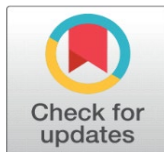


A NEPHROPROTECTIVE EFFECT OF CARISSA SPINARUM AGAINST GENTAMICIN INDUCED OXIDATIVE NEPHROTOXICITY

Soumya Bharadwaj ¹, Ritu Sanwal ²

¹ Assistant Professor, Department of Pharmacology, Siddhartha Institute of Pharmacy, Motherhood University, Roorkee, Dehradun, India

² Assistant Professor, Department of Pharmacology, Siddhartha Institute of Pharmacy, Roorkee, Dehradun, India



Received 17 January 2024

Accepted 18 February 2024

Published 01 March 2024

Corresponding Author

Soumya Bharadwaj,
bharadwajsoumya95@gmail.com

DOI

[10.29121/granthaalayah.v12.i2.2024.5521](https://doi.org/10.29121/granthaalayah.v12.i2.2024.5521)

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Copyright: © 2024 The Author(s). This work is licensed under a [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/).

With the license CC-BY, authors retain the copyright, allowing anyone to download, reuse, re-print, modify, distribute, and/or copy their contribution. The work must be properly attributed to its author.



ABSTRACT

One of the most prevalent issues with the kidneys is nephrotoxicity, which happens when the body is exposed to a toxin or medicine. With the growing availability of powerful therapeutic medications such as aminoglycoside antibiotics, chemotherapeutic agents, and nonsteroidal anti-inflammatory drugs (NSAIDs), a variety of pharmaceuticals can have a negative impact on the kidney, leading to acute renal failure, chronic interstitial nephritis, and nephritic syndrome. Ethiopian native *Carissa spinarum* (Apocynaceae) is traditionally used to treat skin conditions, rheumatism, diarrhoea, chicken pox, and stomachaches. The herbal plant *Carissa spinarum* possesses antioxidant qualities. The term "nephrotoxicity" describes the detrimental effects that different drugs can have on the kidneys, which can result in damage and dysfunction. This illness offers a serious risk to kidney health and can be brought on by exposure to specific medicines, chemicals, or poisons. Understanding the methods by which these substances affect the structure and function of the kidneys—such as oxidative stress, inflammation, and interference with essential cellular processes—is necessary to comprehend the abstract idea of nephrotoxicity. Nephrotoxicity management also involves establishing prevention and management strategies, identifying, and tracking possible nephrotoxic substances, and managing and preventing nephrotoxicity. All things considered, an abstract comprehension of nephrotoxicity entails investigating the complex pathways and circumstances that lead to renal injury and formulating strategies to lessen or offset these detrimental effects on kidney function.

Keywords: *Carissa spinarum*, Cellular Damage, Oxidative Stress, Kidney Function

1. INTRODUCTION

Gentamicin: Aminoglycoside antibiotics are used in clinical practice due to their active bactericidal activity, post-antibiotic effect, reduced bacterial resistance and low cost. This class of drugs usually causes nephrotoxicity, limiting frequent clinical use. Gentamicin is a class of aminoglycoside antibiotics used in the treatment of certain bacterial infections. These can include sepsis, meningitis, pneumonia, urinary tract infections, endocarditis, bone infections, and pelvic inflammatory

diseases. It doesn't work against chlamydia or gonorrhoea. It can be used topically, intramuscularly, or intravenously. [Al-Qarawi et al. \(2008\)](#)

For burns or infections on the outer surface of the eye, topical treatments are useful. Until a bacterial culture identifies the precise antibiotic that is sensitive to infection, it is frequently administered for just two days. Blood tests should monitor the required dose. It works by interfering with the bacteria's ability to make proteins that normally kill them. Gentamicin is most likely to damage the inner ear and kidneys. My ear problems are related to imbalances and hearing loss. These problems may be persistent. If administered during pregnancy, It might damage an unborn child. It seems safe to use, though, if you are nursing. Micromonospora purpurea is the bacterium that first produces gentamicin. Antibiotics are obtained by culturing micromonosporae by penetrating bacteria through the cell wall. Research is currently underway to confirm the biosynthesis of this antibiotic. This is an attempt to increase pronunciation and increase secretion of gentamicin for higher titers. Gentamicin is on the World Health Organization's list of essential medicines. Gentamicin is regarded by the World Health Organisation (WHO) as being necessary for human medicine. Also accessible as a generic medication.

