

A systematic review on Eefooton: A natural formulation used to stop the progression of chronic kidney disease

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Abstract

Chronic Kidney Disease (CKD) is an important global public health problem. More than 2 million people worldwide are estimated to be receiving treatment with dialysis or transplantation for chronic kidney failure, and this population has been growing at an approximate rate of 7% per year. A Case report recently published claimed that use of natural formulation (eefooton). After the Eefooton adjuvant therapy was finished, the patient was monitored for a further three months. Renal function of the patient was enhanced, and CKD progression was slowed down. Following Eefooton therapy, the patient's blood urea nitrogen (BUN) and serum creatinine concentrations dropped while the size of both kidneys rose by 8%. In addition, 2 months after therapy, a further decrease in BUN concentration was seen. This review gives an objective to the reserchers if the eefooton has potential benefits. After performing several literature reviews it was revealing that more research is required to prove the efficacy of eefooton on reversing CKD condition.

Keywords: Eefooton; Chronic Kidney Disease; *Astragalus membranaceus*; *Codonopsis pilosula*; *Ligustrum lucidum*; *Panax quinquefolius*; *Rhodiola sacra*

1. Introduction

A significant issue in terms of worldwide public health is chronic kidney disease (CKD) [1]. It is estimated that more than 2 million people worldwide are receiving treatment for chronic kidney failure through dialysis or transplantation, and this number has been expanding at a pace of about 7% each year [2]. However, the adverse effects of CKD go far beyond kidney failure and also encompass a wide range of morbidity and mortality linked to comorbidities, notably those caused by reduced kidney function and Cardiovascular Diseases (CVD) [3]. In collaboration with other organs, such as the Parathyroid Gland (PTG), intestines, and bones, the kidney plays a key role in preserving calcium and phosphorus homeostasis. It serves as both the primary site for the generation of calcitriol as well as the target organ for a number of hormones, including parathyroid hormone (PTH) (1, 25-dihydroxyvitamin D). Thus, as CKD progresses, a variety of disorders in mineral and bone metabolism emerge and may change serum minerals [4]. Three feedback systems interact intricately in healthy persons to maintain blood calcium and phosphate concentrations that are suitable for bone formation [5]. Mineral homeostasis gradually deteriorates with declining kidney function, leading to abnormal phosphorus and calcium concentrations in serum and tissues as well as abnormalities in hormone levels in

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the blood. These include growth hormone, 25(OH)D, 1,25(OH)2D, and other vitamin D metabolites, as well as PTH, FGF-23, and other vitamin D metabolites. As CKD progresses to stage 3, the kidneys' capacity to appropriately eliminate a phosphate load decreases, resulting in hyperphosphatemia, increased PTH, reduced 1,25(OH)2D, and raised levels of FGF-23. In order to reduce the effects of biochemical and hormonal imbalances, therapy typically focuses on repairing them [6]. Stages 4 and 5 of chronic kidney disease (CKD) start with nonspecific symptoms like nausea and vomiting that get progressively worse as the glomerular filtration rate (GFR) falls below 15 mL/min. This clinical condition develops slowly as kidney function diminishes to the most severe stages. To remove uremic toxins and keep hemodynamic stability, renal replacement therapy, such as dialysis or transplantation, is advised at this point. End-stage renal disease is described as a patient with stage 5 CKD who needs chronic dialysis or a kidney transplant to treat their uremic symptoms (ESRD) [7].

The patient has three management options after their kidneys have failed: hemodialysis (HD), peritoneal dialysis, or transplantation. Transplantation decisions are carefully considered. An already unwell patient undergoing this surgery, who is likely also dealing with comorbid conditions like diabetes or hypertension, may find it difficult [8]. The overall load of physical and psychological symptoms, sadness, and poor quality of life are common among patients on maintenance dialysis [9]. Furthermore, a large portion of individuals with end-stage renal disease are elderly. A 1-year death rate of 41% follows the start of dialysis in individuals over the age of 75, with around 40% of those patients suffering from CKD [10]. It is necessary to find viable palliative therapies for people with CKD and end-stage renal disease. Using natural formulation, according to a case study that was recently released (eefooton) [11]. Following the conclusion of the Eefooton adjuvant therapy, the patient was monitored for three months. Renal function of the patient increased, slowing the course of CKD. The patient's blood urea nitrogen (BUN) and serum creatinine concentrations reduced after Eefooton medication, and both kidney sizes rose by 8%. Additionally, 2 months after therapy, a further decline in BUN concentration was seen. [11].

