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Abstract

Background: The kidney is tasked with a number of metabolic functions in the body. In its role as a detoxifier and primary eliminator of xenobiotics, it becomes vulnerable to developing injuries. Currently, over 1 million people in the world are living on renal replacement therapies (RRTs). The case in sub-Saharan African countries like Nigeria and South Africa is not any better than the global trend.

Materials and Methods: A systematic review of medicinal plants used in the treatment of kidney disorders was conducted. Information were gathered from published scientific journals, books, reports from national, regional and international institutions, conference proceedings and other high profile intellectual resources. MeSH words like 'prevalence of kidney disorders in Africa', 'renal replacement therapy', 'nephrotoxins or nephrotoxicants', 'nephroprotective plants', 'nephroprotective plants in Nigeria or South Africa' and 'nephroprotective phytochemicals' were used to retrieve information from online databases (Google, Pubmed, MEDLINE, Science Direct, Scopus and SID).

Results: Interestingly, our findings revealed that phytotherapy has emerged and is being employed to protect renal functions and delay progression of renal pathological conditions into end episodes where the last resort is RRT. In fact, in recent times, Phytotherapists are not only interested in developing relatively safe, more affordable, easily accessible and potent nephroprotective formulations but also increasing awareness on the prevalence of the disease and educating the populace on the probable preventive measures. More importantly, efforts at scientifically elucidating the pharmacological efficacy of the identified nephroprotective plants yet to be validated must be intensified through informed expert opinions. Till date, there is paucity of information on the concept of nephroprotection in most developing countries where kidney disorder is a major threat. Although, the concept is just emerging in South Africa, evidences have given credence to its application in complementary and alternative system of medicine in Nigeria.

Conclusion: This review, therefore, reawaken researchers' consciousness in the continuous search for auspicious nephroprotective plants that could potentially be excellent candidates in developing new lead drugs to manage and treat renal disorders.

Key words: Bioactive principles, Nephroprotective, Nephrotoxic, Renal replacement therapy, Silent killer.

Introduction

The kidneys are a pair of fist-sized organs located outside the peritoneal cavity on each side of the spine. They are highly specialized organs that maintain the body's homeostasis by selectively excreting or retaining various substances according to specific body needs. The importance of urine formation and excretion as a life-sustaining function is highlighted in situations when kidney function is suddenly lost. The complex nature of renal diseases and their progression to renal failure and end stage renal disease (ESRD) makes its management quite difficult. Many cases of renal disease (largely due to chemical exposure, reckless lifestyles, and complication from metabolic ailments) remain unnoticed until they progress to advance stages when the conventional therapeutic interventions are usually not sufficient to provide ample remedy, hence, the name 'silent killer disease'. The major problem with kidney disease however is its progression to a stage when the last resort is the renal replacement therapy (RRT).

In recognition of the importance of the kidney and its affiliated disorders, the second Thursday of every March has been designated as 'World Kidney Day'. It is a day set aside by international bodies to re-awaken human consciousness on the significance of a healthy kidney and the inherent burden of its disorders to health. This review, thus, examines the common nephrotoxins, and the ambit of traditional systems of medicine in providing affordable, relatively safe, and easily accessible renal healthcare in Nigeria and South Africa. In 2014, the World Health Organization (WHO) estimated about 300 million people as victims of Chronic Kidney Disease (CKD) worldwide with 3.4 million attributable death cases and even more in 2012 and 2013 respectively (WHO, 2014). In sub-Saharan Africa countries including Nigeria, the numbers are more disconcerting. An estimated 36.8 million Nigerians (23 percent) were reported to be suffering from various stages of kidney disease. With this figure, one in seven Nigerians is at risk of the different forms of the disease (WHO, 2014). In South Africa on the other hand, inherited hypertension and Type 2 diabetes account for between 60-65% and 20-25%, respectively of kidney failure in adults (NKFS, 2015). With nephropathy as one of the secondary complications of diabetes, the prevalence of renal disorders is even more daunting in South Africa which tops the list with an average of 8.3% and closely followed by Nigeria (4.5%) in Africa (IDF, 2014). This singular fact has placed these countries in the beam light and as requiring concerted and optimized attention in this region of the world.