1) Specific populations:

- ***Pregnancy and nutrition***

It is not advised to use gentamicin when pregnant unless the advantages outweigh the dangers to the expectant mother. Gentamicin has the ability to pass the placental barrier, and multiple cases of refractory bilateral congenital hearing loss in infants have been documented. Intramuscular administration of gentamicin to mothers may cause dystonia in infants. The safety and activity of gentamicin in lactating women have not been established. Human breast milk contains different amounts of gentamicin than does breast milk for newborns. [Ali \(1995\)](#).

- ***old***

Renal function should be assessed prior to and during treatment due to the older group's low glomerular filtration rate.

- ***Youth***

Gentamicin is not suitable for growing children. Various studies have concluded that they have longer half-life and greater serum levels compared to those in other age groups. When injected into this group, children after long-term treatment can develop hypocalcemia, hyperkalemia.

- ***Contraindications***

A person with a history of hypersensitivity cannot receive gentamicin. Anaphylaxis is one of them, along with any other major toxic reaction or the use of any other antibiotics. People with myasthenia gravis require extra attention throughout these kinds of procedures.

2) Adverse Effects

Gentamicin adverse effect may range to less severe effect to life threatening effect. Some of them are;

- Anemia
- Allergic Reactions
- Neuromuscular Problems
- Nerve damaging

- Kidney damage
- Ear damage

3) Kidney Damage

Kidney damage is a most common type of problem in the people who receive aminoglycoside for a longer time. Gentamicin is one of the most common drug of this group which cause nephrotoxicity. The dose's frequency can be adjusted to lower the risk of nephrotoxicity. [Gaikwad et al. \(2012\)](#)

Factors that increase the chance of nephrotoxicity are following:

- Increasing age
- Reduced renal function
- Pregnancy
- Hypothyroidism
- Hepatic dysfunction
- Volume reduction
- Sodium reduction
- Metabolic Dysfunction

Creatinine and urea levels in the blood are used to assess kidney impairment.

4) Inner Ear

Factors that increase the risk of inner ear damage include:

- Increasing age
- High blood uric acid level
- Kidney dysfunction
- Liver Dysfunction
- Higher dose
- Long courses of therapy
- Strong Diuretics

Gentamicin, a commonly used aminoglycoside, causes tubular necrosis, proximal tubular epithelial edema, cell detachment, renal failure is eventually caused by tubular fibrosis, glomerular congestion, perivascular edoema, and inflammation. It is applied to treat infections that could be fatal. Many therapeutic settings use it as a first-line therapy because to its wide activity, chemical stability, and quick bactericidal action against aerobic gram-positive and gram-negative pathogens. However, higher concentrations of these antibiotics are nephrotoxic. In some cases, these side effects are so severe that the drug must be stopped. It is estimated that up to 30% of patients treated with aminoglycosides for more than 7 days will show some signs of nephrotoxicity. Although new drugs such as third-generation cephalosporins and aztrone can be used as therapeutic and cost-effective aminoglycosides without the nephrotoxicities associated with the latter, aminoglycosides are the most widely used antimicrobials. This may be due to its rapid efficacy and the availability of more information about its pharmacology, toxicity, and therapeutic properties than other new drugs. The pharmacokinetics, pathology and clinical manifestations of gentamicin-induced nephrotoxicity have been extensively studied in both humans and animals. ... Gentamicin is an aminoglycoside, polycation and is highly polar in nature. They are not absorbed

from the gastrointestinal tract, but are rapidly absorbed after intramuscular or subcutaneous injection. They may also be administered intravenously or intrathecally. Plasma protein binding is minimal. Gentamicin crosses the placental barrier, but does not cross the blood-brain barrier into the central nervous system and does not enter the eye. [Kshirsagar & Patil \(2008\)](#)