2. Composition of eefooton

Eefooton (a liquid formula of herbal extracts: *Astragalus membranaceus* 3 g, *Codonopsis pilosula* 3 g, *Ligustrum lucidum* 3 g, *Panax quinquefolius* 1.3 g, and *Rhodiola sacra* 1.3 g) [11].

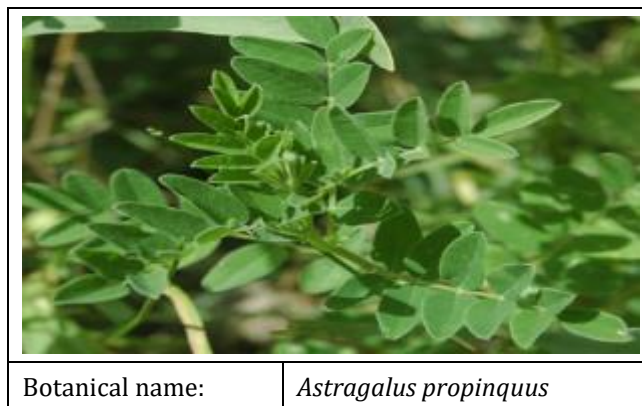
2.1. Evaluation of efficacy and safety of eefooton

2.1.1. *Astragalus propinquus*

Astragalus propinquus (syn. *Astragalus membranaceus* [12]). An annual blooming plant belonging to the Fabaceae family, it is also known as Mongolian milkvetch [13] in that country. It is one of the 50 essential plants used in conventional medicine in Mongolia [13]. It is a perennial plant. Its effectiveness was investigated, and a result was reached since it is only used as a supplement to conventional medicines. Studies have shown that it may reduce proteinuria and raise serum albumin and haemoglobin [14]. To demonstrate its benefits in CKD, however, numerous additional confirmatory preclinical and clinical studies are necessary, and additional research is advised.

Table 1 *Astragalus propinquus*


Scientific classification	
Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Rosids
Order	Fabales
Family	Fabaceae
Subfamily	Faboideae
Genus	<i>Astragalus</i>



2.1.2. *Codonopsis pilosula*

Since ancient times, *Codonopsis pilosula* has been used in traditional Chinese medicine to cure a variety of illnesses, including anaemia, weariness, a weak spleen, and stomach issues. While the aerial parts of *C. pilosula* are always discarded after being harvested in the fall or winter, the roots are thought to have therapeutic properties. According to some research, *C. pilosula* stems and leaves also contain a number of active metabolites, including as saponins, flavonoids, terpenoids, and polysaccharides. Additionally, the extracts from *C. pilosula* aerial portions shown greater antioxidant strength than roots. The stems and leaves of *C. pilosula* were abundant in active components and may be extremely valuable for research and development [15].

Table 2 *Codonopsis pilosula*

Scientific classification	
Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Asterids
Order	Asterales
Family	Campanulaceae
Genus	<i>Codonopsis</i>
Species	<i>C. pilosula</i>
	
Binomial name	<i>Codonopsis pilosula</i>

Medical use

Studies on the root's potential to cure digestive, respiratory, and cardiovascular diseases have been motivated by the historic therapeutic usage of codonopsis. Five animal models of gastric ulcer were used to study the effects of *Codonopsis*


pilosula extract. It was discovered that the extract had a higher efficiency against gastric ulcers brought on by stress, acetic acid, and sodium hydroxide and a much lower effectiveness against ulcers brought on by pyloroligature and indomethacin. The gastric acid pepsin secretion could be decreased by the *C. pilosula* extract as well. One of the potential mechanisms underlying the antiulcer activity of *C. pilosula* extract is the potential suppression of gastrointestinal motility and propulsion [16].

2.1.3. *Ligustrum lucidum*

An evergreen tree, *Ligustrum lucidum*, can reach a height and width of 10 m (33 ft). It is a type of flowering plant belonging to the Oleaceae family of olives that is native to southern China and has spread widely. The opposite, glossy, dark green leaves are 6–17 centimetres (2.4–6.7 in) in length and 3–8 centimetres (1.2–3.1 in) in width. Similar to other privets, the blooms are white or almost white, borne in panicles, and have a potent aroma that some find repulsive [17].