The two frontiers of RRT (dialysis and kidney transplantation) are highly sophisticated and expensive for the average income class. Only limited fraction of the elite population can take the luxury of such a regimen subject to the availability of this facility. That is why most of the patients of kidney disease are left to die mainly in developing countries because of non-availability of RRT facilities or their inability to afford it. A recent report by Saraladevi (2013) suggests that dialysis treatment rate ranges from < 1 per million populations (pmp) for most sub-Saharan countries, with Nigeria and South Africa at 1.3 and 125 pmp respectively. The

growth in dialysis in South Africa is primarily in the private sector, with improved benefits for dialysis for people on medical insurance. The average cost of hemodialysis in Africa is \$100 per session (Saraladevi, 2013). Renal transplantation on the other hand is available in only seven countries in sub-Saharan Africa (South Africa, Sudan, Nigeria, Mauritius, Kenya, Rwanda, and Ghana) with most of the transplants being living donor transplants, except in South Africa, where deceased donor transplants are also encouraged at ratio 2:3, respectively. Lack of legal framework, religious, and social constraints have hindered deceased donor practice in many countries and have led to the low rate of transplantation in these areas. Except with Nigeria and South Africa where at least 70 transplants are performed annually, other nations are challenged with inadequate facilities (Saraladevi, 2013).

The continuous 'brain drain' of healthcare professionals from Africa for greener pasture has also impacted on this menace and has left the continent with inequitable number of qualified nephrologists to patients' population (Eastwood et al., 2005). There are large rural areas of Africa that have no health professionals to serve their populations. Specifically, the proportion of nephrologists per million population for Kenya, Nigeria, Sudan and, South Africa stood at 0.5, 0.6, 0.7, and 1.1, respectively as compared to the United States with reported 16.7 nephrologists pmp (Kletke, 1997; Matri et al., 2008). Orthodox care is funded primarily by private facilities in most African countries, and access to medication is limited by availability of funds, except for Nigeria and South Africa, where public institutions and hospitals are funded by the government to provide these medications to indigent patients (Saraladevi, 2013).

Globally, as at 2010 over 2 million individuals has been treated by RRT at a cost of \$1 trillion. More than 100 countries worldwide do not have any provision for RRT and consequently, more than a million individuals can be assumed to die every year from ESRD. Availability of kidneys for transplantation is another important challenge consistent with RRT. Although, expenditure on RRT is costing about \$1 trillion but the substantial percentage of patients in need of it, still remains untreated and consequently has out-numbered those receiving the treatment. In the early 90s, it was estimated at about 3.78 million and is expected to be doubled by 2020 (WHO, 2005). In Nigeria, the burden of the disease is also alarming with an estimated 15,000 new patients diagnosed annually. With this statistics, less than 1,000 are on dialysis out of 50,000 patients who should ideally be receiving the treatment and this was largely attributed to the capital intensiveness of RRT. For instance in Nigeria, it cost about \$160 (=N=30,000) for a session of kidney dialysis and three sessions are required per week (i.e. =N=90,000 weekly). For a kidney transplant, the cost requirement is put at an average of \$22,500 (R265, 000) and \$27,500 (=N=5.5 million) in South Africa and Nigeria, respectively (IDF, 2014; NKFS, 2015). The alarming increase in the prevalence of CKD that progresses to ESRD requiring RRT demands huge fund allocation and individuals with kidney diseases are at an increasing risk of other systemic diseases which frequently proves to be fatal (Guildford, 1991). More worrisome is the unimaginable number of mortality recorded daily from kidney failure as terminal end if dialysis or transplant is not performed within two weeks of diagnosis (WHO, 2005). As at 2004, over 1.7 million patients worldwide were receiving treatment for ESRD, of which 77% were on dialysis and 23% had functioning renal transplant, and this number is increasing at the rate of 7% every year (WHO, 2005). With this estimated projection, there is an urgent need for increased awareness among the populace, aimed at preventive measures. Societal practices that seem superficially harmless but nephrotoxic should also be discouraged to stem incidences of the disease and alleviate the associated burdens. Furthermore, since most patients on chronic dialysis cannot be sustained beyond the first 2-3 months due to financial constraints, it can thus be said that it is almost next to impossible to provide replacement therapy to all patients requiring it (Saraladevi, 2013). Therefore, the next option for the physicians is to consider suitable alternatives that will either protect kidney functions or slow the progression of the disease and delay the need of RRT. This will ultimately scale down the prevalence and consequently the financial burden of the disease to a significant level. This latter option could be viewed as paving a way for an envisaged concept that is notably termed as nephroprotection (Ahmad et al., 2014).

