This article presents naturopathic treatments for diabetic kidney disease, also known as diabetic nephropathy. From the outset, it should be emphasized that controlling blood sugar and hypertension are the two most important and indispensable strategies in treating diabetic nephropathy. Because there are many resources available covering naturopathic treatments for hyperglycemia and hypertension, they will not be covered here. Instead, this article will focus on specific dietary, lifestyle, and supplement regimens that have been shown to reduce morbidity and mortality in diabetic nephropathy.

Background
Diabetic nephropathy is a common complication in type 1 and type 2 diabetes (20-40% incidence among diabetics) and is one of the leading causes of end-stage renal disease (ESRD) in the US. It is estimated that 50% of type 1 diabetics with overt nephropathy will have ESRD in seven to ten years, and the time course may be shorter among type 2 diabetics. ESRD, when untreated with dialysis or a kidney transplant, has a high mortality rate.

The earliest clinical sign of nephropathy is the detection of albumin in the urine (>30 mg/day but <300 mg/day); this is the microalbuminuria stage. Overt nephropathy typically happens five to ten years after the onset of microalbuminuria and is characterized by persistent presence of albumin in the urine of >300 mg/day and decline in kidney function as measured by glomerular filtration rate (GFR). Diabetic retinopathy is highly associated with nephropathy (60-90% rate of comorbidity), and the absence of the former should increase suspicion that the nephropathy may have other causes.

The key change in diabetic nephropathy is an increase in extracellular material, such as thickening of the glomerular basement membrane, expansion of the mesangium, and signs of glomerular fibrosis. Although the exact causes are unknown, elevated blood glucose is associated with glomerular basement membrane thickening, while glomerular hypertension is associated with sclerosis. Inflammatory cytokines such as transformation growth factor beta (TGF-b) and NF-KappaB also play a role by upregulating cellular hypertrophy and fibrinogenesis.

Allopathically, the mainstays of treatment include the following: (1) blood sugar control; and (2) blood pressure control, preferably with ACE inhibitors and/or angiotensin II receptor antagonists. In terms of diet, the recommendation is protein restriction to 0.8-1.0g/kg/d. (Note that patients on dialysis may have higher protein requirements.)

Prevention
It is best to treat nephropathy during the microalbuminuria stage. Once overt nephropathy sets in, the pathologic changes in the glomerulus are most likely irreversible. Three tests for microalbuminuria screening are available: (1) random spot urinary albumin-to-creatinine ratio (preferred method); (2) 24-hour urine microalbuminuria test; (3) other timed - e.g., four-hour or overnight - urine collection.

The American Diabetes Association (ADA) recommends annual screening for microalbuminuria among type 1 diabetics starting at five years after initial diabetes diagnosis. All type 2 diabetics should be screened yearly, starting at diagnosis, and during pregnancy. Additionally, serum creatinine should be measured at least yearly to estimate GFR in all adults with diabetes whether or not there is albuminuria.
Diet & Lifestyle Interventions

A carbohydrate-restricted, low- 
dietary-iron, polyphenol-enriched 
diet (CR-LIPE) has been shown to (1) 
reduce death or renal transplant by 
nearly 50%, and (2) reduce doubling of 
serum creatinine by half (Table 1). This 
is based on a controlled study done by 
Faccini and Saylor in 2002,16 where 
subjects were type 2 diabetics with 
confirmed renal disease (N = 191) and 
mean follow-up time was 3.9 years.

Features of the CR-LIPE diet include 
the following:

- A 50% reduction of carbohydrates 
from the previous level of intake.
- Replacement of iron-rich red meats 
(beef and pork) with iron-poor 
white meats (poultry and fish) and 
with protein-enriched food items 
known to inhibit iron absorption, 
e.g., dairy, eggs, and soy.
- Elimination of all beverages except 
teas, water, red wine, and milk.

Tea was highly recommended. 
Red wine was not to exceed 150 
ml with lunch and 150 ml with 
dinner. Milk was recommended for 
breakfast. Outside mealtimes, 
water was the only approved 
beverage.