Using butylated hydroxytoluene (BHT) to cause oxidative stress in rats, a study was conducted to look into the antioxidant properties of an ethanol extract of *Ligustrum lucidum* fruits (ELL). ELL has poor antioxidant properties, according to the results. The results showed that ELL at 250, 500, and 1000 mg/kg significantly decreased the levels of blood urea nitrogen (BUN), serum glutamic pyruvic transaminase (sGPT), glutamic oxaloacetic transaminase (sGOT), alkaline phosphatase (sALP), lactate dehydrogenase (LDH), triglyceride (TG), creatinine (Cr), as well (BALF). The quantity of lipid peroxides in the liver and lungs was also markedly reduced. Moreover, ELL markedly increased the concentrations of the antioxidant enzymes glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT) in these organs. While the liver and renal tissues were unaffected by BHT treatment, histopathological analysis of the tissues showed that ELL decreased the incidence of lung lesions. Collectively, the activation of antioxidant enzymes may be how ELL protects rats from acute BHT-induced oxidative damage. There is still room for more research on the extracts of *Ligustrum lucidum* because this study found no conclusive advantages in chronic renal disease [18].

Table 3 *Ligustrum lucidum*

Scientific classification	
Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Asterids
Order	Lamiales
Family	Oleaceae
Genus	<i>Ligustrum</i>
Species	<i>L. lucidum</i>
	
Binomial name	<i>Ligustrum lucidum</i>

In a different investigation, human hepatocellular carcinoma Bel-7402 cells were subjected to a fruit extract from the *Ligustrum lucidum* (LLFE). The outcomes demonstrated that Bel-7402 cell proliferation was suppressed by LLFE in a dose- and time-dependent manner. Caspase-3, -8, and -9 were activated along with apoptosis in Bel-7402 cells as a result of LLFE. A pan caspase inhibitor called Z-VAD-FMK effectively reversed the effects of LLFE-induced apoptosis. In addition, LLFE treatment resulted in an increase in p21 and a decrease in RB phosphorylation, along with a significant and flat morphologic cellular change, positive SA-gal staining, and G0/G1 phase cell cycle arrest in the Bel-7402 cells.


Apoptosis caused by LLFE was somewhat abolished by specific p21 expression suppression by RNA interference, and cell senescence caused by LLFE was dramatically abated. These findings confirm the traditional usage of Nü-zhen-zi for the treatment of hepatocarcinoma and point to it as a possible anticancer herb [19].

2.1.4. American ginseng

American ginseng (*Panax quinquefolius*, *Panacis quinquefolis*) A perennial herb with thick roots, ginseng grows slowly. One of the natural medications that has been the subject of the greatest research and prescription is ginseng. Ginseng may be helpful in treating renal impairment, according to several studies. [20] and hepatotoxicity.[21]. The fragrant American ginseng root looks like a young parsnip that forks as it gets older. The plant typically has three leaves, each with three to five leaflets, and is 6 to 18 in (15 to 46 cm) tall. The length of the leaflets ranges from 2 to 5 in (5 to 13 cm). A large portion of the eastern and central United States, as well as southeastern Canada, are home to American ginseng.[22] In the Appalachian and Ozark regions of the United States, it is primarily found in deciduous forests [23]. In these deciduous forests beneath the hardwoods, American ginseng can be found in full shadow conditions.

The primary physiologically active components of American ginseng are dammarane-type ginsenosides, also known as saponins. 20(S)-Protopanaxadiol (PPD) and 20(S)-Protopanaxatriol are two types of dammarane-type ginsenosides (PPT). When consumed orally, anaerobes in the gut metabolise PPD-type ginsenosides to PPD monoglucoside, 20-O-beta-D-glucopyranosyl-20(S)-protopanaxadiol (M1) [24]. Humans may detect M1 in plasma beginning seven hours after ingesting PPD-type ginsenosides and in urine beginning twelve hours later. These results suggest that M1 is the ultimate metabolite of ginsenosides of the PPD type [25]. According to a recent case study, a 43-year-old lady who had just ingested three ginseng roots with alcohol was admitted to the hospital with possible hepatitis and an acute kidney injury brought on by ginseng [26].

