruk Kabara. "Urtica Pilulifera Upregulates the Expression of Heat Shock Protein (HSP70) In Kidneys of Diabetic Rats." European Scientific Journal 10, no. 21 (2014).

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