Nephrotoxins and Nephroprotective Active Metabolites

The pathological mechanisms of renal disease that compromises its functional capability and the structural integrity has been established to arise mainly through either altered intraglomerular hemodynamics, tubular cell toxicity, inflammation, crystal nephropathy, rhabdomyolysis, or thrombotic microangiopathy (Schnellmann and Kelly, 1999; Schectz et al., 2005; Cynthia, 2008). Table 1 shows some of the known nephrotoxic agents and the pathological mechanism involved in their renal pathogenesis.

Table 1: Common nephrotoxicants and the mechanism (s) of action

Class	Agent	Mechanism of renal injury	Reference(s)
Analgesics (NSAIDs)	Acetaminophen, Aspirin	a, b, d and e	(Perneger et al., 1994; Fored et al., 2001; Rossert, 2001)
Antibiotics: *Aminoglycosides Amphotericin B **β-lactam	*Gentamicin **Cephalosporins, penicillins	*f f **a and e	(Prendergast and George, 1993; Rossert, 2001; Markowitz et al., 2003; Graham et al., 2004)
Antihistamines	Doxylamine, Diphenhydramine	F	(Coco and Klasner, 2004)
Antiretrovirals	Adefovir, cidofovir Indinavir	g a, c	(Rossert, 2001)
Cardiovasculars	Statins, Clopidogrel ACE and ARBs	f, h, d	(Pisoni et al., 2001; Palmaer, 2002; Graham et al., 2004; Manor et al., 2004; Perazella, 2005)
Chemotherapeutics	Cisplatin, Mitomycin-C	b and g, g and h	(Appel, 2002)
CNS stimulants	Caffeine, cocaine etc	F	(Prendergast and George, 1993; Markowitz et al., 2003)
Diuretics	Thiazides Triamterene	a c	(Rossert, 2001; Markowitz and Perazella, 2005)
Heavy metals	Cd, Pb, Hg, U	a, d, e and f	(Perazella, 1999; Tarloff, 2001)
Immunosuppressives	Sirolimus, calcineurin inhibitors	a and g	(Olyaei et al., 1999; Mark, 2009)

NSAIDs= Non-steroidal anti-inflammatory drugs, CNS= Central nervous system, a= acute interstitial nephritis, b= chronic interstitial nephritis, c= crystal nephropathy, d= disturbed intraglomerular hemodynamics, e= glomerulonephritis, f= rhabdomyolysis, g= tubular cell toxicity, and h= thrombotic microangiopathy.

A good understanding of the pathogenic mechanism of action of these insulting agents is imperative to spotting and either managing or preventing renal toxicity and the associated disorders.

Following the experimental demonstration that angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and erythropoietin slow the progression of loss of kidney function in models of kidney diseases, a treatment strategy to preserve renal function instead of providing supportive and passive therapy to the patients was conceived (Remuzzi et al., 1993). The concept of nephroprotection thus emerged and strongly stimulated the clinicians to apply such concept in early detection and subsequent prevention of progression of the disease, mainly through lifestyle adjustment and the use of new pharmacological agents (Raja et al., 2014).

Normalization of kidney function following exposure to toxicological agent involves complex processes which enhance kidney's hemodynamics. A drug or agent that can assuage some or all the mechanisms highlighted in Table 1 may be an excellent nephroprotective agent and expectantly aid both restoration of kidney function and improvement in the structural impairment of the kidney, thus, slowing its progression into degenerating episodes (Remuzzi et al., 1993). Despite the fact that the mechanisms of action of some known orthodox drugs are yet to be substantiated, they still merit the criteria of nephroprotection owing to their overall efficacy on the improvement of renal function (Ahmad et al., 2014). However, the challenge even with those with well elucidated mechanisms (like ACE and ARBs) is the associated toxicities and side effects which have undermined their application to a great extent. A drug categorized to be effective as a nephroprotective agent without having liability to produce serious side effects will be the obvious palliative choice for the patients suffering from renal dysfunction. Accordingly, traditional systems of medicine had offered effective drugs against kidney pathological conditions and thus can be used to protect renal function and prevent/slow the progression of renal diseases to CKD or ESRD (Naveed et al., 2014). Medicinal plants are a source for a wide variety of natural antioxidants and are used to treat diseases throughout the world. Their applications are mainly due to being antimicrobial, anticancer, anti-diabetic, anti-lipidemic, immunomodulatory, hepatoprotective and even renoprotective in action. A number of drugs from herbal sources in Nigeria and South Africa have been shown to be nephroprotective and there is a keen global focus on the development of such. Attention is mostly on protection or prevention as well as accelerating the regeneration of tubular cells against injury to the kidney (Hamid and Mahmoud, 2013). Active principles of plant formulations have proven health benefits and have been elucidated to confer nephroprotection on the nephron of both humans and experimental animal models (Jaya, 2013). While steroid glycosides, terpenoids and flavonoids have been shown to preserve renal cellular macromolecules against oxidative onslaught of reactive metabolites and oxidative stress (Baek et al., 2006; Shelke et al., 2009; Eduardo et al., 2011), the tendency of polyphenols to protect the nephron against glomerulonephritis and altered intraglomerular hemodynamics in cisplatin-mediated nephrotoxic rats has been demonstrated (Subal et al., 2010). Table 2 presents some of these principles and their probable/specific mechanism of action.