Table 4 *Panax quinquefolius*

Scientific classification	
Kingdom	Plantae
(unranked)	Angiosperms
(unranked)	Eudicots
(unranked)	Asterids
Order	Apiales
Family	Araliaceae
Subfamily	Aralioideae
Genus	<i>Panax</i>
Species	<i>P. quinquefolius</i>
	
Binomial name	<i>Panax quinquefolius</i>

Benefits

Several clinical investigations have proven the effectiveness of ginsenosides. An advantage of anti-inflammatory drugs is that they can enhance glomerular endothelial barrier function, reduce renal cell apoptosis brought on by ischemia and reperfusion to safeguard kidney function in AKI, prevent excessive extracellular matrix (ECM) buildup in renal tubular cells, including collagen and fibronectin, as well as fibrotic markers, especially TGF-1, inhibit apoptosis of

glomerular mesangial cells, and lessen damage to pod The kidney is where ginsenosides work to protect it (Figure 1). Together, ginsenosides have the potential to be a kidney protective treatment rather than a preferred medicine [27].

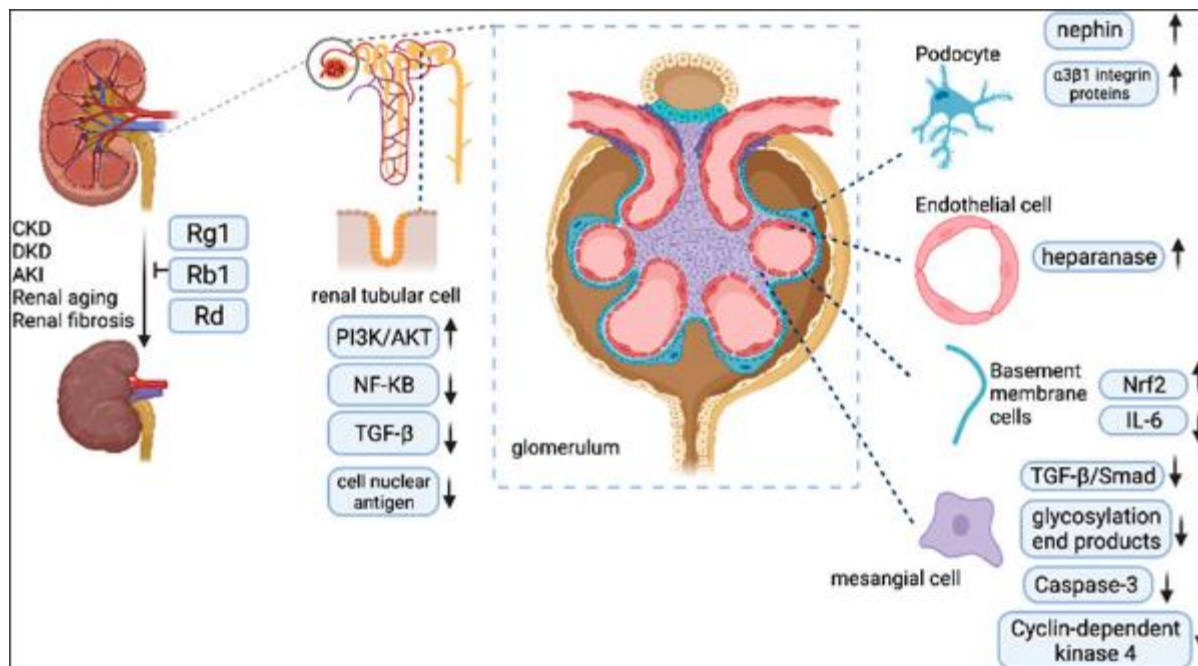


Figure 1 Kidney-protected effects of ginsenosides

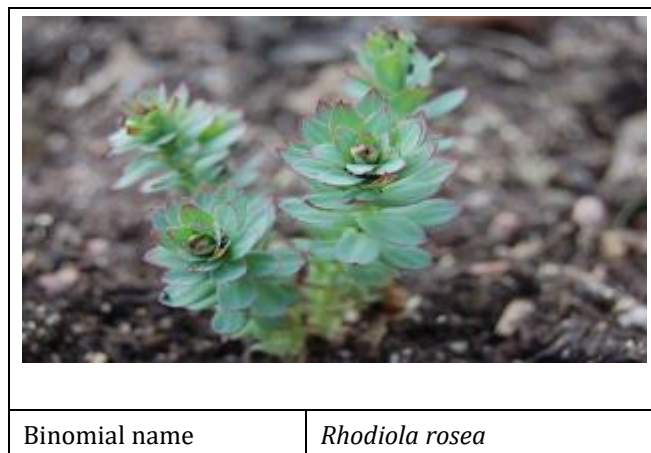
The results of a study employing diabetic rats produced with streptozotocin (STZ) and using heat-processed American ginseng (H-AG) on diabetic renal damage suggest that H-AG may have therapeutic effects on pathological conditions related to diabetic nephropathy [28].

