

Nephroprotection: Meaning and Scope in Unani System of Medicine

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Abstract

The concept of protection and tonicity of an organ as described in Unani medicine has a specific notation that can be understood through the theories philosophies that govern the system. This will help understand the significance of the theory and its practical application and also the nature and mechanism of drugs action and thereby their actual therapeutic value. Evidences are accumulating to demonstrate that the drugs described to be useful in various renal disorders because of their nephroprotective and nephrotonic effect as described in Unani or other traditional medicines, have even more wide and diverse therapeutic uses than that depicted by the modern medicine practitioners. Many scientific studies have demonstrated that Unani medicine have ample potential to become an important source of managing many renal diseases and their complications. This paper gives a brief account of the concept of nephroprotection and explores the potentiality of Unani drugs that can be used to treat the renal diseases or at least arrest their progression to chronic or end stage renal disease.

Key words : Nephroprotection, Nephrotoxicity, Unani System of Medicine.

Introduction

The complex nature of renal diseases and their progression to renal failure (both acute and chronic) and end stage renal disease (ESRD) makes their management quite difficult. The majority of cases of renal disease remain unnoticed unless they progress to advance stage when the conventional therapeutic interventions are usually not sufficient to cure them completely. But the major problem with kidney disease is its progression to a stage when virtually no option works at all except the renal replacement therapy (RRT).

Two major components of RRT viz. dialysis and kidney transplantation are highly sophisticated and thereby too costly to be affordable for the patient of average income group. Only small chunk of elite class can take the luxury of such a regimen, that too subject to the availability of the facility in its reach. That is why most of the patients of kidney disease are left to die mainly in developing and poor countries, because of non-availability of RRT facilities in their region or their inability to pay for it. About 100 countries have been identified not to possess such facility at all (Lameire et al., 2005). In India the projected number of deaths due to chronic kidney diseases (CKD) is on a rise. In 1990 it was 3.78 million and is expected to become 7.63 million in 2020

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(WHO, 2005). Availability of kidneys for transplantation is another important problem consistent with RRT. Although, expenditure on RRT is costing about 1 trillion dollar, annually but the substantial percentage of patients in need of it, still remains untreated and consequently untreated patients have outnumbered those who are receiving the treatment. In nut shell therefore, it can be said that it is almost next to impossible to provide replacement therapy to all patients requiring it. The next option left with the physicians is to think of alternatives and the best way to come out of such a situation or at least scale down the prevalence and consequently the financial burden to a significant level, is to protect the kidney function, slow the progression of disease and delay the need of RRT (Remuzzi *et al.*, 1993 Hanneman *et al.*, 1991). This second option actually paved the way for envisaging a concept that is broadly termed as nephroprotection. It aims at protecting the kidney from noxious stimuli, treating the kidney diseases or at least checking the progression of renal diseases and delaying the need of RRT. However the concept of nephroprotection in modern medicine is relatively new and can hardly be traced before eighties whereas traditional medicines especially Unani medicine offers various protective and curative options of management.

Concept of Nephroprotection in Unani System of Medicine

The concept of protection of an organ, and the *quwa* (faculty) consistent with it, so as to maintain its structure and function has been a distinguishing feature of Unani system of medicines since ancient times. Drugs that are supposed to be tonics and protective for particular organ are used for this purpose and are also combined with other drugs having related pharmacological effects, with an aim to strengthen the organ and its *quwa* to make them efficient enough to fight the noxious stimuli and protect the organ from aversive effect or at least minimize the harmful effects of various untoward elements. Thus, the protective approach to prevent, treat are slow down the progression of disease is the main stay in Unani system of medicine. The concept of nephroprotection in Unani system of medicine is meant to invigorate and strengthen the kidney and help the preservation of its *quwa* involved in maintaining the normal function of the kidney. Thus, when impairment in renal function and structure takes place protective agents help to bring the normalcy back by improving the inherent protective and defensive abilities of the organ.