The risk of nephrotoxicity is related to the concentration of aminoglycosides in the neocortex. Saturated cortical absorption suggests that high but transient aminoglycoside concentrations may be less nephrotoxic than persistently low concentrations. Nephrotoxicity is usually reversible because the cells surrounding the proximal tubule can be regenerated, but trough concentrations <2 mg/L are appropriate. [Mahabale & Chaudhari \(1987\)](#)

2. CARISSA SPINARUM

Name: *Carissa spinarum*

Synonymy: *Carissa diffusa*.

Family: Apocynaceae

Indian names: In India, it is also known as waka, kalivi, kavali karavada, and kharnu (Himachal Pradesh). Kali (Andhra Pradesh); Karekaya, Garji, Pencil, Karwant (Maharashtra), Karondhu, Garna, Karunda (Hindi); karamarda, avighna (Sanskrit); kalakkai, kalachedi; Karmachha (Bengali); Karmarda (Guzrat). The thorn bush of *Carissa spinarum* Linn. As a rule, it grows in forests and wastelands at an altitude of up to 1500 meters. They are very drought tolerant. It produces small fruits that anyone can eat and is sold in many places. [Pushpagadan & Kumar \(2005\)](#)

Shape

upright prickly shrub with forked branches up to 23 m high; Wood is very hard. The bark can be hand peeled lengthwise from light brown to green, exposing the white to light green tree underneath. The spine is 3.2cm long, the base is brown to green, and the tip is dark brown. The leaves are ovate, 4.5 cm long, 2.5 cm wide, and leathery. venous delusion - idolatry; margin, full; petiole length 3 mm; Leaves that release a white milky juice when separated from the stem. Fruit, egg-shaped berry, 9 mm long, 6 mm diameter, weight 642 mg, volume 586 µl; fruit color hyacinth blue 40; Scarlet Pulp 19/2; Juice, red shrimp 616/3. Seeds are lanceolate, 5-6 mm long, 4 mm diameter, black, weighing 28 mg, and volume 42 µl.

Flowering and fruiting season

This plant typically flowers in the months of April and May. It can even begin towards the end of July in certain circumstances. On the other hand, mid-May was the peak flowering period. It takes a long time for small fruits to grow and ripen. November is when ageing starts and ends in January. These were most likely the fruits of July's flowering. [Yadav et al. \(2016\)](#)

Chemical makeup of the developing embryo

The fruit has a 64% water content, while the fruit juice has a 25.8% total soluble solids content. Comparing this amount to other fruits, it is significantly higher. 1.51 grammes of acid, 10.80 grammes of total sugar, 10.77 grammes of reducing sugar, 0.03 grammes of non-reducing sugar, 0.42 grammes of tannins, 1.39 grammes of pectin, and 1.83 milligrammes of vitamin C are all present in fresh fruit. Fruit makes up 4.09%. 1.621% is the fruit's total mineral content, measured in ash. Similarly, fresh fruit has the following proportions: 0.057, 0.504, 0.051, 0.052, and 0.007 for phosphorus, potassium, calcium, magnesium, and iron, respectively. [Yarnell \(2007\)](#)

Root chemical composition

Digitoxigenin D, glucose, carissone, carindone, carinol, odoroside H, and digitalose. Fatty acids, specifically palmitic, stearic, oleic, arachinic, and linoleic acids, make up the chemical composition of seeds. Ursolic acid and triterpene alcohol make up the chemical composition of the sheet.

Flowers' chemical makeup

Nerolidol, dihydrojasnone, myrcene, limonene, camphene, canene, dipentene, farnesol, citronellal, β -ionone, neryl acetate, linalool, and geranyl acetate. (Fatima A. et al., 2013).