Table 2: Bioactive principles implicated in nephroprotective functions

Active principle	Mechanism of action	Reference (s)
Alkaloids	Stems deleterious effect of N-acetyl- <i>p</i> -benzoquinoneimine on tubular macromolecules and improves antioxidant defense system in acetaminophen-treated rats	(Palani et al., 2009; Zhao, 2013)
Amino acids	Improves altered glomerulonephritis in cisplatin-induced nephrotoxicity	(Yogesh et al., 2011)
Catechols	Rescues rhabdomyolysis and acute interstitial nephritis in doxorubicin-mediated acute nephrotoxicity	(Ajith et al., 2008)
Carotenoids	Boosts antioxidant status and attenuates cisplatin-induced renal oxidative stress	(Ranjan et al., 2009; Naghizadeh et al., 2010)
Diterpenoids	Repairs and assuages architectural onslaught of reactive metabolites on kidney functions	(Rao, 2006)
Flavonol glycosides	Improves acute nephritis injury	(Shirwaikar et al., 2004)
Flavonoids	Preserves kidney's cellular macromolecules against oxidative insults.	(Shelke et al., 2009; Kannappan et al., 2010)
Glycosides	Restores renal function capacity and speeds up recovery from glomerulonephritis, tubular cell toxicity and altered intraglomerular hemodynamics	(Yadav and Khandelwal, 2009)
Polyphenols	Preserves the renal tubule against glomerulonephritis and altered intraglomerular hemodynamics in cisplatin-mediated nephrotoxic rats	(Subal et al., 2010)
Saponins	Ameliorates renal carcinogenesis and improves kidney function in N-nitrosodiethylamine-treated animals	(Pracheta et al., 2011)
Steroid glycosides	Reduces tubular cell toxicity and crystal nephropathy in cisplatin-induced nephrotoxicity	(Baek et al., 2006)
Sterols	Enhances speedy restoration of renal cellular functions via antioxidative action	(Paterson, 2008; Subal et al., 2010)
Tannins	Prevents and palliates gentamicin-induced nephrotoxic insults on kidney	(Kakasaheb and Rajkumar, 2011)
Terpenoids	Halts ravaging effect of generated oxidants, induced antioxidant enzymes and modulates mitochondrial pathway in chromium-mediated nephrotoxicity	(Eduardo et al., 2011)
Vitamins B and C	Repairs tubular cell toxicity, ameliorates fluoride nephrotoxicity, aids renal excretion of other toxins and improves antioxidant defense system	(Jiménez-Escrig et al., 2001)

With the elucidation and isolation of these active metabolites from medicinal plants, attention is now given to the traditional system of medicine in providing alternative therapies to augment the increasingly expensive orthodox medical services

(Fasola and Egunyomi, 2005). This was well buttressed by the submission of WHO that about 80% of the population in developing nations seek exclusive treatment in folkloric medicine (WHO, 2000). Keeping this in view, researchers across the globe are now focusing on developing herbal renoprotective drugs of plant origin with antioxidant properties for the prevention and cure of kidney disorders (Raja et al., 2014). The exploitation of the antioxidative potentials of these plants is inseparable from the fact that oxidative stress is mostly implicated in episodes of renal tubular necrosis (Hamid and Mahmoud, 2013). Hence, it can be postulated that medicinal plants with excellent antioxidant activities due to the presence of bioactive principles may extenuate the risk of many chronic and degenerative diseases including nephropathy.

