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A CRITICAL REVIEW OF THE NEPHROPROTECTIVE ROLE OF A POLYHERBAL FORMULATION- *PATOLADI GANA*

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ABSTRACT

Nephrotoxicity is one of the most common kidney problems which is increasing gradually due to the increase in usage of several potent therapeutic drugs like aminoglycosides, antibiotics, chemotherapeutic agents, NSAIDs, and due to some systemic diseases, such as hypertension, hypercholesterolemia, diabetes mellitus, etc. The usage of these drugs and systemic diseases are inevitable, so nephroprotection may play an important role in this area. Current therapies for nephrotoxicity include peritoneal dialysis, hemodialysis, and kidney transplantation, which are costly regimens linked to high morbidity. Therefore, it is beneficial to administer nephroprotective drugs along with nephrotoxic drugs to reduce their toxicity without affecting the therapeutic efficacy. There are synthetic nephroprotective drugs available, but the use of natural nephroprotective agents is safer as they act without adversely influencing the body. Therefore, it was a literary search for a formulation in Ayurveda that has nephroprotective action. *Patoladi Gana* is a formulation from *Ashtaang Hridya* which is a combination of *Patol, Kutaki, Chandan, Murva, Guduchi,* and *Patha*. Various research studies show the efficacy of these contents in *Mutravaha Strotas Dushti Vikar* i.e., nephrotoxicity. So, by studying literature from both Ayurveda

& Contemporary sciences, the present literary study was an attempt to establish nephroprotective potential and to highlight the mechanism of nephroprotection of this ayurvedic formulation i.e., *Patoladi Gana.*

Keywords: Nephrotoxicity, Nephroprotective, *Patoladi Gana, Mutravaha Strotas Dushti, Vishaghna*

INTRODUCTION:

Nephrotoxicity occurs when kidney-specific detoxification and excretion do not work properly due to the damage or destruction of kidney function **[1]**. In the current era, it is one of the most commonly rising conditions as patients are exposed to a variety of drugs like aminoglycoside, antibiotics, chemotherapeutic agents, and NSAIDs for diagnostic and therapeutic purposes. Looking at this, nephroprotective drugs may play an important role in this area **[2]**.

In Ayurveda, nephroprotective medicinal plants and their formulations have been traditionally used for the prevention and treatment of renal disorders **[3]**. Ayurveda is enriched with various anti-toxic formulations which need to be evaluated for various toxicities. *Patoladi Gana* is one of them mentioned by *Vagbhat* **[4]**. It contains *Patol, Kutaki, Chandan, Murva, Guduchi* and *Patha.* This drug has been selected for the study as it is *Vishaghna* according to Ayurveda. Most of the drugs in this formulation show anti-oxidant, anti-inflammatory, immunomodulatory and nephroprotective activities **[5, 6, 7, 8]**.

The present review is about the assessment of the nephroprotective activity of *Patoladi Gana.*

MATERIALS AND METHODS:

This study is a literary review to establish the nephroprotective role of *Patoladi Gana.* Literature has been reviewed from both Ayurveda & Contemporary sciences. Also, various related websites have been searched.

CONCEPTUAL STUDY:

Modern Perspective of Nephrotoxicity:

Nephrotoxicity means renal toxicity. The kidney is a very important organ that has an important role in the body for blood filtration to excrete waste products, balance electrolytes in the body, control blood pressure, and stimulate the production of red blood cells. Most drugs are excreted by the kidneys, so the use of drugs that exceed the therapeutic dosage can damage the kidneys **[9]**. In the pathophysiology of several kidney diseases, oxidative stress plays a critical role. Systemic diseases such as hypertension, diabetes mellitus, environmental toxins, radiation, smoking, as well as consumption of alcohol induce oxidative stress in the kidney **[10]**.

Elevated BUN and Creatinine Levels are diagnostic of Nephrotoxicity **[11]**.

Mechanisms of Nephrotoxicity: General mechanisms that cause nephrotoxicity include changes in glomerular hemodynamics, renal ischemia, tubular necrosis, inflammatory tissue injury, tubular cell injury due to toxins or medications, degeneration due to some disorders like diabetes mellitus, hypertension, polycystic kidney disease, glomerulonephritis, etc which causes an irreversible decrease in the number of functional nephrons and obstruction of renal excretion **[1, 12, 13]**. Oxidative stress plays a critical role in drug-induced nephrotoxicity by inducing glomerular and tubular damage or indirectly associated with inflammation and endothelial dysfunction. Antioxidants have been shown to be effective in animals for kidney protection **[10]**.

