JOURNAL OF NATURAL REMEDIES
DOI: 10.18311/jnr/2023/33881
SHORT REVIEW

Siddha Therapeutic Approach to Diabetic Nephropathy – A Review

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Abstract

Diabetic Nephropathy (DN) is a severe kidney illness that presents with proteinuria, enlarged glomeruli, reduction in the process of glomerular filtration, and fibrosis of the kidneys. Approximately one-third of all instances of diabetes globally are brought to diabetic nephropathy, a common cause of end-stage kidney disease. In *Siddha*'s literature, the complications of Diabetes mellitus were expressed as ten *Avathaigal* in the *Neerizhivu noi* chapter. The feature of *Avathaigal* 1 to 7 depicts some of the clinical outcomes of Diabetic Nephropathy. The manifestation of clinical features in final stage Diabetic Nephropathy includes oliguria, fatigue, anorexia, nausea, vomiting, itching and dryness of skin, drowsiness, numbness and swelling in the limbs, muscle twitching or cramps, bone pain, breathlessness, increased thirst, sleep disturbance, and sexual problems. Oxidative stress is the standard mechanism involved in developing diabetic kidney disease. Most of the *Siddha* medicines used for managing diabetic Nephropathy are herbal formulations, and they protect against damage to the renal tubules due to their significant antioxidant property. This review summarizes the pathophysiology of Diabetic Nephropathy and the evidence for using *Siddha* herbal formulations to treat diabetic Nephropathy. For treating early-stage diabetic Nephropathy, *Siddha* practices primarily emphasize using herbal formulations; however, yoga therapy, diet, and other exercises are also included in *Siddha* treatment modalities.

Keywords: Blood Urea, Diabetic Nephropathy, Herbal Medicines, Serum Creatinine, *Siddha*

1. Introduction

Diabetes complications, including Diabetic Kidney Disease (DKD), are common[1]. In the entire world, it is the main contributor to chronic and end-stage renal disease. Glomerular hyperfiltration, progressive albuminuria or elevated albumin to creatinine ratio, and falling GFR are all parts of the typical course of diabetic kidney disease. Then progresses to the final stage of renal disease[2]. Genetic predisposition, poor metabolism of glucose, and altered glomerular hemodynamics all contribute to the development of kidney disease, with oxidative stress being a prevalent mechanism. It affects both Type 1 and Type 2 diabetics[3].

According to the *Siddha* medicine, there are 4448 disease classifications, and Meghaneer is one among them[4]. Based on the derangement of 3 vital senses of humor, there are 20 forms of *meghaneer* with four being under *vatham*, six under *pitham*, and ten under *kapham*[5]. *Pithaneer*, which includes *Madhumegam* is distinguished by passing sweet urine[6]. According to Yugi and Agasthiyar, the etiology of the illness is brought on by dietary changes, lifestyle choices, and actions. With a strict diet and yoga therapy, powerful *Siddha* medications can reduce the disease's severity. According to the Yugi Vaidya Chinthamani book, Type 2 Diabetes mellitus can be linked to 10 of the indications and symptoms of *Madhumegam avathaigal*, including Polyuria (excessive urine), Polydypsia (excessive thirst), and Polyphagia (excessive eating). Most of the morbidity and death linked with diabetes mellitus reported in contemporary science are caused by long-term micro and macrovascular complications.

Article Received on: 27.05.2023 Revised on: 20.09.2023 Accepted on: 26.09.2023

In Yugi Vaidya Chinthamani, under *Avathaigal*, they can also be related to and appreciated[7].

Diabetic Nephropathy (DN) is classified into five stages: Stage 1, high renal perfusion or hypertrophy of the kidney; Stage 2, the average rate of urinary elimination of albumin; Stage 3, also known as early DN, microalbumin present in the urine; Stage 4, DN, which stands clinical or dominant, plenty of albumin in the urine; and stage 5, End-Stage Kidney Disease (ESRD). Early stage DN, Stage 3 nephropathy, treatment steps must be taken to prevent progression to the ESRD phase[8]. Diabetic Nephropathy is irreversible when it progresses to the fourth stage or clinical albuminuria and requires renal replacement therapy. Thus, the most important safeguard against kidney failure is early therapy before or during Stage 3 DN[9]. The system involving renin, angiotensin, and aldosterone has received some attention as a significant target for successful therapy. However, medical guidelines for preventing early DN have historically concentrated on lowering blood pressure, controlling dyslipidemia, and lowering serum glucose levels. Even if these treatment methods slow down DN's development, they cannot reverse or stop it[10].

In the *Siddha* system, many plant-based medications are used to treat diabetic nephropathy. Glycosides, terpenoids, alkaloid compounds, and flavonoids in plants have the potential to treat diabetic nephropathy[11,12]. This review article aims to consolidate information on *Siddha's* therapeutic approach and prevention of Diabetic Nephropathy by using various *Siddha* herbal formulations. In addition, this article revealed the clinical and pharmacological data favouring using particular herbal formulations to treat diabetic nephropathy.

2. Aims and Objectives

This study sought to discover and assemble promising *Siddha* medications that have demonstrated efficacy in clinical trials and single and compound formulations/ regimes that help early-stage diabetic nephropathy.

