

## Propolis against Urolithiasis

Timucin Atayoglu A<sup>1\*</sup>, Guner Atayoglu A<sup>2</sup>, Oguzhan Gunduz<sup>3</sup>, Ismail Evren<sup>4</sup>, Sibel Silici<sup>5</sup> and Noor Buchholz<sup>6</sup>

<sup>1</sup>Holistic & Integrative Medicine Association, Istanbul, Turkey

<sup>2</sup>State Family Health Center in Kucukcekmece Province, Istanbul, Turkey

<sup>3</sup>Department of Urology, Uskudar State Hospital, Istanbul, Turkey

<sup>4</sup>Department of Urology, Bakirkoy Dr Sadi Konuk Education and Research Hospital, Istanbul, Turkey

<sup>5</sup>Faculty of Agriculture, Erciyes University, Kayseri, Turkey

<sup>6</sup>Endourology & Stone Service, Barts and The London NHS Trust, London, UK

\*Corresponding author: Timucin Atayoglu A, President of Holistic & Integrative Medicine Association, Istanbul, Turkey, Tel: +90 (212) 696 14 15; Fax: +90 (212) 470 00 38; E-mail: dratayoglu@apider.org

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### Abstract

Urolithiasis is a common presentation in Family Medicine. People who suffer from this problem very often seek natural treatments. Many natural remedies have been used to treat urolithiasis problems throughout history. Propolis is one of the bee products and a potential preventive and therapeutic agent for different health conditions. The aim of this review is to discuss the possibility that propolis may assist the prevention and treatment of urolithiasis as well. Several compounds have been identified in propolis and we reviewed the scientific literature on them to evaluate the potential effect of propolis against urolithiasis. The active components of propolis that have been identified so far mainly include polyphenols and flavonoids. There is a relatively great amount of scientific data on these components showing their anti-inflammatory, XOD-inhibitory, renoprotective, diuretic, anti-microbial, anti-oxidant and immunomodulator activities. The synergistic effect of active compounds of propolis may be promising for urinary stone disease as further studies are encouraged on their bioavailability, stability in different preparations, along with safe and effective doses for prevention or treatment of urolithiasis on animals and human.

**Keywords:** Urolithiasis; Stone disease; Propolis; Natural treatment

### Introduction

Urolithiasis is a common condition in primary health care. It affects all cultural and racial groups. The incidence in the developed world is about 10 to 15%, but because of the increased risk of dehydration in hot climates, coupled with a diet lower in calcium and higher in oxalates, the estimated lifetime risk of developing urolithiasis for individuals born in the Middle East can be as high as 20 to 25% [1]. After a first stone episode, up to 50 percent of patients have at least a second stone within 10 years, and up to 80 percent have more stones within 20 to 30 years [2].

Many natural remedies have been used against urinary calculous problems. An effective medicine for urolithiasis may prophylactically inhibit the formation of new crystals; may alleviate pain whilst also facilitating stone passage by diuresis or ureteral relaxation; and furthermore, it may be protective against urolithiasis complications such as infection and kidney damage.

The crystalline components of urolithiasis can be classified into five types: calcium oxalate, calcium phosphate, bacterial related, purine, or cystine. The majority of urinary stones are mixtures of two or more of these components, with calcium oxalate combined with apatite being the most common [3,4]. Urolithiasis literature has largely defined the composition and frequency of occurrence of urinary stones and there have been many studies on the possible mechanisms of crystal aggregate formation [5]. For calculi formation there are some mechanisms that have been proposed such as the development of

calculi attached to papillary epithelium and the development of calculi in cavities without any attachment to urothelium [6].

The physical chemistry of calculous formation has been intensively studied. It has become clear that the pathophysiology of renal calculous disease cannot be explained by crystallization processes alone and many aspects of this complex phenomenon remain unclear [7].

In recent years a honey-bee product called Propolis has attracted attention due to its beneficial effects for different health conditions. More than 200 components have been found in propolis, mainly composed of phenolic compounds, terpenes, essential oils and especially flavonoids are responsible for the biological activity of propolis [8,9]. Propolis compounds have recently become the subject of investigation in order to determine its therapeutic application [10]. Phenolic compounds are known to be secondary metabolites of the plants [11]. Flavonoids are natural products with potential benefit for human health and they present an important part of the human diet [12].

The active components of propolis that have been identified so far have cardioprotective, vasoprotective, antioxidant, antiatherosclerotic, antiinflammatory, antiangiogenic actions, etc. This paper discuss the possibility that propolis may assist in the prevention and treatment of urolithiasis.