2.1.5. *Rhodiola rosea*

The perennial blooming plant *Rhodiola rosea*, often known as golden root, rose root, roseroot, Aaron's rod, Arctic root, king's crown, lignum rhodium, orpin rose, belongs to the Crassulaceae family. It has multiple stems sprouting from a short, scaly base and grows between 5 and 40 centimetres (2.0 and 15.7 in) tall, meaty, and multi-stemmed. Flowers are roughly 1 to 3.5 millimetres (0.039 to 0.138 in) long, with 4 sepals and 4 petals that range in hue from yellow to greenish yellow and occasionally have red tips. They bloom in the summer. A single thick root may produce several shoots that might range in height from 5 to 35 centimetres (2.0 to 13.8 in). *R. rosea* has separate male and female plants since it is dioecious [29].

Table 5 *Rhodiola rosea*

Scientific classification	
Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Order	Saxifragales
Family	Crassulaceae
Genus	<i>Rhodiola</i>
Species	<i>R. rosea</i>
Kingdom	Plantae



Chemical constituents

Underground regions of *R. rosea* include over 140 chemical substances. Phenols, organic acids, terpenoids, phenolic acids and their derivatives, flavonoids, anthraquinones, alkaloids, tyrosol, and salidroside are all present in roots. [30][31]. Salidroside exerts nephroprotective effects in diabetic kidney disease patients by inhibiting apoptosis in the proximal Renal tubular cells, according to a study [32]. Hypertension and diabetes mellitus were found to be the major comorbidities in valvular heart disease patients and further leads to nephropathy [33].

3. Discussion

One noteworthy herb that can be found among food and medicinal plants is *Astragalus membranaceus* (AM). Its advantages come from bioactive substances that strengthen immune system performance, preventing and healing various ailments, and enhancing health, there are no evidences of AM extracts that it can reverse the CKD and its complications. More research is required to show its benefits in Nephroprotectivity. Diabetic Kidney Disease (DKD) is a multifactorial diabetic complication with numerous mechanistic pathways contributing to disease pathogenesis. Despite tremendous advancement in delineating these pathways that contribute to DKD, clinicians are still a long way away from having a new drug in their prescribing guidelines [34]. Evidence suggests that diets emphasizing the consumption of plant-based foods might protect against chronic conditions like asthma development and improve asthma symptoms through their effects on systemic inflammation, oxidation, and microbial composition [35]. Here no evidence are seen in limiting progress of CKD. Overall, few study results show that *Codonopsis pilosula* has a cytoprotective effect on melanocytes under oxidative stress by increasing autophagy and microphthalmia-associated transcription factor (MITF) expression in addition to having an anti-melanogenic effect on healthy melanocytes and no evidence on nephrons. *Ligustrum lucidum* has antioxidant properties, American ginseng contains dammarane-type ginsenosides, or saponins, as the major biologically active constituents, upon consumption of its roots caused Hepatitis and Kidney injury. The renin-angiotensin-aldosterone system (RAAS) mechanisms are prime factors for progression and worsening of the CKD, steps should be taken to prevent the over activity of RAAS by using many of the newer therapeutic agents show promise in preventing or stabilizing cyst growth, providing much needed hope in this currently relentless condition [36]. No such evidence is available with plant based therapies. However ginsenosides are capable of being a remedy for kidney protection and not a drug of choice in kidney failure. Few studies reveals that salidroside of *Rhodiola rosea* has nephroprotective effects through inhibition of apoptosis in the proximal Renal tubular cells in diabetic kidney disease patients and may show benefits. Antiplatelet therapies [37] in DM, antihypertensives and management of sugar and blood pressure can benefit disease progression.

4. Conclusion

In this review, we conclude that while there are very few individual studies of Eefooton ingredients that show benefits in kidney dysfunction, there are no direct indications in various research and literature reviews that suggest potential benefits and clarification of reversing CKD by using Eefooton formulation. *Ligustrum lucidum* possesses antioxidant, hepatoprotective, and nephroprotective characteristics, however additional research is needed to demonstrate its efficacy in reversing CKD. H-AG might be helpful for diabetic nephropathy-related pathological disorders. By inhibiting apoptosis in the proximal Renal tubular cells, the salidroside in *Rhodiola rosea* has nephroprotective actions.

Compliance with ethical standards

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Disclosure of conflict of interest

All authors declare that they have no conflict of interest.

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