The faculties at their equilibrium are poised inherently to maintain the normal functions of that organ / system and make it strong enough to fight and remove the untoward elements that come to its contact. That is why for every organ/

system a group of tonic drugs has been proposed that safeguards its larger interest and bring it near to its equilibrium, if some derangement in its function or structure has taken place. If the normalization does not take place then the drugs possessing specific actions are used to treat the disease or inhibit its progression. Thus, we can say that simultaneous protective and curative approach to prevent, treat or slow the progression of disease is the hallmark of Unani System of Medicine.

According to Unani system of medicine all the organs have been endowed with four faculties which work in coordination to maintain the function and the structure of the organ. These faculties are:

- *Quwwat-e-Hazimah*
- *Quwwat-e-Jazibah*
- *Quwwat-e- Masikah*
- *Quwwat-e-Dafeah*

Apart from these four faculties that are responsible to maintain the normal functioning of all the organs, kidney has also been bestowed upon with an additional faculty namely *quwwat-e- mumayyizah* (separating and distinguishing faculty), by virtue of which kidney separates the blood from impurities and wastes which are the sequels of the ongoing metabolic process in the body or come from the deliberately administered drugs and chemicals for therapeutic purposes, or passively ingested toxicants from the environmental pollution and exposure to various hazardous toxic substances. When the process of separation completes, *quwwat-e- dafeah* helps the wastes excrete out, as early as possible. It suggests that a number of forces that complement each other, operate continuously in a synchronized way to maintain the functioning of kidney and also to protect it by not allowing the wastes and toxins which the kidney is constantly exposed to, to stay for sufficient period of time to cause local injury. The renoprotection by view point of Unani Medicine comprises of the protection of the various faculties the kidneys are imbued with, to maintain its functioning. In case of mild degree of kidney disorder the drugs categorized to be kidney tonics, are sufficient enough to deal with the situation to bring the normalcy. However, when gross impairment in kidney function or it matrix takes place anyhow, because of the high toxic effect of a substance or because one of the natural faculties are undermined owing to some local or systemic disease of the body, then the drugs having other pharmacological actions along with the tonic one, are used. Drugs ascribed to

possess diuretic, anti-inflammatory, antioxidant, cathartic etc along with tonic effect are frequently used with an aim to treat the pathology and invigorate the kidney to bounce back to its normal state to perform its assigned work. Further, in case of progression of kidney diseases some other drugs are included in the regimen along with the drugs mentioned above, to directly ameliorate the compromised condition by promoting the healing of injured tissue, removal of toxins and reducing the pressure of work on kidney by diverting the wastes to some other system or organs of the body (Arzani, 2006; Ibn Hubal, 2007). However, despite a comprehensive approach of treatment described in literature and being practiced by the physicians it has been accounted by the practitioners that the treatment of renal injury itself is very difficult because of several reasons such as:

- (a) Kidney is the passage of urine and other waste product therefore the drugs intended to be effective do not stay at the site of action for sufficient period of time.
- (b) The matrix of kidney is too hard therefore the drugs did not diffuse easily to the site of action.
- (c) The waste material excreted by kidney is usually noxious and corrosive in nature which delay or partially hamper the process of healing.
- (d) Kidney always remains busy in its work, while healing process requires a degree of rest (Khan, 2003; Ibn Rushd, 1987).

The kidney disease also occurs due to change in *mizaj* (temperament), *Amraze Aliah*, (compound disease) or weakening of the any of five faculties. When the faculties become weak, kidney does not get sufficient nutrition from fluids and following diseases may occur:-

- *Sou-e-Mizaje Kulyah*
- *Waram-e-Kulyah*
- *Hasat-e-Kulyah*
- *Waj'-e- Kulyah*
- *Huzal-e-Kulyah*
- *Iltehab-e-Hauze kulyah*
- *Sudad-e-Kulyah* (Tabari, 2006; Khan, 2003; Ibn Rushd, 1987)

However, despite recognition of drug induced nephrotoxicity and concerted efforts directed towards developing therapeutic or prophylactic agents to induce protection against chemically induced nephrotoxicity, conventional therapeutic options available are still very limited. In the absence of reliable and effective modern nephroprotective drugs efforts are currently canalized toward exploring drugs from alternative and complementary medicines to treat and/or prevent the disease.