- Exclusive use of polyphenol- 
enriched extra-virgin olive oil for 
both dressing and frying.
- Except for carbohydrate restriction, 
this diet was fed ad libitum (up to 
the discretion of subjects).

The control group ate a standard 
protein-restricted (0.8g/kg/d) diet, 
isocaloric for ideal body weight 
maintenance. When the macronutrient 
profiles of the CR-LIPE vs. control diet 
were analyzed, it was shown that the 
CR-LIPE diet resulted in significantly 
less carbohydrates (35% vs. 65%), 
more protein (25-30% vs. 10%), and 
slightly more fat (30% vs. 25%).

The authors postulate that the key 
mechanism explaining these life-
saving benefits is the fivefold 
reduction in serum ferritin (as a measure 
of body iron stores) due to reduced iron 
intake, absorption inhibition by milk, 
polyphenols, and tannins in tea. Iron 
in high amounts has been linked with 
oxidative stress, while iron depletion is 
linked with insulin sensitization. Low 
carbohydrate intake is also associated 
with a reduction in risk factors for 
morbidities associated with diabetes 
such as decreasing hyperlipidemia, 
insulinemia, and glycemia.

This CR-LIPE diet differs widely 
from the ADA’s recommendation of 
protein restriction. The former diet 
results in approximately 25-30% of 
daily intake from protein, while the 
ADA’s recommendation of 0.8g/
kg/d results in approximately ten 
percent of daily intake from protein. 
Reviewing the bibliography of ADA’s 
position statement,17 the advice to 
decrease protein intake is based on the 
following:

1) A randomized control trial with 
N = 121, with follow-up at six and 
12 months, shows that protein 
restriction decreased albuminuria 
by 28% and 18%, respectively. The 
author’s conclusion to this study is 
that “Substantial protein restriction 
in primary care, type 2 diabetic 
patients with no nephropathy is 
barely feasible. However, even a 
small reduction has a substantial 
and potentially beneficial effect on 
albuminuria.”18

2) A meta-analysis with a pooled 
N = 108 and follow-up times 
ranging from nine to 33 months 
showing that protein restriction 
among insulin-dependent diabetics 
reduced the decline in GFR or 
urinary albumin excretion or 
creatinine clearance.19

3) A randomized control trial 
with N = 82, with follow-up of 
four years, shows a ten-percent 
incidence of ESRD or death in the 
protein restriction of 0.6 g/kg/d 
group vs. 27% in the “usual protein 
intake” group of about 1.02 g/
kg/d.20

The ADA’s protein restriction 
recommendation is based on evidence 
level B.21

The CR-LIPE study directly 
compared the effects of a CR-LIPE 
diet vs. standard protein restriction 
of 0.8/kg/d, and concluded that CR-
LIPE is superior to standard protein 
restriction in terms of improving 
overall survival rates. CR-LIPE captures 
the combined effects of various dietary 
and biochemical interventions, i.e., 
macronutrient changes, high poly-
phenol intake, and reduction in 
oxidative stress via iron reduction. 
The CR-LIPE study, published in 2002, 
has not been repeated to date and will 
need more corroborating evidence 
before it may be widely adopted. Also, 
it should be noted that the CR-LIPE diet 
has not yet been studied in the setting 
of ESRD or dialysis.

A few small pilot crossover- 
designed studies indicate that a 
soy-based protein diet may be 
beneficial to individuals with diabetic 
nephropathy. A small (N = 14), seven- 
month crossover study in male type 2 
diabetics with nephropathy found that 
a soy-based diet significantly reduced 
urinary albumin excretion.22 Similar 
results were found in another small 
(N = 14), seven-week crossover study, 
which showed that replacement of 
portions of animal protein with soy 
and vegetable proteins, in a setting of a 
low-protein diet, reduced albuminuria 
and urinary urea nitrogen.23 A small 
(N = 12) twenty-week crossover study 
of type 1 diabetes found that a soy-
based diet significantly reduced 
proteinuria.24 Larger-scale 
studies are needed to more clearly 
elucidate the role of soy protein in the 
setting of diabetic nephropathy.