Dessert quality

Both the fruit and the seeds are consumed simultaneously. The quality is decent and the taste is pleasant. utilisation Small Carissa spinarum Linn fruits. It is a popular food that is also available for purchase in some places. It is incredibly nutrient-dense and a fantastic source of protein. The exceptionally high total soluble solids content suggests that this wild fruit can be processed and dehydrated. This shrub can grow on extremely stony, barren soils and is naturally very tough and drought tolerant. In order to protect the soil, it can therefore be utilised for afforestation. When paired with other tannin-rich materials like the branches and bark of *Embllica officinalis*, the leaves, which have a high tannin content of 915 percent, show great promise as a tannin source.

Pharmacological Uses

- Antiarthritic activity - Root/ Ethanolic extract- Phenylbutazone
- Anticonulsant- Root/ Ethanolic extract-Diazepam and phenobarbitone
- Hepatoprotective- Root/ Ethanolic extract- Silymarin
- Antioxidant- Root/ Ethanolic extract -Silymarin
- Antibacterial-Leaves/ Methanol extract- Cefotaxime

3. NEPHROTOXICITY

The kidney is the most vital organ in the human body. It plays a role in the metabolism of carbs, proteins, lipids, and other nutrients in addition to eliminating metabolites and hazardous waste from the body. The tubular cells that produce glucose through gluconeogenesis are the primary process. People frequently experience elevated susceptibility to toxins as a result of exposure to specific poisonous and toxic situations in the environment or to different physiological states, such as metabolic activity, increased chemical buildup in tubular fluid, and excessive blood flow to organs. [Najeem \(2021\)](#)

Renal tubules, renal arteries, renal corpuscles, and renal spaces are all altered in renal cells. A normal kidney structure contains millions of nephrons, all of which are primarily responsible for filtering waste products from the body and generally preserving the body's fluid balance. Nephrons also regulate blood pressure and bone health in addition to blood pH and hormones that stimulate the production of red blood cells. Renal pathology is linked to kidney disease diagnosis and characterisation, not tumours. When drug damage does not infect the kidneys, nephrotoxicity is distinguished from kidney disease.

- **Nephrotoxicity:** One of the most frequent causes of kidney disorders is nephrotoxicity, which happens when the body is exposed to a toxin or medicine. The body's ability to eliminate waste products and extra urine is

compromised when kidney impairment takes place. As a result, all blood electrolytes, including potassium and magnesium, will rise. A growing number of effective therapeutic drugs, such as aminoglycoside antibiotics, chemotherapeutic agents, and NSAIDS, have the potential to negatively impact the kidney, leading to acute renal failure, chronic interstitial nephritis, and nephritic syndrome. Nephrotoxicity can also occur as a result of exposure to heavy metals including lead, mercury, arsenic, and cadmium as well as chemical reagents such sodium oxalate, carbon tetra chloride, and ethylene glycol. (Kanchan Gaikwad et al., 2005).

- **The mechanism by which drugs induce nephrotoxicity is biochemical:-**

Based on molecular and biochemical events, nephrotoxicity can be classified into three primary phases.

- **Take Action Steps:** Toxins linked to vital biological molecules, including proteins, lipids, RNA, and DNA, result in the functional deactivation of these molecules. Venoms can interact with developing biomolecules in two ways: irreversibly (through covalent bonding) or reversibly (via charge-charge interactions) throughout various stages of reproduction. The significance of these interactions sets the stage for the production of ROS, lipid peroxidation, and free radicals. This significantly affects the flowability, integrity, permeability, and other membrane-related activities.
- **Stage of propagation:** Several biomolecular pathways that may or may not be reversible are disrupted by toxins and biomolecule interactions. It is capable of healing once the traumatic input is eliminated. Reduced ATP levels and an increase in free calcium concentration in the cytoplasm are the causes of renal cytotoxicity. This results in modifications to the cytoskeleton and internal proteins as well as blisters in the cell.
- **Actions to take:** Cell necrosis is the final result of primary poisoning. Organelles are harmed by toxins, which also degrade the plasma membrane, allowing cell contents to seep out. Vasoconstriction brought on by oxidative stress induces a hypoxic cellular state that eventually results in renal damage and renal apoptosis at the cellular level.