Nephroprotective Plants from Nigeria and South Africa

Globally, folkloric medicine has been and is still finding relevance in providing preventive and palliative measures against nephrotoxicity. Phytotherapists with keen interest in renal disorders and those informed of the unawareness and ignorance of majority of the victims are striving not only to educate the world on this 'silent killer' but also proffer extenuating panacea to its daunting effects. Notably, reviews on nephroprotective medicinal plants revealed appreciable success mainly from India and some other Asian countries and have implicated more than 300 plants with remarkable effects against several renal disorders. While Ajith et al. (2008) and Palani et al. (2009) have demonstrated respective therapeutic efficacy of *Zingiber officinale* and *Pimpinella tirupatiensis* on drug-induced nephrotoxicity and oxidative stress, others have reported pharmacological significance of medicinal plants in annihilating oxidative insults on renal tubular cells and preserving overall kidney functions (Gaikwad et al., 2012; Mohana et al., 2012; Talele et al., 2012; Jaya, 2013; Raja et al., 2014).

In Nigeria and South Africa, traditional systems of medicine are also not wanting in offering formulations/drugs for different forms of kidney diseases (Musabayane et al., 2007; Al-Qattan et al., 2008; Usman et al., 2009). Some of the identified renoprotective herbs in these countries are being embraced by physicians, and have been demonstrated to exhibit remarkable diuretic and antioxidative effect against known toxicants (Simpson, 1998; Kadiri et al., 2015). Plants such as curcumin, pawpaw, and bitter leaf are commonly and routinely cultivated in these countries and have been reported to have excellent nephroprotective capability on the kidneys. Assertions from some of these studies are highlighted as follows:

***Carica Papaya* Linn (Caricaceae)**

Carica papaya is a dicotyledonous, polygamous, large, tree-like plant, with a single stem of average height 5-10 m. The leaves are large, 50-70 cm in diameter, deep palmately lobed, spirally arranged and confined to the top of the trunk. The flowers appear on the axils of the leaves, maturing into large fruit. A typical fruit of *C. papaya* is ripe when it feels soft and its skin has attained amber to orange appearance. Globally, the fruit is consumed either in its fresh form or the form of juices, jams, and crystallized dry fruit (Nakasone and Paull, 1998). The nephroprotective effect of its aqueous seed extract on CCl₄-perturbed renal damage has been reported (Olagunju et al., 2009). The authors attributed the effect elicited by the plant to its phytoconstituents and opined that it could have been via antioxidative and/or free radical scavenging mechanism(s).

Zea Mays* L. (Poaceae), *Stigma Maydis

Zea mays, *Stigma maydis* (Corn silk) is one of the several plant parts commonly used in the management of kidney stones, bedwetting and urinary infections. GCMS analysis of its aqueous extract revealed the presence of maizenic acid, β -carotene, ascorbic acid, gluten, o-diethyl phthalate, 2-methyl-naphthalene, thymol, 3'-o-methyl-maysin, cyanidin, cinnamic acid, hordenine, luteolinidin, pelargonidin and betaine as major adaptogenic phytonutrients (Sabiu et al., 2016a). Although, corn is a common staple food in Nigeria and South Africa, the pharmacological significance of its silk is still hugely underutilized. However, its membrane stabilization and detoxification potential of acetaminophen-mediated oxidative onslaughts in the kidneys of Wistar rats has just been recently reported (Sabiu et al., 2016b).

***Agathosma Betulina* (Bergius) Pillans**

Agathosma betulina is a flowering plant in the family Rutaceae. It is native to the lower elevation mountains of western South Africa, where it occurs near streams in fynbos habitats. It is an evergreen shrub growing to 2 m tall. While its flowers are white or pale pink with five petals, the fruit is five-parted capsule which split open to release its seeds. The leaves are opposite, rounded, about 20 mm long and broad, and are strongly aromatic. The essential oil from its leaves is golden in colour, with a strong-sweetish, peppermint-like odour and rich in isomenthone and diosphenol as major adaptogenic constituents. Leaf extracts of *A. betulina* taste like blackcurrant and is normally used as flavouring agent for teas, and has great reputation for treating kidney and urinary tract diseases (Moolla and Viljoen, 2008).