3. Materials and Methods

The accessible *Siddha* literature in the *Siddha* Regional Research Institute library in Thiruvananthapuram served as the basis for the collection of literature. The Tamil Nadu Dr. M.G.R. Medical University's online library of grey literature and electronic databases like PubMed and Medline were also used to collect data. *Avathaigal* in *Neerizhivu*, *Siruneeraga noi*, diabetic nephropathy, herbal remedies, blood urea, and serum creatinine were used as search terms. All of the information was gathered, assembled, and examined. Additionally, the effectiveness of clinical studies on *Siddha* medicines for treating early-stage diabetic nephropathy has been compiled and reviewed.

4. Pathophysiology of Diabetic Nephropathy

Diabetic nephropathy's pathogenesis involves various interactions between metabolic and hemodynamic variables (Figure 1). Metabolic factors such as advanced end products of glycation and their binding sites affect glucose-dependent pathways. Numerous vasoactive hormones, such as renin and angiotensin system components, are among the hemodynamic variables[13]. These molecular and signalling mechanisms, including Protein kinase C and nuclear factor kappa light chain stimulator of activated B lymphocytes with concurrent reactive oxygen species production, are anticipated to interact with these metabolic and hemodynamic parameters. The podocytes and tubulointerstitial, in particular, are presumably pathologically harmed by these contributory components in the glomerulus. Since selective blockers of the different pathways are accessible, diabetic nephropathy prevention and treatment may benefit from these new pharmaceutical approaches. To stop the evolution of diabetic nephropathy, maintaining good blood pressure and glucose control remains the cornerstone of treatment[14]. In people with Type 1 and Type 2 diabetes who are hypertensive and normotensive, drugs that interfere with the renin and angiotensin system have proved helpful as renoprotective drugs.

5. Assessment of *Madhumega Avathaigal* in Comparison with Complications of Diabetes Mellitus

According to *Siddha* philosophy, *Neerizhivu noi* is caused by the derangement of *Iyya* humor, which first