Nephroprotective Phytoconstituents from Different Medicinal Plant:

- **Curcuma longa:**

Curcuma longa, a perennial plant of to the Zingiberaceae family (also known as gingerbread), is commonly grown in Asia, India, China, and other tropical regions. It can reach a height of 3 to 5 feet. The primary curcuminoid in turmeric, a well-known Indian spice that is related to ginger, is called curcumin. Desmethoxycurcumin and bisdesmethoxycurcumin are the other two curcuminoids. Turmeric's yellow colour is caused by polyphenols called curcuminoids. Turmeric can be found in dried Curcuma longa. Due to its flavour and colour, turmeric is frequently used in food. It has a long history of usage in the Chinese and Ayurvedic medical systems for the treatment of colic, jaundice, dyspepsia, hematuria, flatulence, and bleeding. Curcumin possesses antiviral, antifungal, anti-inflammatory, and antioxidant properties. Research has demonstrated that curcumin protects the kidneys.

- **Panax ginseng:**

Panax ginseng is a member of the Araliaceae family and is native to Russia and East Asia. A lot of Asia harvests too much of it. China, Japan, and Korea all grow it for medical uses. It is a deciduous perennial that grows in shade and has tan roots, tiny

white blooms, and five-toed leaves. Triterpene glycosides, also known as saponins or ginsenosides, are part of its chemical makeup. Since ancient times, Asian cultures have used ginseng to treat a variety of ailments, including fatigue, mental stress, blood sugar regulation, libido enhancement, and longevity. However, current clinical research is concentrating on ginseng's potential benefits for blood sugar regulation, cancer prevention, human health, immune regulation, and fatigue. The nephrotoxicity caused by cisplatin was greatly lessened by ginsenosides Rh4 and Rk3. [Jado et al. \(2020\)](#)

- **Nephrotoxic substances and related nephropathy:**

One of the most prevalent kidney conditions is renal toxicity, which is characterised as kidney illness or dysfunction brought on by direct or indirect exposure to hazardous medications and chemicals found in the environment or in industry. The kidneys are particularly susceptible to the effects of environmental pollutants because of their concentration and excretory function. These pollutants cause harm to the kidneys, raise blood levels of electrolytes (potassium and magnesium), and impair the body's ability to eliminate waste materials and extra urine. [Gaikwad et al. \(2012\)](#)

- **Nonsteroidal anti-inflammatory drugs (NSAIDs):**

The main nephropathy induced by NSAIDs such as aspirin, ibuprofen, and indomethacin cause tubulointerstitial nephritis, systemic/renal acute renal failure, potassium retention and high blood pressure. menstruum: The main solvents are carbon tetrachloride (CCl₄), tetrachlorethylene and toluene. CCl₄ in the proximal tubule is converted to free radicals trichloromethyl and trichloromethylperoxyl. These free radicals cause direct renal tubular damage and hypertension with cell necrosis. Toluene causes hyperanionic gap acidosis, hyperacidosis, distal renal tubular acidosis, and severe hypokalemia. Tetrachlorethylene poisoning causes acute renal failure due to tubular necrosis.

- **Glycol:**

Calcium oxalate crystals build up in the renal tubules as ethylene glycol is broken down into glycolic acid and oxalic acid. Acute renal failure and blockage result from this. Severe interstitial inflammation brought on by crystals can also result in hematuria, proteinuria, hyperglycemia, or anuria.

- **Anti-tumor agents:**

These consist of nitrourea, alkylating agents, radiopaque agents, antimetabolites, and antibiotics that fight tumours. Although cisplatin is an effective alkylating anticancer drug, its clinical use is restricted due to its renal toxicity. Cisplatin has been shown to reduce antioxidant enzymes and antioxidants by increasing lipid peroxidation and the metabolites of reactive oxygen radicals.