***Ficus Thoningii* (Blume) (Moraceae)**

F. thoningii is a multistemmed, evergreen tree with a dense, rounded to spreading crown. It is native to Africa with distribution across the upland forests of tropical and subtropical regions, at altitudes of between 1,000-2,500 m (ATD, 2011). While the leaves are rounded or tapering, 4.5-12 cm long, hairless or finely hairy with a prominent midrib, the fruits are round, 10-20 mm in diameter, usually hairy and turn yellowish and rarely pink when ripe (Schmidt et al., 2002). Study of its stem-bark ethanolic extract on blood glucose, cardiovascular and kidney functions of rats, and on kidney cell lines of the proximal (LLC-PK1) and distal tubules (MDBK) revealed remarkable renoprotective activities and presented the plant as a source of probable lead compound in the management of kidney diseases (Musabayane et al., 2007).

C. schweinfurthii is a tall forest tree growing wild in Africa with characteristic straight and cylindrical bole exceeding 50 m (Orwa et al., 2009). The Leaves are pinnate, clustered at the end of the branches, and may be 15-65 cm long, with 8-12 pairs of leaflets. It produces fruit that is similar in appearance to olives, green in color, and red-purple when fully matured. Okwuosa et al. (2009) have demonstrated the potency of its stem bark extracts against acetaminophen-induced renal injuries in rats. Improved renal function indices and preserved histoarchitectural features were their major assertions.

***Sclerocarya birrea* (A. Rich) Hochst. (Anacardiaceae)**

S. birrea is a highly valued cultural and ethnomedicinal plant in Africa. It is commonly found in semi-arid, deciduous and savannah regions of sub-Saharan Africa. In South Africa, *S. birrea* occurs in the lowlands of KwaZulu-Natal and bears edible fruit that has formed an integral component of the southern African diet. Literatures have indicated the presence of polyphenols, tannins, coumarins, flavonoids, triterpenoids and phytosterols as medicinally-important chemical constituents in its various extracts and standardized fractions. Treatments with stem-bark ethanolic extract of *S. birrea* resulted in decreased plasma urea and creatinine concentrations of streptozotocin-diabetic rats with concomitant increase in glomerular filtration rate (Gondwe et al., 2008).

***Pseudocedrela kotschy* (Schweinf.) Harms (Meliaceae)**

P. kotschy is a Savanna woodland plant, chiefly of the Guinea zone on moister heavy soils of valleys. It is commonly 20-30 m high with wide crown. While the crown is rounded with ascending branches, the bark is thick, silvery-grey and fairly regularly fissured into small square pieces. Antioxidative and nephroprotective activities of ethanolic roots extract of *P. kotschy* against oxidative stress and nephrotoxicity in rats have just been recently documented (Ojewale et al., 2014).

Vernonia Amygdalina*, *Citrullus Colocynthis*, *Psidium Guajava* And *Ficus Mucoso

Vernonia amygdalina (Asteraceae), commonly known as bitter leaf is a shrub that grows up to 3 m high in the African tropics. It has petiolate leaves of about 6 mm diameter and elliptic shape. The leaves are green with a characteristic odour and bitter taste. Saponins, alkaloids, terpenes, steroids, coumarins, flavonoids, phenolic acids, lignans, xanthenes, anthraquinone, edotides and sesquiterpenes are the pharmacologically-active constituents of *V. amygdalina*.

C. colocynthis L. (Cucurbitaceae) is a tropical plant, native to Asia and Africa. Its fruit contains bitter glycoside which has found therapeutic significance against an array of diseases. Biologically-active phytonutrients like alkaloids and flavonoids have also been identified and isolated from its various extracts.

P. guajava (Myrtaceae) is a semi deciduous tropical tree commonly called guava. Its antioxidative potentials which are closely associated with its numerous tannins, polyphenolic compounds, flavonoids, pentacyclic triterpenoids, guajaverin, quercetin, free sugars, vitamins B1, B2, B6 and C have been documented.

F. mucoso (Moraceae) is a tree that usually grows to a height of 30 m on mountains and stands isolated in farmlands. While it flowers in June, the fruits become matured in August. Phytochemical screening of its extracts revealed triterpenes, flavonoids, chromones and alkaloids as major bioactive constituents.

An investigation into the probable nephroprotective attributes of *V. amygdalina*, *C. colocynthis*, *P. guajava* and *F. mucoso* in streptozotocin-induced diabetic animals revealed auspicious submissions and lent support to the nephroprotection concept of medicinal plants. However, *P. guajava* elicited the best and most prominent effect in preventing glomeruli disruption and also preserved nephro-histoarchitectural morphology of the animals (Komolafe et al., 2013).