Lifestyle Intervention

Smoking Cessation

Cigarette smoking is associated 
with proteinuria and quicker pro-
gression of all types of chronic kidney 
diseases.25,26 Furthermore, cigarette 
smoke condensate worsened experi-
mental renal injury and increased 
proteinuria.27

Table 1: Comparison Between CR-LIPE Diet and Control Diet Results

<table>
<thead>
<tr>
<th></th>
<th>CR-LIPE Diet</th>
<th>Control Diet</th>
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<tbody>
<tr>
<td>Kidney transplant or death</td>
<td>20%</td>
<td>39%</td>
</tr>
<tr>
<td>Percentage who doubled creatinine</td>
<td>21%</td>
<td>39%</td>
</tr>
</tbody>
</table>
Diabetic Kidney Disease

Biologically Based Interventions

Antioxidant Therapy

Studies have shown that diabetes and diabetic complications are associated with greater oxidative stress\(^\text{28-30}\) and reduced levels of antioxidants.\(^\text{31-39}\) Recently, a unifying mechanism has been proposed suggesting that both macrovascular and microvascular (including nephropathy) diabetic complications are all mediated via an intracellular increase in reactive oxygen species.\(^\text{40}\) This link between oxidative stress and progression to diabetic nephropathy is supported by at least one subsequent study.\(^\text{41}\)

A recent review article, specifically written to assist clinical nephrologists in the treatment of glomerular proteinuria, lists antioxidants such as d-alpha-tocopherol, alpha-lipoic acid, selenium, and vitamin C as potential antiproteinuric agents.\(^\text{42}\)

Several clinical studies demonstrate that antioxidant supplementation can help improve kidney function among individuals with diabetic nephropathy. Treatment with vitamins C (200 mg q.d.) and E (100 IU q.d.) for 12 weeks,\(^\text{43}\) or vitamins C (1,250 mg q.d.) and E (680 IU q.d.) for four weeks,\(^\text{44}\) or vitamin E (1,200 IU q.d.) for four months,\(^\text{45}\) or vitamin C (500 mg b.i.d.) for nine months\(^\text{46}\) have all been shown to significantly reduce urinary albumin excretion ratio among diabetics. The addition of zinc (30 mg q.d.) and magnesium (200 mg q.d.) to vitamins C and E therapy resulted in a synergistic reduction of urinary albumin excretion.\(^\text{47}\)

In type 1 and type 2 diabetics, treatment with alpha-lipoic acid (600 mg q.d.) for 18 months halted progression of urinary albumin concentration (UAC), compared to controls whose UAC nearly doubled.\(^\text{48}\) This dose of alpha-lipoic acid has been shown to exert significant antioxidant activity even in the setting of poor glycemic control and a wide range of albuminuria.\(^\text{49}\)

A three-month trial comparing alpha-lipoic acid (600 mg q.d.) or selenium (100 mcg q.d.) or D-alpha-tocopherol (1,200 IU q.d.) to a control group found significantly diminished urinary excretion rates in each of the three antioxidant groups.\(^\text{50}\)

Phytotherapy

Plant-based treatments for diabetic nephropathy are supported by human and animal research models. Several studies examining phytotherapy interventions for diabetic nephropathy have been conducted in China. Injections of ginkgo biloba extracts combined with conventional western medical interventions have been found to decrease urinary albumin excretion in early stages of diabetic nephropathy.\(^\text{51}\) A three-month study found administration of Fructus arctii and Radix astragalus led to significantly reduced urinary albumin excretion in individuals with diabetic nephropathy.\(^\text{52}\) A decoction of Radix astragalus and Rhizoma ligustici chuanxiong (150 ml QD) for six months significantly decreased urinary albumin excretion in type 2 diabetic individuals with microalbuminuria.\(^\text{53}\) A Traditional Chinese Medicine formulation combined with conventional western medical interventions led to significant improvement in urinary albumin excretion, total 24-hour protein excretion, and renal function.\(^\text{54}\)