- **Aminoglycosides:**

To treat gram-negative bacterial infections, gentamicin, kanamycin, amikacin, and streptomycin are frequently utilised. Their ototoxicity and nephrotoxicity, however, severely restrict their therapeutic applicability. Renal failure brought on by gentamicin-mediated nephrotoxicity is characterised by a gradual but noticeable rise in tubular necrosis, reactive oxygen species production, hypoosmolality, and blood creatinine levels.

- **Antibacterial agents:**

Tetracycline, pentamidine, acyclovir, trimethoprim, sulfadiazine, and rifampicin.

4. CONCLUSIONS

The purpose of this review was to assess the pharmacological effects of Carissa spinarum methanolic extract on Wistar rats' nephrotoxicity caused by gentamicin. The primary goal of the research was to determine whether orally administering Carissa spinarum methanolic extract may counteract the nephrotoxicity caused by the antibiotic Gentamicin.

Conclusions drawn from the study are as follows:

This review set out to evaluate the pharmacological effects of a methanolic extract of Carissa spinarum on the nephrotoxicity that gentamicin causes in wistar rats. Finding out whether giving Carissa spinarum methanolic extract orally may offset the nephrotoxicity brought on by the antibiotic Gentamicin was the main objective of the study.

CONFLICT OF INTERESTS

None.

ACKNOWLEDGMENTS

None.

REFERENCES

- Al-Qarawi, A.A., Abdel-Rahman, H., Mousa, H.M., Ali, B.H., & ElMougy, S.A. (2008). Nephroprotective Action of Phoenix Dactylifera in Gentamicine-Induced Nephrotoxicity. *Pharmaceutical Biology*, 46(4), 227-230. <https://doi.org/10.1080/13880200701739322>
- Ali, B. H. (1995). Gentamicin Nephrotoxicity in Humans and Animals: Some Recent Research. *General Pharmacology*, 26(7), 1477-1487. [https://doi.org/10.1016/0306-3623\(95\)00049-6](https://doi.org/10.1016/0306-3623(95)00049-6)
- Bhattacharjee, S.K. (2004). *Handbook of Medicinal Plants*. Pointer Publishers.
- Chopda, M.Z., & Mahajan, R.T. (2009). *Wound Healing Plants of Jalgaon District*.
- Chopra, R.N., Nayar, S.L., & Chopra, I. C. (1999). *Glossary of Indian Medicinal Plants*. National Institute of Science Communication (CSIR).
- Dragsted, L.O., Strube, M., & Larsen, J.C. (1993). Cancer-Protective Factors in Fruits and Vegetables: Biochemical and Biological Background. *Pharmacol Toxico*, 1, 116-35. <https://doi.org/10.1111/j.1600-0773.1993.tb01679.x>
- Fatima, A., Singh, P.P., Agarwal, P., Irchhaiya, R., Alok, S., & Verma, A. (2013). Treatment of Various Diseases by Carissa Spinorum L. - A Promising Shrub. *International Journal of Pharmaceutical Sciences and Research*. [https://doi.org/10.13040/IJPSR.0975-8232.4\(7\).1000-03](https://doi.org/10.13040/IJPSR.0975-8232.4(7).1000-03)
- Gaikwad, K., Pradeep, D., Pushpalata, C., Joshi, Y. M., Kadam, V. (2012). A Review on Some Nephroprotective Medicinal Plants. *International Journal of Pharmaceutical Sciences and Research*. [http://dx.doi.org/10.13040/IJPSR.0975-8232.3\(8\).2451-54](http://dx.doi.org/10.13040/IJPSR.0975-8232.3(8).2451-54)
- García, B., Barcia, E., Pérez, F., Molina, I. T. (2006). Population Pharmacokinetics of Gentamicin in Premature Newborns. *Journal of Antimicrobial Chemotherapy*, 58(2), 372-379. <https://doi.org/10.1093/jac/dkl244>