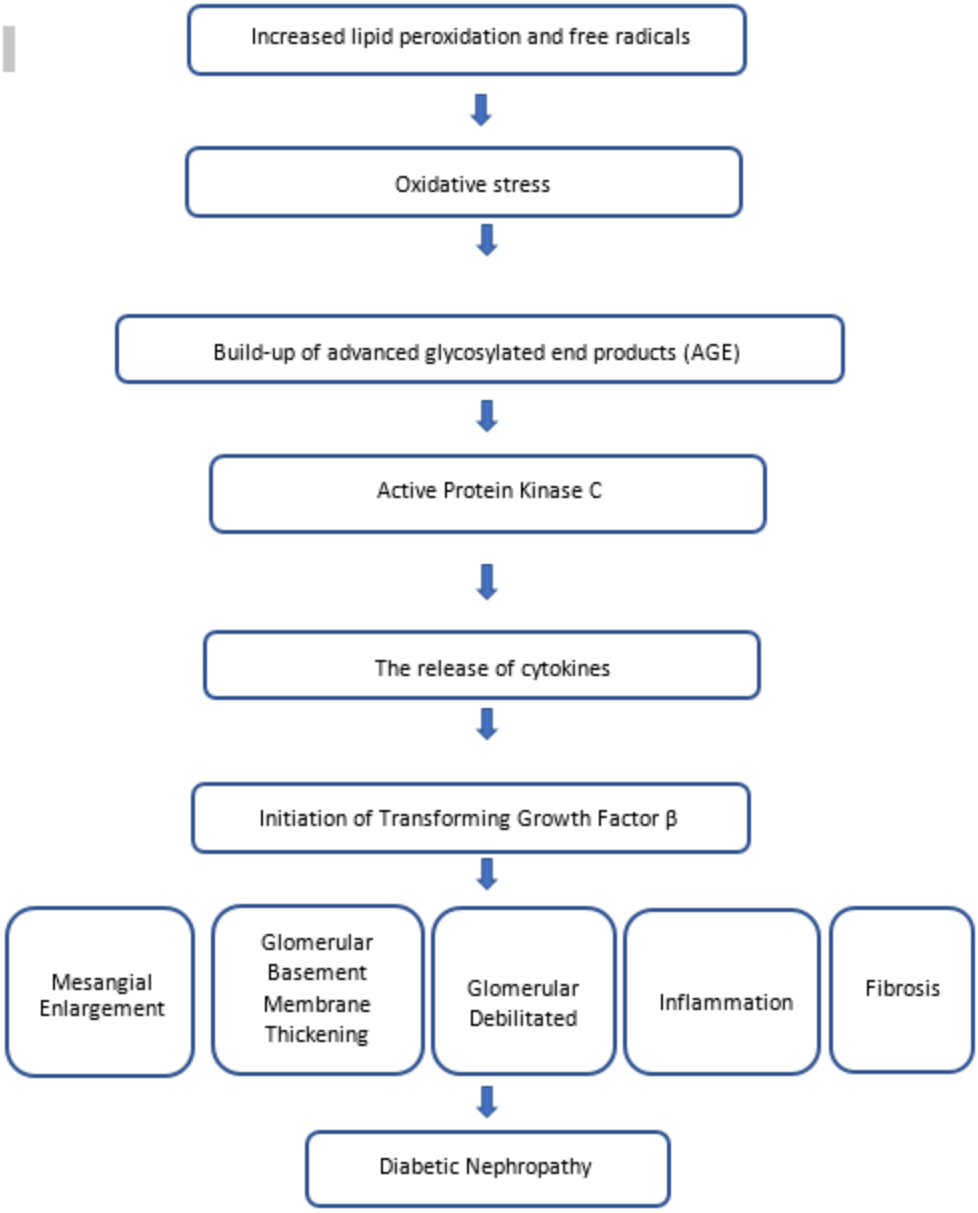

Figure 1. Pathogenesis of diabetic nephropathy.

affects vital forces in the body like the *Keezhnokku kal* (excretory system) and *Paravu kal* (circulatory system) before moving on to the body's constituents, known as the Seven *Udal thadhukkal* (*Saaram* (nourishing liquid), *Cheneer* (blood), *Oon* (muscles), *Kozhuppu* (fat), *Enbu* (bone), *Moolai* (marrow), *Sukilam/Sronitham* (semen/ova) resulting in functional disability and emaciation[5,12].

In describing the effects of diabetes mellitus, *Avathaigal* ten in *Neerizhivu noi* highlights some of the clinical implications of chronic renal disease. Anorexia, oliguria, exhaustion, nausea, vomiting, itchiness and dry skin, bone pain, increased thirst, drowsiness, limb numbness and swelling, muscle spasms or cramps, disturbed sleep, and problems with sex are some of the clinical features that manifest in the final stage of diabetic nephropathy. (Table 1). Additionally, *"Pala nirankalil neer kalithal"* is one of the premonitory symptoms of *Neerizhivu* described in *Siddha*'[5], which depicts the meaning that the physical appearance of abnormality in urine can be correlated to the changes of urine seen in diabetic nephropathy patients.

Table 1. Comparison of *Avathaigal* in *Neerizhivu*[15] with diabetic complications

Sl. No.	*Avathaigal* in *Siddha*	Meaning in English	Complications of Diabetes
1	*Noy tūkkuvatārkku muṟkūrika uṭal paruttu koṇṭē varum. Nīr puḻai akaṉṟu varum.*	Obesity and dilation of the urethral canal	Obesity, phimosis, paraphimosis, stricture urethra
2	*Ciṟunīr peruki keṭṭu iḻiyum veṇīr(cukkilam) keṭṭu uṭaliṉ oli kuṉṟi kāṇum.*	The body dries up and loses its lustre due to the excessive secretion and flow of urine combined with vital fluid (semen).	Polyurea, increased urethral discharge prostatitis, balanitis, balanoposthitis, urethritis. Cutaneous manifestations of Diabetes mellitus, Prenuptial fissures, acanthosis nigricans, acrochordons, diabetic dermopathy, eruptive xanthoma, rubeosis facies, scleroderma diabetic rum, bullous, diabetic rum,
3	*Nāvarāṭciyuṭaṉ vayiṟṟil kāṟṟu kūṭi perukum.*	Tongue dryness. Due to the development and accumulation of too much gas, patients can suffer from abdominal distension.	Polydipsia, diabetic gastroparesis, gastroesophageal reflux disorders, oesophageal dysmotility enteropathy, glycogenic hepatopathy, hepatogenous diabetes.
4	*Nīrvēṭkai mikuntu muppiṇi toṭarum.*	Delirium (a toxic state) develops after dehydration due to severe tissue fluid loss.	Dehydration (mild/mod/severe), excessive diarrhoea, recurrent vomiting.
5	*Ciṟunīr peruki yiḻintu vintu naṭṭamuṇṭākum.*	Unrest is brought on by the loss of essential fluid in the urine.	Diabetic cytopathy, cystitis, interstitial cystitis, polyurea, day/nocturnal, erectile dysfunction, diabetic bladder, frequency of urination, need to urinate.
6	*Paṭukkaiyil kiṭakka voṭṭātu. Mōrccai uṇṭākum.*	Breathlessness and restlessness	Restless legs syndrome, sleep disturbance, uremia, encephalopathy, breathlessness (rest/ exertion), restlessness
7	*Vāy kumati cūvaiyāṟṟu perumūcci uṇṭu uṭal cūrum.*	Nausea, tastelessness, laboured breathing, exhaustion.	An impaired taste sensation, ageusia, diabetic peripheral neuropathy, diabetic ketoacidosis pneumomediastinum, fatigue, and lactic acidosis.
8	*Uṭalil kaḻalai kaṭṭikaḷ uṇṭākum.*	Carbuncle and multiple abscess formation.	Diabetic carbuncle, bladder, breast, colon, endometrial, liver, pancreatic, and other cancers, multiple abscesses
9	*Oḻukkam tavaṟal, peru kaḻiccal, puḻu cēral ivai uṇṭākum.*	Confusion altered mental status and generalized emaciation; in Type 2 diabetic patients, the frequency of *Ascaris lumbricoides* and *Giardia lamblia* was greater.	Living conditions for diabetics - diabetic diarrhoea, diabetic foot, diabetic ulcer, worm infestations, infective complication, bacterial, viral, and fungal infections.
10	*Ilaippu nōy cayam uṇṭāy noyyiṇaṇai koḷḷumēntirariyum.*	Emaciation (*shayam*) with copious expectoration that is intractable and difficult can result in mortality.	Pulmonary tuberculosis is extrapulmonary and finally death.