### Data

Propolis have antiinflammatory, XOD-inhibitory, renoprotective, diuretic, antimicrobial, antioxidant and immunomodulator

compounds. There is a close relationship between inflammation and urinary calculous formation [13]. Strong anti-inflammatory activity of propolis has been well established by a number of studies [10,14-16]. This antiinflammatory activity can be explained by the presence of active flavonoids such as caffeic acid phenethyl ester (CAPE) and cinnamic acid derivatives [10,17]. Its activity can be well correlated with its effects on the release of various mediators of inflammation [17].

Flavonoids have been investigated for their hypouricemic action [18,19]. Mo et al. [18] showed that oral administration of quercetin, puerarin, myricetin, morin and kaempferol significantly reduced liver uric acid level in hyperuricemic animals. In addition, quercetin, morin, myricetin, kaempferol and puerarin exhibited significant inhibition on the liver xanthine oxidase (XOD) activities. It seems to be likely that some flavonoids reduce serum urate levels by mainly inhibiting XOD activity while some others might act via other mechanisms apart from inhibiting enzyme activity simply. Analysis of the chemical structure showed that a planar structure with the hydroxyl groups played a crucial role in hypouricemic activity of flavonoids [19]. The XOD inhibitors decrease the production of uric acid, by interfering with xanthine oxidase. Furthermore, XOD has been implicated in the tissue oxidative injury after ischemia-reperfusion. Two flavonoids, quercetin and silybin, characterized as free radical scavengers, exert a protective effect preventing the decrease in the dehydrogenase/oxidase ratio observed during ischemia-reperfusion [19,20]. Yoshizumi et al. showed that propolis has XOD inhibitory activity. Therefore intake of propolis may be effective for the prevention and the treatment of hyperuricemia [20].

Infection stones make up approximately 15% of urinary stone diseases and are thus an important group [21]. *Escherichia coli*, the main bacteria found in recurrent urinary tract infections (UTI), is now frequently resistant to several currently used antibiotic treatments making new solutions essential. Jean-Philippe Lavigne et al. evaluated the association propolis and proanthocyanidins type A to reduce bacterial anti-adhesion activity of *E. coli* on urothelial cells and concluded that administration of PACs plus propolis once daily offers some protection against bacterial adhesion, bacterial multiplication and virulence in the urinary tract, representing a strategy to prevent recurrent UTI [22].

The flavonoids in propolis are powerful antioxidants [23]. Animal studies have demonstrated the likely role of oxidative tissue damage in the pathophysiology of stone disease [24]. Holoch et al. evaluated the association between serum antioxidant levels and the self-reported prevalence of kidney stones in a large cross-sectional population in a retrospective cohort study. When analyzed by quartile, the lower levels of antioxidants were associated with a history of kidney stones and may indicate a role for these antioxidants in preventing stone formation [25]. Ozyurt et al. reported that acute administration of CAPE an active component of propolis extract altered the indices of oxidative stress differently in renal ischaemia-reperfusion injury [26]. CAPE was also found to be protective against cisplatin-induced antioxidant enzyme reductions. Treatment with free-radical scavenger CAPE attenuated the increase in plasma blood urea nitrogen and kidney nitric oxide levels, and showed histopathological protection against cisplatin-induced acute renal failure. CAPE caused a marked reduction in the extent of tubular damage. It is concluded that administration of cisplatin imposes an oxidative stress to renal tissue and CAPE confers protection against the oxidative damage. This

mechanism may be attributed to its free-oxygen-radical scavenging activity [27].

Wei Zhu et al. [28] demonstrated the beneficial effects of propolis in hepatorenal function. They tested the effects of propolis on experimentally-induced type 1 diabetes mellitus in rats and observed an apparent reduction in levels of blood urea nitrogen and urine micro albuminuria-excretion rate, as well as AST and ALT. Moreover, oxidative stress in kidney was improved to various degrees by propolis [28].

Cross-sectional studies have shown that urinary stones are more frequently found in hypertensive patients than in normotensive subjects, but the pathogenic link between hypertension and urolithiasis is still not clear [29]. Some flavonoids are effective in decreasing blood pressure and increasing water and electrolytes excretion. It was shown that intake of quercetin would affect the body fluid amount via the Na<sup>+</sup> reabsorption in the kidney [30].

## Conclusion

Integrative and preventive therapies are possible with modern treatment modalities against urolithiasis. Family physicians who want to pursue more detailed study in integrative medicine need to be familiar with the evidence based natural therapies.

The synergistic effect of active compounds of propolis may be promising for urolithiasis and in this context further studies are encouraged on their bioavailability, stability in different preparations, and safe and effective doses for prevention or treatment of urolithiasis in animals and humans.

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