Animal model studies have shown the following: polyphenols have been shown to reduce transforming growth factor-beta and prevent fibrosis and deterioration of renal function,\(^\text{55}\) as well as reduce uremic toxic products in renal failure.\(^\text{56}\) Quercetin and turmeric have been shown to attenuate the severity of nephropathy, most likely through their antioxidant properties.\(^\text{57-58}\)

Polyunsaturated Fatty Acids

Several clinical studies have shown that the use of eicosapentaenoic omega-3 fatty acids (EPA) have been able to improve urinary albumin excretion ratios for type 2 diabetics at doses of 900 mg/day\(^\text{59}\) and 1,800 mg/day.\(^\text{60}\) A seven-year, multicenter (N = 192), prospective study has shown that diabetic nephropathy regression (reversal of microalbuminuria to normoalbuminuria, or macroalbuminuria to micro- or normoalbuminuria) is associated with a higher polyunsaturated fatty acid to saturated fatty acid ratio, while nephropathy progression (normoalbuminuria becoming micro- or macroalbuminuria or microalbuminuria becoming macroalbuminuria) is associated with a reversal of that same ratio.\(^\text{61}\) Specifically, one type 1 diabetic patient and four type 2 diabetic patients regressed from macroalbuminuria to microalbuminuria, and one type 2 diabetic patient regressed from macroalbuminuria to normoalbuminuria. These results are particularly interesting as they are inconsistent with the conventionally held belief that overt nephropathy is irreversible. Further research is needed to explore if there are circumstances that may allow for reversal of overt nephropathy.

While outside the scope of this article to discuss in detail, it should be noted that several of the interventions listed above have other known benefits in altering the pathophysiology and comorbidities associated with diabetes, for example, diabetic neuropathy and alpha-lipoic-acid.\(^\text{62-64}\) Therefore, the benefits of supplementing with the above biologically based interventions may extend beyond diabetic nephropathy.

Clinical Context

A comprehensive naturopathic approach to diabetic nephropathy treats the whole person by identifying causative and contributing factors that may exist in the physical, psycho-emotional, and spiritual planes. These factors can be addressed by utilizing a wide range of treatment modalities including, but not limited to, homeopathy, constitutional hydrotherapy, glandular therapy, counseling, and environmental medicine. The complexity involved in implementing these modalities in clinical practice precludes their inclusion in the present discussion and will be left for further writings.
Conclusion

Diabetic nephropathy is a major complication of diabetes and can result in significant morbidity and mortality if untreated. Control of blood sugar and hypertension are the two established basic clinical problems that need to be addressed in treating diabetic nephropathy.

In this article, we have highlighted and presented the evidence for other interventions:

1. Prevention through yearly screening for microalbuminuria and possibly through early adoption of treatment interventions discussed in this article is important, given the prevailing opinion that glomerular changes are irreversible once overt nephropathy sets in.

2. Diet has a major impact on mortality rates. The current standard recommendation is protein restriction. There is also emerging evidence that a more multifaceted diet, incorporating carbohydrate restriction, iron depletion, and polyphenol supplementation, may be superior. The study that supports this needs to be corroborated on a larger scale before widespread adoption.

3. Smoking cessation is a major lifestyle intervention. This includes exposure to second-hand smoke.

4. Supplementation with antioxidants, certain phytotherapeutics, and omega-3 fatty acids has been shown to reduce urinary albumin excretion. Although the exact mechanisms are unknown, there is evidence it might be through mediation of oxidative stress.

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Notes
3. Ibid. 1590.
4. Ibid.

Dear Tenant,

Effective immediately, you may no longer reside in my intestine.

Sincerely,
The Landlord

Bioray, Inc
The natural detox company
ARTEMESIA & CLOVE An Herbal Supplement
Traditionally known as a broad spectrum anti-parsitic herbal.*
3:1 Concentrate 2 Fluid Ounces (60 ml)

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Diabetic Kidney Disease

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