6. Current Treatment for Diabetic Nephropathy and Why There is a Need for Alternative Therapy

Modern medicine has licensed ten kinds of glucose-lowering medications for treating diabetes. Patients who fail to obtain optimal glycemic control through diet and exercise should consider oral therapy[16]. Oral hypoglycemic medications may have a positive initial reaction. After that, however, many individuals may see a decline in their efficacy. The drug category includes meglitinides, sulfonylureas, metformin (a biguanide), bile acid sequestrants, Thiazolidinediones class of Drugs (TZDs), agonists of dopamine, alpha-glucosidase inhibitors, Dipeptidyl Peptidase IV (DPP-4) inhibiting agents, Sodium-Glucose Transporter Protein 2 (SGLT2) inhibitors and oral Glucagon-Like Peptide one (GLP-1) receptor agonists. Aside from

that, injections can provide GLP-1 receptor, amylin, GIP receptor, dual, and GLP-1 receptor agonists. These medications do have several adverse effects, however. Sulfonylurea, for instance, induces weight gain as a result of hyperinsulinemia. Alpha-glucosidase inhibitors may cause diarrhoea, while thiazolidinediones may raise LDL cholesterol levels. Biguanide produces weakness, weariness, and lactic acidosis[17].

When glycemic control is inadequate, even at the highest dosage of an oral drug, insulin is usually administered to the patient in addition to the oral medication. However, insulin frequently has adverse side effects like weight gain and hypoglycemia. In addition, intense insulin therapy may also lead to an uptick in atherogenesis.

These therapies have several problems, including the development of resistance, unfavourable effects, and a lack of responsiveness in a significant patient population segment. Additionally, none of the glucose-lowering medications can effectively manage the hyperlipidemia that the condition commonly causes. As a result, alternative therapies have been shoved to control diabetes more effectively and safely owing to the limitations of currently available oral antidiabetic drugs in terms of efficacy and safety and the rise of the illness as a global epidemic.

6.1 Role of *Siddha* in Diabetic Nephropathy Management

When used in clinical settings, the currently available oral anti-hyperglycemic medications showed recognizable adverse effects[17]. The medical community still faces difficulties in treating Diabetes mellitus with drugs with no side effects, leading to a rise in the demand for natural medicines with anti-hyperglycemic activity with fewer adverse effects. As a result, the *Siddha* medicine employs numerous polyherbal combinations to treat Madhumegam and its *Avathaigal* (Complications)[18]. The therapeutic aspect of the *Siddha* system is based on the subjects' body constitution and the disease's pathogenesis[24]. The treatment is usually initiated with the diagnosis of an imbalance in humor and its maintenance with cleansing therapies and lifestyle approaches. Then the drugs to balance the deranged humor, ameliorate the physical condition and quality of life of subjects, and be used with a dietary restriction schedule[19]. An individual's *naadi* (pulse) and *thegi* (Body constitution) are considered when prescribing a course of treatment based on the *Siddha* system of Medicine. The eight folds of diagnosis (*Envagai thervu*) are *naa* (tongue examination), *niram* (Complexion), *mozhi* (voice), *vizhi* (Eyes), *naadi* (Pulse), *sparisam* (Touch), *malam* (Stools), and *moothiram* (Urine) which are used to diagnose the ailment[20]. The *Siddha* system places a strong emphasis on a person's food (*pathyam*) and lifestyle (*Naal ozhukkam* and *Kaala -Ozhukkam*)[21] because these factors affect how effectively medications work. The disturbance of *Iyya* humor, one of the three types of body composition, is thought to be the root of *Neerizhivu noi* (Diabetes), first impacting natural processes like the excretory and circulatory systems before influencing the body's elements[5]. Seven *udal thadhukkal* (*Saaram* or nourishing juice, *Cheneer*, blood, *Oon*, muscles, *Kozhuppu*, fat, *Enbu*, bone, *Moolai*, Marrow, *Sukilam/Suronitham*, Semen/ova) resulting in functional disability and emaciation[20]. The *Siddha* system of medicine incorporates dietary, exercise, and lifestyle modifications into its treatment protocols because they are all necessary to successfully control diabetic nephropathy.