Ayurvedic Perspective of Nephrotoxicity:

Nephrotoxicity means *Mutravaha Srotas Dushti* which occurs due to *Rasadidhatu Kshinata* and *Kshat* (Injury) **[14]**. *Mutravaha Srotas* is one of the most important and functional *Srotas*. Its main functioning organs are *Vrikka* and *Basti* **[15, 16]**. *Vrikka* is a very important part of this *Strotas* and it is developed from *Rakta* and *Meda Dhatu* **[17]**. *Basti* acts as a reservoir of urine and it is developed from *Rakta* and *Kapha* **[18]**. Vitiation of these *Dhatus* or injury to the S*trotas* can lead to nephrotoxicity.

Patoladi Gana:

The group of herbs means *Gana* and it is named based on its first ingredient. *Patoladi Gana* is one of 33 *Ganas* frequently used. The contents of this *Gana* are *Patol, Kutaki, Chandan, Murva, Guduchi,* and *Patha* which pacify *Kapha, and Pitta* and act on *Kushtha* (Skin diseases), *Visha* (toxin), *Jwara* (fever), *Vami* (Vomiting), *Arochak* (Anorexia), and *Kamala* (Jaundice) **[4]**.

Table 1: Botanical name, Family, and Parts used of *Patoladi Gana* [19,20]

Sr No	Drug	Botanical name	Family	Part used
1	*Patol*	Trichosanthes dioica	Cucurbitaceae	Whole plant
2	*Kutaki*	Picrorrhiza kurroa	Scrophulariaceae	Rhizomes
3	*Chandan*	Santalum album	Santalaceae	Stem bark
4	*Murva*	Clematis gouriana	Ranunculaceae	Leaves
5	*Guduchi*	Tinospora cordifolia	Menispermaceae	Stem
6	*Patha*	Cissampelos pareira	Menispermaceae	Stem

Table 2: *Rasa, Guna, Veerya, Vipak, Karma* (Pharmacological properties) of contents of *Patoladi Gana* [21]

Attributes	*Patol*	*Kutaki*	*Chandan*	*Murva*	*Guduchi*	*Patha*
Rasa	*Tikta*	*Tikta*	*Tikta, katu*	*Tikta, Kashay*	*Tikta, Katu, Kashay*	*Tikta, Katu*
Guna	*Laghu, snigdh*	*Laghu, Ruksha*	*Laghu, Ruksha*	*Guru, Ruksha*	Fresh-*Snigdha,mrudu* Dried- *Laghu, Ruksha,*	*Laghu, Tikshna*
Veerya	*Ushna*	*Sheet*	*Sheet*	*Ushna*	*Ushna*	*Ushna*
Vipak	*Madhur*	*Katu*	*Katu*	*Katu*	*Madhur*	*Katu*
Action on *dosha*	*Tridoshghna*	*Vatakara,Pittakaphaharak*	*Pittaghna, Vatkar*	*Tridoshghna*	*Tridoshghna*	*Tridoshghna*

Table 3: Chemical constituents and Pharmacological actions of contents of *Patoladi Gana*

S.N.	Content	Chemical constituents	Pharmacological actions
1	*Patol*	phenolic acids, polyphenols, flavonoids, alkaloids, glycosides, tannins.[22]	anti-inflammatory, antioxidant, and immunomodulatory activity, anti-toxic, and antimicrobial [23]
2	*Kutaki*	picrosides I, II, III, kutkoside, flavonoids, alkaloids, glycosides.[24]	antioxidant, immunomodulatory, anti-inflammatory, nephroprotective, [25]
3	*Chandan*	phenolics, flavonoids, alkaloids, tannins, α-santalol, β-santalol.[26]	antioxidant, antibacterial, anti-inflammatory, and analgesic [27]
4	*Murva*	alkaloids, flavonoids, terpenoids, saponins, glycosides, phenol. [28]	anti-inflammatory, and antioxidant activity.[29]
5	*Guduchi*	alkaloids, diterpenoid lactones, steroids, glycosides, polysaccharides.[30]	anti–inflammatory, antimicrobial, nephroprotective antioxidant [31]
6	*Patha*	alkaloids, flavonoids, tannins, volatile oils, glycosides, etc. [32]	anti-inflammatory, antivenom, anti-urolithic, analgesic,antioxidant [33]