- Gupta, A. K., & Sharma, N. (2004). Tendon Reviews on Indian Medicinal Plants 1- 4 ICMR.
- Jado, J. C., Humanes, B., González-Nicolás, M. Á., Camaño, S., Lara, J. M., López, B., Cercenado, E., García-Bordas, J., Tejedor, A., & Lázaro, A. (2020). Nephroprotective Effect of Cilastatin Against Gentamicin-Induced Renal Injury in Vitro and in Vivo Without Altering its Bactericidal Efficiency. *Antioxidants* (Basel, Switzerland), 9(9), 821. <https://doi.org/10.3390/antiox9090821>
- Jain, S.K. (1991). Dictionary of Indian Folkmedicine and Ethnobotany, 1-311.
- Khan, M. R., Rizvi, W., Khan, G. N., Khan, R. A., Shaheen, S. (2008). Carbon Tetrachloride-Induced Nephrotoxicity in Rats: Protective Role of *Digera Muricata*. *Journal of Ethnopharmacology*, 122, 91-99. <https://doi.org/10.1016/j.jep.2008.12.006>
- Khare, C.P. (2007). Indian Medicinal Plants Springer Science Business Media LLC. <https://doi.org/10.1007/978-0-387-70638-2>
- Kirtikar, K. R., & Basu, B. D. (1995). Indian Medicinal Plants, (1), 5-6.
- Kshirsagar, S.R. & Patil, D.A. (2008). Flora of Dule and Nandurbar District, Maharashtra.
- Kshirsagar, S.R., & Patil, D.A. (2008). Flora of Jalgaon District, Maharashtra.
- Kumar, M. M., Kushwah, H.K., & Manjusha, R., Ravishankar, B. (2009). An Experimental Evaluation on Nephroprotective Activity of Nagaradi kashaya AYU, 30(1), 55-61.
- Mahabale, T.S., & Chaudhari, K.K. (1987). Gazetteer of India. Maharashtra state Botany and Flora of Maharashtra.
- Moona, A. (2009). Latheef Madhukkal HH, Sithara Ravindran A Review of Nephroprotective Plants. B Pharm Project and Review, 1- 27.
- Najeem, P. (2021). A Systematic Review on Nephroprotective Plants. *International Journal of Research Publication and Reviews*, 2(6), 174-184.
- Negi, K., & Asma, M. (2020). Nephroprotective and Therapeutic Potential of Traditional Medicinal Plants in Renal Diseases. *Journal of Drug Research in Ayurvedic Sciences*, 5(3), 177-185. <http://dx.doi.org/10.5005/jdras-10059-0079>
- Prajapathi, P., Sharma, A. K., & Kumar, T. (2003). A Hand Book of Medicinal Plants (Ed. 1st). Agrobios.
- Pushpagadan, P., & Kumar, B. (2005). Ethnobotany, CBD, WTO and the Biodiversity Act of India, Ethenobotany, 17, 2-12.
- Sundararajan, R., Akhil, B., & Ravindranadh, K. (2014). A Review on Phytoconstituents for Nephroprotective Activity. *Gitam Institute of Pharmacy*.
- Taayade, S. K., & Patil, D. A. (2006). Ethenomedicinal Wisdom of Tribals of Nandurbar Districts (Maharashtra). *Natural Product Radiance*, 5(1), 64-69.
- Yadav, D., Sharma, A. K., Srivastava, S., & Tripathi, Y. B. (2016). Nephroprotective Potential of Standardized Herbals Described In Ayurveda: A Comparative Study. *Journal of Chemical and Pharmaceutical Research*, 8(8), 419-427.
- Yarnell, E. (2007). Abascal Herbs for Relieving Chronic Renal Failure. *Alternative and Complementary Therapies*, 13(1), 18-23. <https://doi.org/10.1089/act.2007.13106>