7. Evidence to Authenticate the Role of *Siddha* Herbal Formulations in Diabetic Nephropathy

7.1 *Sirupeelai Kudineer*

Thrithodam (TO), *Neeradaippu/Moothira Kiricharam* (XB) (urinary diseases), and *Pandu* (QA) (anaemia) are the indications for *Sirupeelai* (*Aerva lanata*)[5,22]. The majority of all are discovered as late-stage consequences of diabetes mellitus. The *Siddha* medication *Sirupeelai* (*Aerva lanata*) (Figure 2) has a hot potency (*Veppa veeriyam*), a bitter (*kaippu*) flavour, and a diuretic and lithotriptic effect[22]. The increased *Iyya* humor can be balanced by *kaippu* (bitter) flavour components, while the *Vali* humor can be aggravated. *Sirupeelai* can help the body eliminate unbalanced metabolic wastes and other impurities by balancing *Iyam* and reawakening the *Keenokkukal* (The vital force responsible for downward movements). The herb Sirupeelai's primary effect is a diuretic, which is crucial for flushing out water and stagnant waste products from circulation and improving renal function. *Aerva lanata*, on the other hand, is a rich

Figure 2. *Sirupeelai (Aerva lanata)* plant.

source of flavonoids, including alkaloids, kaempferol, isorhamnetin, tannic acid, and quercetin, among others, according to the results of its phytochemistry[23]. According to earlier research, the flavonoids and tannins in herbs are responsible for energetic antioxidant activity and may help with renal tubule regeneration. *Aerva lanata* has been found to have pharmacological qualities that include nephroprotective, hypoglycaemic, hepatoprotective, diuretic, antimicrobial, antioxidant, anti-inflammatory, antidiabetic, antiparasitic, anti-urolithiasis, and hypolipidemic effects[23]. Studies on *Aerva lanata*'s nephroprotective properties proved that high blood urea and serum creatinine levels fell dose-relatedly, and the histological abnormalities were restored[24]. The herb's antioxidant activity also points to a rejuvenating effect on the kidneys, which results in the regeneration of renal tubules and nephrons[25]. This medication may also help to promote the preservation of *thiridhodam*'s (the three senses of humor) equilibrium and stop additional cellular damage. The case study report on using *Sirupeelai kudineer* in treating early-stage diabetic nephropathy revealed a considerable improvement in the patient's symptoms and decreased blood urea and serum creatinine levels[26].

7.2 *Surai Karuppu*

Surai (Lagenaria siceraria) (Figure 3) has diuretic action and it is indicated for *Neerkattu* (XC) and *Veekkam* (TL)[22]. *Surai Karuppu*, *surai kai* fruit is cut into pieces, charred into ashes, and given to treat kidney damage caused by impurified mercurial medicines[27]. It also reduces the elevated creatinine level in serum. *Surai Karuppu* treats *pitha-kapha* diseases since it is used in the *Karuppu* form (activated charcoal) and acts as a chelating agent[28]. According to some researchers, oral activated charcoal can be used safely and successfully in clinical settings to reduce serum levels of phosphorus, urea, and creatinine. Studies have shown that *Lagenaria siceraria* possesses antioxidant and diuretic activities, which help to prevent kidney damage and facilitate the removal of impurities through urine. It can be used in the treatment of diabetic nephropathy along with other antidiabetic medicines. When fine powdered, the carbon particles are called activated charcoal because the fine powdering renders more surface area with more pores. Urea, creatinine, or any impurities in the blood are trapped in the pores of activated charcoal by adsorption and eliminated from the human body.

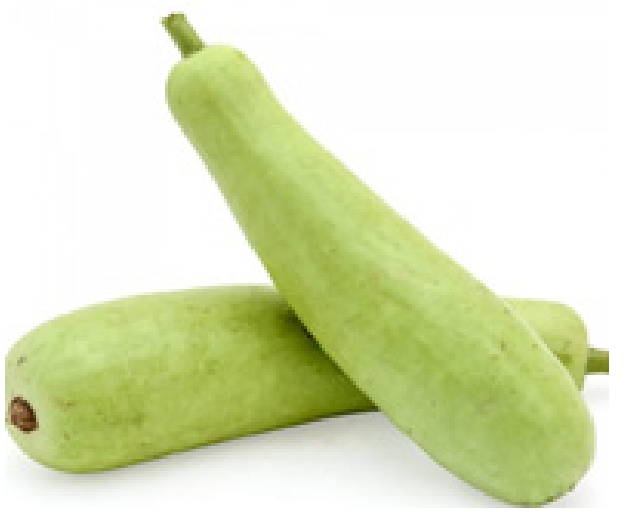

Figure 3. *Surai kai (Lagenaria siceraria)* fruit.

7.3 *Neermulli Kudineer*

The *Siddha* medicine *Neermulli Kudineer* (NMK) is a classical polyherbal one having eleven ingredients, namely *Nerunjil samoolam (Tribulus Terrestris), Nelli vattral (Phyllanthus emblica), Neermulli samoolam (Hygrophila auriculata), Parangipattai(Cassia Auriculate), Manathakkali vattral (Solanum nigrum), Sarakkondrai puli (Cassia fistula), Sombu (Foeniculum vulgare), Vellari vithai (Cucumis sativus), Surai kodi (Lagenaria siceraria), Kadukkai thol (Terminalia*