In modern medicine Antihypertensive Converting Enzyme (ACE) inhibitors and Angiotensin II Receptor Blockers (ARBs) are mainly used to induce renoprotection, however these agents are neither the drugs of choice for this purpose nor can be used exclusively to produce renoprotective effects, rather they are mainly effective in nephropathies associated with blood pressure and diabetes etc (George *et al.*, 2000) It implies that by treating a patient with the above mentioned drugs it is obligatory to induce a pharmacological effect that may not be necessarily needed by him. The associated toxicities of these agents also limit their use to a great extent. Although, ARBs are comparatively safer than ACE inhibitors but some of the side effects are common to both the drugs such as neutropenia, proteinuria, angioneurotic edema, hyperkalemia especially in patients with renal impairment etc. (George *et al.*, 2000), which undermine the therapeutic utility of these agents. A drug categorized to be effective specifically as a nephroprotective agent without having liability to produce some serious side effects will be the obvious choice for the patients suffering from renal dysfunction or failure.

In view of the limitations of Western medicine and the alarmingly increasing cases of renal disorders, development of effective and safe drugs to treat renal disorders has become the priority area of research. Unani system of medicine possesses many effective and safe diuretics and nephroprotective drugs which are in use since hundreds of years in renal disorders. However, these drugs have been neither described with necessary details for their role in renal disorders nor scientifically investigated for various pharmacological activities; therefore, in order to evaluate their different pharmacological effects concerning kidney ailments a comprehensive scientific study is inarguably inevitable.

Further, since the Western medicine as described above still doesn't have satisfactorily effective and safe drugs which can cure renal disorders completely, therefore the study of Unani drugs gains importance in respect of characterizing and identifying a better group of drugs that can fill this lacuna.

It is being appreciated that Unani System of Medicine can offer some effective drugs from its treatise to be useful in diverse pathological conditions of kidney and thus can be used to protect the renal function and prevent/slow the progression of renal diseases to CKD or ESRD. A number of drugs from herbal sources have been shown to possess promising nephroprotective and related effects in some recent studies and researchers are making it a point to concentrate seriously on the development of nephroprotective agents from traditional sources.

A number of poly herbal formulations and single drugs mentioned in Unani literature and being practiced by physicians have been demonstrated to produce some important effects such as diuretic, anti-inflammatory, antioxidant nephroprotective etc against known toxicants. Some of the drugs such as Jawarish zarooni sada (Afzal *et al.*, 2004), Banadequl buzoor (Anwar *et al.*, 1999), Bisehri Booti (*Aerva lanata* Juss) (Shirwaikar *et al.*, 2004), Revand Chini (*Rheum officinalis*) (Yokozawa *et al.*, 1991), Zanjabeel (*Zingiber officinale*) (Narora *et al.*, 1992), Asgand (*Withania somnifera*) (Panda *et al.*, 1997), Khare khasak (*Tribulus terrestris*) (Nagarkatti *et al.*, 1942), Haleela (*Terminalia chebula*) (Yokozawa *et al.*, 1995), Sahajna (*Moringa olifera*) with a little opium, (*Papaver somniferum*), Giloo (*Tinospora cordifolia*) are useful in the inflammation of kidney (Sevanand *et al.*, 1996) have been shown to possess nephroprotective and related effect of varying degree.

The protective effect of Asgand (*Withania somnifera*) on cadmium induced toxicity in mice kidney has been studied to demonstrate a promising result (Panday *et al.*, 1997). Similarly, curcumin isolated from turmeric has been reported to produce protective effect against adriamycin induced nephrotoxicity (Venkatesan *et al.*, 2000). A Unani drug Kabab chini (*Piper cubeba*) was investigated for nephroprotective activity in chemically induced nephrotoxicity showed significant nephroprotective effect against gentamicin and cisplatin induced nephrotoxicity (Zaid *et al.*, 2012). These reports are although of preliminary nature but showing great potential of Unani Medicine to deliver promising agents that can be used to treat the kidney diseases or at least, preserve its function and slow the progression of diseases. Therefore, the study of Unani diuretics, tonics and nephroprotective drugs gains importance as one of the means of characterizing and identifying a better group of drug that can be used as nephroprotective agent. Some of the important studies showing interesting results are being presented in the table given below:

