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# Adenine-rich diet: a potential mechanism for renal fibrosis progression

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## Abstract

Chronic kidney disease (CKD) is a major health problem but there are many modalities to prevent and manage CKD progression. Diet is one of these factors, which needs to be evaluated more. Adenine is a water-soluble nucleoprotein that exists in both vegetables and animal foods, which triggers and aggravates fibrosis process besides other metabolic derangements such as diabetes mellitus affection that accelerates glomerular filtration rate decline rapidly.

## Keywords

Kidney fibrosis, adenine, uric acid

Chronic kidney disease (CKD) is a major health problem that costs much with poor prognosis and leads to glomerular filtration rate (GFR) decline following increased extracellular matrix (ECM) protein synthesis by multiple mechanisms partly related to inflammation and cell transformation (epithelial and endothelial to mesenchymal cells) and excrete matrix protein by integrin linked kinase (ILK) modulation. The trigger factor for such process is signals from epithelial cell to interstitial parts to promote fibrogenesis, and adenine can trigger renal fibrosis simultaneously by increasing ILK expression [1]. Adenine is a nucleobase and purine precursor that increases serum uric acid level [2]. Adenine is absorbed and metabolized to an insoluble compound that precipitates in renal tubules to promote tubular occlusion and tubular epithelium physical injury. It has been shown that adenine-rich diet in mouse brings pathologic changes simultaneously with weight decline and hypertension and leads to smaller kidney ultimately. ILK expression was increased in the renal cortex simultaneously with hyper blood pressure after adenine use and ILK depletion can be protective against adenine-rich diet adverse effects [1]. There is a broad spectrum of clinical manifestations following adenine-rich diet in rats such as decreased food intake, polyuria, polydipsia, and nephrogenic diabetes insipidus by interfering Aquaporin-2 (AQP-2) and salt transporter function (NKCC2) leads to prerenal azotemia. All of these symptoms besides decreased fluid intake can be inciting for chronic kidney disease pathogenesis in long term [3]. Adenine or vitamin B4 is available as nicotinamide adenine dinucleotide (NAD) along with vitamin B2 and B3 plays a role in producing energy but its dose has not been defined by recommended dietary allowance (RDA) and doses as much as 25–75 mg per day were used in healthy adults [4]. Adenine is a precursor of uric

acid that contributes to kidney fibrosis by inducing inflammation, endothelial dysfunction, oxidative stress, and activation of the renin-angiotensin system that alter renal hemodynamics via afferent arteriolopathy as the onset of kidney fibrosis progression. Allopurinol as a uric acid synthesis blocker can reverse kidney fibrosis following adenine-rich diet [5]. Adenine can also make glucose intolerance by intermediary role in free fat acid (FFA) metabolism in obese mice but adenine nucleotide makes hyperglycemia by different mechanisms such as hyperuricemia, a metabolite of adenine nucleotide, which stimulates hepatocyte gluconeogenesis in diabetes by inhibition of the phosphorylation of adenosine monophosphate–activated protein kinase (AMPK) [6].

## Conclusions

Renal fibrosis is an insidious phenomenon, influenced by diverse mechanisms. Adenine is a component of many kinds of foods, which plays a role in renal fibrosis development by many mechanisms. We haven't had enough information about adenine benefit and limitation in vulnerable patients to CKD such as diabetes and pre-existing renal dysfunction for any reasons.

## Abbreviations

CKD: chronic kidney disease

ILK: integrin linked kinase

## Declarations

### Author contributions

The author contributed solely to this work.

### Conflicts of interest

The author declares that he has no conflicts of interest.

### Ethical approval

Not applicable.

### Consent to participate

Not applicable.

### Consent to publication

Not applicable.

### Availability of data and materials

Not applicable.

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