DISCUSSION:

Pathophysiology of Nephrotoxicity- Ayurveda perspective

According to Ayurveda, Vitiation of *Dhatus* or injury to the S*trotas* can lead to nephrotoxicity. In modern science, there are various mechanisms of nephrotoxicity which include Ischaemia, Degeneration, Necrosis, Inflammation, and Obstruction, etc. Decreased cardiac output causes renal ischemia which results in the destruction of epithelial cells and then renal failure. In some metabolic disorders, Immunologic disorders, and Renal vascular diseases degenerative changes occur which leads to an irreversible decrease in the number of functional nephrons which in turn leads to nephrotoxicity. Inflammatory conditions like glomerulonephritis, Interstitial nephritis can develop insoluble immune complexes due to

antigen-antibody reaction which blocked glomeruli and causes renal failure. Necrosis is the result of Inflammation and ischemia in which damaged epithelial cells may slough off and plug the tubules and thus cause renal failure. Obstruction can be due to stones or plugging of nephrons due to sloughing of epithelial cells which also causes nephrotoxicity.

As per Ayurveda, vitiated *Vata* can cause stiffening or stenosis of renal arteries which leads to ischemia. Thus, reduced blood flow can damage the epithelial cells of nephrons. Vitiated *Vata* also causes degenerative changes in epithelial cells due to which there is a decrease in the number of functional nephrons. Thus, vitiated *Vata* is responsible for Nephrotoxicity by the mechanism of Ischaemia and degeneration.

Vitiated *Pitta* when enters *Ras* and *Rakta Dhatu* circulates all over the body. It also vitiates *Kleda* through its *Ushnatikshnadi* properties. Such vitiated *Kleda* when drawn into the *Mutravaha Srotas*, gets affected and causes inflammation and afterward necrosis. Thus, vitiation of *Pitta* causes Nephrotoxicity by the mechanism of Inflammation and Necrosis.

Vitiated *Kapha* blocks the glomerulus and causes obstruction which can cause nephrotoxicity. There are various causes for obstruction such as Immune complex invasion of the glomerulus, plugging of nephrons due to destructed tubular epithelial cells, glomerular sclerosis, stones, etc. But as per Ayurveda, vitiated *Kapha* is mainly responsible for such obstruction.

Thus, vitiated *Doshas* can cause vitiation of *Dhatus* which leads to nephrotoxicity.

Nephroprotective action of *Patoladi Gana*:

It is a formulation in Ayurveda that contains *Tiktarasatmak, Katu Vipaki,* and *Ushna Veerya Dravyas* i.e., *Patol, Kutaki, Chandan, Murva, Guduchi,* and *Patha.* It is *Tridoshaghna* specially P*ittakaphashamak, Dhatwagnideepan, Dhaatuprasadak, Aampachan, Strotoshodhan, Vranashodhan, Raktashodhak, Mutrajanan, Shothahar, Kothaprashaman* and *Vishaghna* in nature. Looking at the pathophysiology, its nephroprotective action can be described in the following ways:

Action on *Hetu*: *Visha* (Toxin) is one of the causes of nephrotoxicity. Toxins like medicines, metals, etc can be nephrotoxic if not used properly (if used in high doses or with long time use). Even infection also acts as a toxin as it causes an Insoluble immune complex which entrapped in the glomerulus and thereby unable to filter and causes renal failure. Long-term toxicity (*Dushi Visha*) vitiates all three *Doshas. Patoladi Gana* is

Tridoshghna and V*ishaghna* in nature. So, by *Guna* and *Prabhav* it acts as nephroprotective and thus its action is *Hetupratyanik Chikitsa.*