Though substantive focus is yet to be given to nephrophytotherapy in South Africa, efforts are ongoing in our laboratory in this regard. A comprehensive list of some selected plants being embraced as nephroprotective agents in Nigeria and those currently exploited in South Africa is presented in Table 3.

Table 3: Commonly used nephroprotective plants in Nigeria and South Africa

Plant name	Part used	Implicated active principle(s)	Country	Reference (s)
<i>Adansonia digitata</i>	Leaves, fruit pulp, bark	Alkaloids, tannins, saponins, sterols, flavonoids, vitamin C	Nigeria	(Olowokudejo et al., 2008; Adebisi et al., 2012; Kadiri et al., 2015)
<i>Aerva lanata</i>	Whole plant	Phenols, tannins, saponins, flavonoids, phytosterols	Nigeria	(Olowokudejo et al., 2008; Guarav et al., 2013)
<i>Agathosma betulina</i> Berg.	Leaves	Flavonoids	South Africa	(Posthumus et al., 1996; Simpson, 1998)
<i>Allium sativum</i> L.	Cloves	Phenols, flavonoids	Both	(Al-Qattan et al., 2008)
<i>Annanas comosus</i>	Whole plant	Alkaloids, flavonoids, phenols, tannins, phytosterols, glycosides, amino acids	Nigeria	(Kataki, 2010; Kadiri et al., 2015)
<i>Arachis hypogaea</i>	Nuts, leaves	Glycosides, phenols, saponins	Nigeria	(Borokini et al., 2013; Rajinikanth et al., 2013; Kadiri et al., 2015)
<i>Azadirachta indica</i>	Leaves	Alkaloids, flavonoids, phenols, tannins, saponins	Nigeria	(Harry-Asobara and Samson, 2014; Kadiri et al., 2015)
<i>Bixa orellana</i> L.	Seeds, leaves	Alkaloids, flavonoids, anthraquinones, tannins, sterols, saponins	Nigeria	(Tamil et al., 2011; Dike et al., 2012)
<i>Canarium Schweinfurthii</i>	Stem-bark, fruits, leaves	Tannins, sterols, cardiac glycosides	Nigeria	(Okwuosa et al., 2009; Ayoade et al., 2015)