chebula), Thandrikkai thol (Terminalia bellerica) which has demonstrated remarkable success in the clinical conditions such as ascites, inflammation, edema, urinary retention or suppression of urine, and associated problems after anaemia, which are treated by the *Siddha* system of medicine[5,22,29]. These are mainly brought on by the buildup of interstitial fluids in our body brought on by impaired *vatham* and increased *pitham* and *Kabam* humor[5]. Anaemia, liver and spleen pathology, tumours, cardiovascular illnesses, and renal diseases are the leading causes of all these clinical problems. For initial care of all these disorders, diuretics must be used. As a result, ancient physicians utilized NMK as a strong diuretic in *Siddha* medicine. By boosting the urine flow and volume, NMK works as a diuretic to encourage the removal of extra water, salt, toxins, and stored metabolic products from the body. Additionally, it lessens fluid retention and edema, lowers high blood pressure, and soothes discomfort and burning sensations[30]. NK has antipyretic, anti-inflammatory, antiviral, antidiabetic, and immunomodulatory actions. It can effectively treat dengue fever and chikungunya. It also reduces joint pain, swelling, muscle pain, and headache. NK also treats infertility, irregular periods, and white discharge[30]. *Neermulli Kudineer*, known as *Nerunjil Kudineer*[31], treats various kidney-related conditions. Studies revealed that NK400mg/Kg had substantial nephroprotective effects. That might result from the kidneys' effective antioxidant potential, which lowers lipid peroxidation and oxidative stress[32].

7.4 *Karisalai Karpa Mathirai*

Ancient *Siddha* text, *Bogar 7000*, refers to *Karisalai Karpa Chooranam* (KKC), a strong poly herbal *Siddha* medicine made of seven different medicinal plants. The ingredients of Karisalai karpa mathirai are *Vellai Karisalai Samoolam (Eclipta alba), Manjal Karisalai Samoolam (Wedelia chinensis), Neeli Samoolam (Indigofera tinctoria), Kottakaranthai Samoolam (Sphaeranthus indicus), Vallarai Samoolam (Centella asiatica), Kuppaimeni (Acalypha indica), Siru Serupadai (Coldenia procumbens)* (Figures 4 and 5)[33]. In addition to being prescribed for *Paandu* (Anaemia), *Kaamalai* (Jaundice), *Kalleral Veekkam* (Hepatomegaly), *Sobai* (Generalised edema), and Skin illnesses to assist in strengthening the immune system, this medication is primarily used internally to treat hepatic-related ailments. In the *Siddha* system, it is a potent remedy for rejuvenation known as *Kaayakalpam*[34]. In the pathogenesis of diabetic nephropathy, which leads to end-stage renal disease, oxidative stress plays a significant role. According to studies, *Karisalai Karpa Choornam* has considerable antioxidant activity, which aids in repairing renal damage and regenerating renal tubules[34]. *Karisalai Karpam* tablet reduces serum glutamic oxaloacetate transaminase, alkaline phosphatase, glutamic pyruvic transaminase, and total bilirubin, direct bilirubin. The levels of antioxidant enzymes were also found to have significantly increased. At higher doses, *Karisalai Karpam* prevented glutathione depletion in liver tissue. Results confirmed that *Karisalai Karpam* contained oxidative damage to the tissues by increasing the antioxidant defence mechanism[35]. It gives good results in diabetic nephropathy conditions owing to its antioxidant properties.

7.5 *Seenthil Choornam*

The traditional *Siddha* scripture *Agasthiyar Paripooranam – 400*[36] mentions the medicine *Seenthil Chooranam* (SC) for the conditions of *Megam* (Diabetic mellitus), rheumatism, orchitis, bronchitis, asthma, Tuberculosis (TB), cough, and various skin diseases. *Seenthil (Tinospora cordifolia), Karisalai (Eclipta prostata),* and *Poonagam* (Earthworm) are the components of *Seenthil Choornam*. SC has potential antidiabetic,

Figure 4. *Vellai Karisalai Samoolam (Eclipta alba), Manjal Karisalai Samoolam (Wedelia chinensis), Siru Serupadai (Coldenia procumbens), Neeli Samoolam (Indigofera tinctoria).*

Figure 5. *Kuppaimeni (Acalypha indica), Kottakaranthai Samoolam (Sphaeranthus indicus), Vallarai Samoolam (Centella asiatica).*

hepatoprotective, and anti-inflammatory activities. SC with honey is also used to manage sinusitis and ulcers in the nasal passages. Furthermore, SC and sufficient sugar will reduce dandruff and alopecia. Finally, it effectively treats various fevers and splenomegaly. According to studies, the active substances isolated from the *Seenthil* plant exhibit a strong nephroprotective effect by modulating gene expression, lowering blood glucose levels, stabilizing renal indices, and reducing inflammatory cytokines in diabetic nephropathy rats[37].