Table 1 : Unani drugs which are scientifically evaluated for nephroprotective effect

S. No.	Herbs	Protective effect
1.	<i>Tribulus terresteris</i>	Possess protective effect against the gentamicin induced nephrotoxicity in both structural and functional terms. (Nagarkatti <i>et al.</i> , 1942)
2.	<i>Boerhavia diffusa</i>	Clinically proved to be useful and safe drug in patients of nephritic syndrome (Singh <i>et al.</i> , 1972)
3.	<i>Withania somnifera</i>	Significantly reduced toxicity caused by cadmium (Panday <i>et al.</i> , 1997)
4.	Banadequl Buzoor	The formulation was found to decrease the serum urea and serum creatinine levels significantly (Anwar <i>et al.</i> , 1999)
5.	Jawarish Zarooni Sada	The formulation was found to decrease the serum urea and serum creatinine levels significantly (Afzal <i>et al.</i> , 2004)
6.	<i>Piper cubeba</i>	Showed significant protective effect against cisplatin and gentamicin induced nephrotoxicity (Zaid <i>et al.</i> , 2012)
7.	<i>Moringa oleifera</i> and <i>Tinospora cordifolia</i>	Useful in the inflammation of kidney (Melookunnel, 1996).
8.	<i>Ficus racemosa</i>	Significantly protects the toxicity produced by Cisplatin (Gowda <i>et al.</i> , 2011).
9.	<i>Aegle marmelos</i>	Normalized the serum creatinine, urea and blood urea nitrogen levels in gentamicin toxicity (Kore <i>et al.</i> , 2011).
10.	<i>Moringa oleifera</i>	Showed moderate protection in both curative and prophylactic models against Cisplatin induced toxicity (Sreedevi <i>et al.</i> , 2011).
11.	<i>Carica papaya</i>	Owed nephroprotective effect on CCl4 induced nephrotoxicity (Olagunjua <i>et al.</i> 2009).
12.	<i>Cassia auriculata</i>	Reduced the blood urea and serum creatinine level effectively in both the curative as well as the preventive regimen (Shirwaikar <i>et al.</i> , 2005).
13.	<i>Eruca sativa</i>	A potent antioxidant and renal protective activity and preclude oxidative damage inflicted to the kidney (Alam <i>et al.</i> , 2007).

14.	<i>Hemidescus indicus</i>	Showed nephroprotective activity against gentamicin induced nephrotoxicity (Magala <i>et al.</i> , 2004).
15.	<i>Allium sativum</i>	Showed dose dependent reduction in the elevated blood urea and serum creatinine levels and normalized the histopathological changes in the curative regimen. (Maldonado <i>et al.</i> , 2000).
16.	Glycyrrhizin	Offered protective effect against gentamicin induced toxicity (Sohn <i>et al.</i> , 2003).
17.	<i>Pongamia pinnata</i>	Demonstrated protective effect against cisplatin and gentamicin induced renal injury (Shirwaikar <i>et al.</i> , 2003).
18.	<i>Solanum nigrum</i>	Exhibited significant hydroxyl radical scavenging potential, thus suggesting its probable mechanism of cytoprotection (Prasanth Kumar <i>et al.</i> , 2001).
19.	<i>Terminalia chebula</i>	Reduced the serum concentrations of urea nitrogen, creatinine, methyl guanidine and guanidinosuccinic acid significantly (Yokozava <i>et al.</i> , 1995).

Conclusion

It can be concluded that the concept of nephroprotection as described in Unani literature, is comprehensive and can be used to understand the subject matter in its entirety. The concept of quva and maintenance of the equilibrium in the body and specific organs may be used as a theoretical model to understand the physiopathology of many pathological conditions of many diseases including the renal disorders. Further, a number of drugs used in the management of renal disease by the Unani physicians have been validated by modern scientists who have reported very interesting effect possessed by these drugs. These drugs may be developed as a better substitute of ARBs and ACE inhibitors which have failed to produce the desired response.

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