<i>Canna indica</i> L.	Leaves, root	Alkaloids, flavonoids, terpenoids, cardiac glycosides, steroids, tannins, saponins, phlobatannins	Nigeria	(Dike et al., 2012; Ali, 2015)
<i>Carica papaya</i> L.	Leaves, seeds	Alkaloids, phenols, flavonoids, tannins, terpenoids, saponins	Nigeria	(Olagunju et al., 2009; Subal et al., 2010; Dike et al., 2012)
<i>Citrullus colocynthis</i>	Seed shaft	Alkaloids, flavonoids	Nigeria	(Dallak and Bin-Jaliah, 2010; Komolafe et al., 2013)
<i>Croton zambesicus</i> Muell Arg.	Root	Alkaloids, saponins, terpenes, tannins, phlobatannins, anthraquinones, cardiac glycosides	Nigeria	(Jude et al., 2011)
<i>Ekebergia capensis</i>	Leaves	Saponins, alkaloids, flavonoids, tannins	South Africa	(Fitzpatrick et al., 1995)
<i>Ficus exasperata</i> Vahl	Leaves	Saponins, steroids, glycosides, tannins	Nigeria	(Shagal et al., 2011; Dike et al., 2012)
<i>Ficus mucoso</i>	Leaves	Flavonoids, monoterpenoids	Nigeria	(Gojayeve et al., 2011; Komolafe et al., 2013)
<i>Ficus thonningii</i>	Leaves	Alkaloids, anthraquinones, flavonoids, saponins, tannins	Both	(Musabayane et al., 2007; Usman et al., 2009)
<i>Foeniculum vulgare</i> L.	Leaves	Phytoestrogens	South Africa	(Musabayane, 2012)
<i>Gongronema latifolium</i>	Leaves	Flavonoids, saponins, polyphenols	Nigeria	(Ugochukwu et al., 2003; Ezeonwu and Dahiru, 2013)
<i>Harpagophytum procumbens</i>	Tubers	Phenols, flavonoids	South Africa	(Joffe, 2005; Motlhanka, 2012)
<i>Harungana madagascariensis</i> L.	Root	Glycosides, flavonoids, alkaloids, saponins and tannins	Nigeria	(Okoli et al., 2002; Adeneye et al., 2008)
<i>Helichrysum ceres</i> S.	Leaves	Polyphenols, tannins, triterpenes, saponins	South Africa	(Musabayane et al., 2003)
<i>Ipomoea batatas</i>	Tubers	Triterpenes, steroids, alkaloids, anthraquinones, flavonoids, saponins, tannins, phenols	Nigeria	(Márcia et al., 2011; Borokini et al., 2013)
<i>Launaea taraxacifolia</i>	Leaves	Cardiac glycosides, terpenoids, tannins, saponins, flavonoids, steroids	Nigeria	(Adinortey et al., 2012; Borokini et al., 2013)
<i>Mallotus oppositifolius</i> Mull. Arg.	Leaves	Flavonols	Nigeria	(Iwu, 2000; Dike et al., 2012)
<i>Mangifera indica</i> L.	Leaves, bark	Saponin, steroids, tannin, flavonoid, cardiac glycosides, anthraquinone	Nigeria	(Aiyelagbe et al., 2009; Dike et al., 2012; Kadiri et al., 2015)
<i>Morinda lucida</i>	Leaves, bark	Alkaloids, tannins, saponins	Nigeria	(Chukwuemeka et al., 2013; Kadiri et al., 2015)
<i>Ocimum gratissimum</i>	Leaves	Polyphenols, flavonoids, fatty acids	Nigeria	(Ezeonwu and Dahiru, 2013; Venuprasad et al., 2014)
<i>Olea europaea</i> L.	Leaves	Triterpenes, flavonoids, glycosides	South Africa	(Benavente-Garcia et al., 2000; Bennani-Kabchi et al., 2000)
<i>Opuntia megacantha</i>	Leaves	Phenols, flavonoids	South Africa	(Bwititi et al., 2001)
<i>Parkia biglobosa</i>	Leaves	Tannins, steroids, cardiac glycosides, alkaloids	Nigeria	(Ajaiyeoba, 2002; Kadiri et al., 2015)
<i>Persea Americana</i> Mill.	Leaves	Tannins, saponins, flavonoids, alkaloids, glycosides	Both	(Owolabi et al., 2010; Yasir et al., 2010)
<i>Pseudocedrela kotschy</i>	Leaves, root	Alkaloids, flavonoids	Nigeria	(Ojewale et al., 2014)
<i>Psidium guajava</i>	Leaves	Glycosides, flavonoids, terpenoids	Nigeria	(Komolafe et al., 2013)
<i>Sclerocarya birrea</i>	Stem-bark	Alkaloids, flavonoids, triterpenoids, vitamin C	South Africa	(Gondwe et al., 2008)
<i>Sida acuta</i>	Leaves, root	Alkaloids, phytosterols, tannins, flavonoids, saponins	Nigeria	(Borokini et al., 2013)
<i>Sutherlandia frutescens</i>	Leaves	Amino butyric acid, flavonol, glycosides, triterpenoid, saponins	South Africa	(Herbert, 2006; van Wyk and Albrecht, 2008)
<i>Syzigium spp.</i>	Seeds	Flavonoids	South Africa	(Mapanga et al., 2009)
<i>Terminalia catapa</i>	Leaves, bark	Alkaloids, saponins, tannins, steroids	Nigeria	(Muhammad and Mudi, 2011; Kadiri et al., 2015)
<i>Uvaria afzelii</i>	Leaves, bark	Tannins, saponins, cardenolides, alkaloids	Nigeria	(Olowokudejo et al., 2008; Temitope et al., 2014)
<i>Vernonia amygdalina</i>	Leaves	Tannins, flavonoids	Nigeria	(Eleyinmi et al., 2008; Komolafe et al., 2013)
<i>Zea mays</i>	Silk	β -carotene, ascorbic acid, thymol, cinnamic acid, betaine	Both	(Sabiou et al., 2016a, b)

Conclusion

Generally, efforts at increasing awareness about kidney disease and its complications in communities and among health professionals should be intensified. This is imperative as many are unaware of the severity of the disorder, which probably serves as a barrier to appropriate preventive measures. Although, thorough clinical trials and expert opinions may be necessary on medicinal plants to gain medical significance as preferred class of drugs, their overall auspicious and remarkable nephroprotective attributes have presented them as excellent candidatures to develop new lead drugs in the treatment and management of renal disorders in Nigeria and South Africa.

Conflicts of Interest

The authors have declared that no conflict of interest exists.

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