7.6 *Nilavembu Kudineer*

An authentic herbal *Siddha* medicine called *Nilavembu kudineer* has nine herbs in equal amounts[31]. The ingredients of *Nilavembu kudineer* are *Nilavembu (Andrographis paniculata), VilamichaiVer (Plectranthus vettiveroides), Vetiver (Vetiveria zizanioides), Milagu (Piper nigrum), Chukku (Zingiber officinale), Parpadagam (Mollugo cerviana), KoraiKizhangu (Cyperus rotundus), Santanam (Santalum album), Peyputtal (Trichosanthes cucumerina).* NK exhibits antipyretic, anti-inflammatory, antiviral, antidiabetic, antioxidant, and immunomodulatory properties[38,18]. It can effectively treat dengue fever and chikungunya. It also reduces joint pain, swelling, muscle pain, and headache. In addition, NK also treats infertility, irregular periods, and white discharge[39]. *Siddha* practitioners use *Nilavembu kudineer* as a supplementary drug for the effective management of diabetic Nephropathy owing to its antidiabetic and antioxidant properties; it was seen that NK reduces blood urea and serum creatinine in diabetic nephropathy patients.

7.7 *Poonai Meesai Choornam*

Siddha medical practitioners extensively use this plant drug to alleviate symptoms of renal disorders. The study carried out to evaluate the nephroprotective activity of orthosiphon stamineus revealed the drug's strong diuretic activity, which results in the excretion of sodium and potassium, as well as its effective nephroprotective action by lowering elevated serum creatinine, blood urea, urinary protein levels, and the severity of renal damage. The *Poonai meesai* plant is shown in Figure 6.

7.8 *Aavarai Kudineer*

The ingredients of *Aavarai Kudineer* are *Avarai samoolam (Cassia auriculata), Kondrai pattai (Cassia fistula), Naval pattai (Syzygium cumini), Koraikizhangu (Cyperus rotundus), Kostam (Saussurea lappa), Marutham pattai (Terminalia arjuna), Kadalalingil ver (Salacia reticulate).* Traditional herb for medicinal purposes *Senna auriculata* (L.) Roxb., also known as *Cassia auriculata* L., is frequently used in *Siddha* systems of medicine to treat various diseases[40].

Nearly every component of the plant, including the flowers, leaves, seeds, barks, and roots, has been used for medicinal purposes. Diabetes, dysentery, skin conditions, asthma, rheumatism, and metabolic diseases are all treated by it[22]. Some of the pharmacological properties of its extracts and isolated components include nephroprotective, anti-diabetic, anti-oxidant, anti-inflammatory, antihyperlipidemic, hepatoprotective, cardioprotective, anti-cancer, antimutagenic, antibacterial, and immunomodulatory effects[40]. Studies have shown

Figure 6. *Poonai meesai (Orthosiphon stamineus)* plant.

Figure 7. *Keezharnelli (Phyllanthus niruri)* plant.

that multi-property antioxidants ameliorate diabetic nephropathy changes in humans.

7.9 *Keezhanelli ver Kudineer*

Keezhanelli (Figure 7) has diuretic and deobstruent action. So it is used to treat edematous conditions and diabetes[22]. *Phyllanthus niruri* has been shown to have anti-diabetic, antioxidant, and kidney-protective properties[41]. Polyphenols were found in plant extracts after phytochemical analysis, and it was established that *P. niruri* leaf extract shields the kidney from the oxidative stress brought on by diabetes.

7.10 *Mookkirattai Kudineer*

Mookkirattai (Boerrhavia diffusa) (Figure 8) has a bitter taste and hot potency. It is a potent diuretic used to treat oliguria and edematous conditions of the body[22]. A study conducted on the *Boerrhavia diffusa* plant established the nephroprotective potential with particular relevance to the antioxidant mechanism of the plant. Traditional practitioners extensively use this plant drug to alleviate symptoms of renal disorders. *B. diffusa* protected against structural and functional kidney damage induced by gentamicin, possibly due to its antioxidant properties.

7.11 *Kollu Kudineer*

Kollu (Macrotyloma uniflorum) has diuretic and lithotriptic action. It is effective in treating *kapha* diseases[22]. The most potent antioxidants are the phenolic acids found in *M. uniflorum* seeds, which scavenge free radicals and reactive oxygen species. According to the findings, the aqueous extract of *Macrotyloma uniflorum* inhibits degenerative alterations in the renal system and promotes glomerulus activity[42]. Kollu seeds are famous for their diuretic properties. It protects renal tubular damage in diabetic nephropathy patients and helps to eliminate waste through urine.

7.12 *Mullangi Chaaru*

Mullangi (Raphanus sativus) (Figure 9) has a diuretic action, and it is also indicated to treat *Kapha, vatha* diseases, *Neeradaippu* (oliguria), and edematous conditions of the body[22]. The ethanolic extract of *Raphanus sativus* was found to have a nephroprotective impact on the tissue defence system in rats with galactosamine-induced kidney injury. It dramatically boosted antioxidant levels while decreasing kidney indicators. It also helped to repair renal tubular damage. These findings imply that *R. sativus* has nephroprotective properties, which may be due to the extract's antioxidant content.