Action on *Doshas*: Pathophysiology of nephrotoxicity shows that Ischaemia and Degeneration occur due to vitiated *Vata*, Necrosis and Inflammation occur due to vitiated P*itta,* and Obstruction occurs due to vitiated K*apha. Patoladi Gana* is T*ridoshagna* in nature, especially *pitta Kapha Shamak. Patol* with its *Madhur Vipak* and *Ushna Guna, Guduchi* with its *Snigdha* and *Ushna Guna,* and *Patha* and *Murva* with its *Ushna Veerya* pacify V*ata* and thus prevent ischemia and degeneration. *Kutaki* and *Chandan* pacify *Pitta* due to *Tikta Rasa* and *Sheeta Veerya*. *Patol* and *Patha* due to *Tikta Ras* while *Guduchi* with its *Tikta, Kashaya Rasa* pacifies *Pitta Dosha* and thus prevents necrosis and inflammation. Most of the contents of *Patoladi Gana* pacify *Kapha Dosha* due to their T*ikta, Katu* and *Kashay Ras, Katu Vipak, Laghu, Ruksha, Ushna,* and *Tikshna Gunas*. Thus, obstruction is prevented. In this way, *Patoladi Gana* helps to break the pathogenesis of nephrotoxicity caused by various mechanisms. Due to its *Tridoshaghna* nature, it acts as nephroprotective and its action is *Doshapratyanik Chikitsa.*

Action on *Mutravaha Srotas*: *Vrikka* and *Basti* are the main functioning organ of *Mutravaha Srotas*, Kidneys are developed from *Rakta* and *Medadhatu* and *Basti* is developed from *Rakta* and *Kapha.* Vitiation of these *Dhatus* can lead to nephrotoxicity. *Patoladi Gana* is *Pitta* and *Kaphashamak, Aampachak, Lekhan, Vranashodhan, Dhatwagnideepan,* and *Dhatuprasadak*. It acts on *Mutradhatu* and causes diuresis due to *Strotoshodhan* and thus acts as *Shothaghna.* It also alleviates *Rakta* and *Pittadushti* by destroying *Avaran* of *Kapha* and thus acts as V*ishaghna* and *Raktaprasadak*. Thus, *Patoladi Gana* acts as nephroprotective by its *Dhatuprasadak* action which is *Balya* for *Doshadushya Samurchhana Sthan.*

Action as per Contemporary science: Oxidative stress damages renal tissue and furthers inflammation leading to tissue injury **[10]**. It generates free radicals which overpower the inbuilt protective mechanism and this gives rise to nephrotic damage, and necrosis and causes nephrotoxicity. Thus, antioxidants and free radical scavengers, are useful in reducing nephrotoxicity. Several research papers show that the contents of *Patoladi Gana* have an antioxidant and anti-inflammatory activity which is useful in nephroprotection. Most of the Chemical constituents of *Patoladi Gana* like Phenolic

acids **[34]**, Flavonoid glycosides, **[35]** Tannins, **[36]** Alkaloids, **[37]** α-Santalol, and β-Santalol, **[38]** Picroside II, **[39]** Iridoids exhibit,**[40]** Diterpenoid lactones, Steroids, Glycosides Aliphatic compounds, Polysaccharides **[41]** have anti-oxidant, anti-allergic, anti-inflammatory, anti-helminthic, anti-viral and anti-microbial activities. They are beneficial to human health due to their potential antioxidants and prevent the damage of cells resulting from free-radical oxidation reactions. They also promote the anti-inflammation capacity of human beings. Thus, the antioxidant and anti-inflammatory activity of *Patoladi Gana* is useful in nephroprotection.

CONCLUSION:

As per Ayurveda, *Patoladi Gana* protects kidneys from toxins due to *Tridoshaghna* nature especially *Pitta-Kaphashamak* and *Dhatuprasadak* action especially *Raktaprasadak* and *Vishaghna* nature. It acts on nephrotoxicity by *Hetupratyanik and Doshapratyanik Chikitsa*. Also, by *Dhatuprasadak* action it is *Balya* for *Doshadushya Sammurchhana Sthan*.

As per contemporary science, the administration of antioxidants along with nephrotoxic drugs is beneficial to reduce their toxicity without affecting the therapeutic efficacy. The use of synthetic antioxidants in long term is unsafe for human health, so herbal medicines should be preferred. As *Patoladi Gana* has antioxidant activity, it can be useful in reducing nephrotoxicity.

By taking all literature into consideration, it can be concluded that *Patoladi Gana* is a nephroprotective drug.

This is a literary study only; further Pre-clinical and Clinical studies should be carried out to validate its nephroprotective role.

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