7.13 *Thumbai Chooranam*

Thumbai (*Leucas aspera* Spreng.) is an anti-inflammatory stimulant used to treat jaundice, malaria, headache, cough, asthma, eye diseases like conjunctivitis, diabetes, otalgia, skin illnesses, snake bite, toothache, and wounds. It is indicated for all types of chronic *kapha* diseases. *Thumbai* can balance elevated *Iyya* humor in kidney diseases[22]. The significant antidiabetic, antipyretic, wound-healing, antioxidant, hepatoprotective, and nephroprotective activity of the extract of the *Leucas aspera* plant was established

Figure 8. *Mookkirattai (Boerrhavia diffusa), Kollu (Macrotyloma uniflorum).*

Figure 9. *Mullangi (Raphanus sativus), Thumbai (Leucas aspera* Spreng*).*

by biochemical parameters, physical parameters, and histopathological studies. Traditional practitioners use *Thumbai choornam* to reduce elevated renal parameters in nephropathies[43].

7.14 *Thiripala Churnam Mathirai*

Thiripala churnam, a well-known polyherbal *Siddha* formulation consisting of fruits of the three *plants Nellikkai (Emblica officinalis), Kadukkai (Terminalia chebula),* and *Thandrikkai (Terminalia bellerica)* (Figure 10), cures piles, wounds, gum bleeding, stomach ulcers, skin disease, constipation, and liver disease[22]. The

Figure 10. *Kadukkai (Terminalia chebula), Nellikkai (Emblica officinalis),* and *Thandrikkai (Terminalia bellerica).*

medication is both a preventative and a therapeutic option for diabetes. Furthermore, the powdered microscopy results can be used to identify starch grains, a type of polysaccharide that plays a role in managing pre-diabetes (IGT)[41]. *Triphala churnam* has been found in animal experiments to have a considerable nephroprotective impact due to its capacity to suppress oxidative stress and TGF-β in diabetes. In addition, *Triphala churnam* was found to minimize kidney damage in histopathological investigations[44].

8. *Siddha* Yoga Therapy as an Adjunctive Therapy for the Treatment of Diabetic Nephropathy

The prevalence of Type 2 Diabetes Mellitus (T2DM) has been steadily increasing, owing primarily to the sedentary and stressful lifestyle people currently lead. Diabetes, the most common endocrine and metabolic disorder, causes multiple organ systems to malfunction. Yoga, as adjuvant therapy, appears to provide significant benefits for diabetes patients, according to emerging research. Yoga has been researched and found to help manage T2DM symptoms and consequences. Many diabetic problems have been claimed to be eased by yoga while improving their Quality of Life (QoL)[45]. All glycemic markers (FBS, PPBS, and HbA1c) were considerably lower in individuals receiving adjuvant yoga therapy, which can increase insulin sensitivity in tissues and muscles and improve peripheral consumption and utilization[46]. These treatments are beneficial because of the healthy changes brought about by the psycho-physical mechanisms, while they are non-invasive and promote relaxation in patients with no adverse consequences. Uncontrolled diabetes often results in the prevalent and challenging-to-treat condition of diabetic nephropathy. Renal impairment is indicated by increased serum and blood levels of urea and creatinine. The study found that individuals who got adjuvant yoga therapy had significantly better glycemic indices and renal function tests than those who did not[47]. Patients with renal issues have significantly decreased physical fitness, which hurts their daily activities and capacity to execute job duties. In people with renal disease, regular exercise has been found to enhance physical fitness, walking capacity, cardiovascular parameters (such as heart rate and blood

pressure), health-related QoL, and various nutritional factors. Specific yoga poses listed in *Siddha* literature, such as *Kalappai Asanam* (*Halasana*), *Villasanam* (*Dhanurasana*)[48], and *Pavanamuktasana*, are regarded highly useful for the prevention of diabetes and its complications[49]. Yoga is a nonpharmacological, cost-effective approach to managing blood dyslipidemia. It has been reported to lower cholesterol levels in those with diabetes and those who are fat, which benefits everyone but is especially beneficial for those with renal disorders[50]. In one study, oxidative stress was lowered in the population after yoga therapy, which was found to be helpful in renal patients. It was discovered that adjuvant yoga therapy is safe and can improve renal function and QoL in CKD patients. Yoga may therefore aid in the prevention and management of chronic illnesses like diabetes by reducing anxiety and depression, promoting autonomic balance, improving physical health, and boosting brain centre functioning. Yoga practitioners develop a calm mind, which promotes self-awareness, and this internalized focus causes changes in neuro-hormonal systems that diminish sympathetic activity. Yoga was reported to reduce serum creatinine levels in dialysis patients because of decreased oxidative and mental stress, sympathetic hyperactivity, and inflammatory markers[47]. For patients with renal sickness, the yoga-based programme for rehabilitation is an easy, secure, and efficient clinical therapy strategy.

9. Conclusion

This review shows that traditional *Siddha* medicine can help manage diabetic nephropathy, besides being safe, cost-effective, and readily available. Most of the *Siddha* medicines used for managing diabetic nephropathy are herbal formulations. Due to their strong antioxidant qualities, they shield the renal tubules from harm, which is important because the formation of oxidative stress as well as free radicals is a significant contributor to diabetic nephropathy. Furthermore, the treatment protocols outlined and practised in *Siddha* have been time-tested and have shown positive outcomes in managing early-stage diabetic nephropathy. Therefore, the compound formulations or single drugs mentioned in *Siddha* literature for managing diabetic nephropathy shall be subjected to retrospective analysis to explore the scientific background behind the therapeutic aspects.

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