Propolis against Urolithiasis

Timucin Atayoglu A1, Guner Atayoglu A2, Oguzhan Gunduz3, Ismail Evren4, Sibel Silici5 and Noor Buchholz6

1Holistic & Integrative Medicine Association, Istanbul, Turkey
2State Family Health Center in Kucukcekmece Province, Istanbul, Turkey
3Department of Urology, Uskudar State Hospital, Istanbul, Turkey
4Department of Urology, Bakirkoy Dr Sadi Konuk Education and Research Hospital, Istanbul, Turkey
5Faculty of Agriculture, Erciyes University, Kayseri, Turkey
6Endourology & 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

Rec date: Jul 25, 2014; Acc date: Dec 29, 2014; Pub date: Dec 31, 2014

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 immune-modulator 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 immunemodulator...
Inhibitors decrease the production of uric acid, by interfering with making new solutions essential. Jean-Philippe Lavigne et al. evaluated antioxidant enzyme reductions. Treatment with free-radical scavenger and virulence in the urinary tract, representing a strategy to prevent 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].

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 inhibiting activity 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 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]. Ozurt 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 microalbuminuria-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+ 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.

Acknowledgements

The authors are grateful to the members of Turkish Apitherapy Association for their valuable contribution to the work with many useful suggestions.

References

1. Lieske JC, Segura JW (2004) "Evaluation and Medical Management of Kidney Stones”. In Potts, JM. Essential Urology: A Guide to Clinical Practice. Ed: 1st. Totowa, New Jersey: Humana Press. pp. 117–152.
2. Sutherland JW, Parks JH, Coe FL (1985) Recurrence after a single renal stone in a community practice. Miner Electrolyte Metab 11: 267–269.
3. Mandel N (1996) Mechanism of stone formation. Semin Nephrol 16: 364-374.
4. Nurse DE, McNerney PD, Thomas PJ, Mundy AR (1996) Stones in enterocystoplasties. Br J Urol 77: 684-687.
5. Mandel N (1998) Mechanism of stone formation. Semin Nephrol 16: 364-374.
6. Grases F, Costa-Bauzá A, García-Ferragut L (1998) Biopathological crystallization: a general view about the mechanisms of renal stone formation. Adv Colloid Interface Sci 74: 169-194.
7. Verkoelen CF, van der Boom BG, Schröder FH, Romijn JC (1997) Cell cultures and nephrolithiasis. World J Urol 15: 229-235.
8. Marcucci MC (1995) "Propolis: chemical composition, biological properties and therapeutic activity". Apidologie 26: 83–99.
9. Ankova VS, De Castro SL, Marcucci MC (2000) "Propolis: recent advances in research on chemistry and plant origin". Apidologie 31: 3–15.
10. De Almeida EC, Menezes H (2002) Anti-inflammatory activity of propolis extracts: A Review. J. Venom. Anim. Toxins 8.
11. Hermann K (1970) Über das vorkommen und die bedeutung von flavonen, flavonolen and flavanonen in lebensmitteln. Z Lebensm Unters Forsch 144: 191–202.

12. Stavric B, Matula T I (1992) Flavonoids in foods: their significance for nutrition and health. In: Ong A S H, Packer L. (Eds.), Lipid-Soluble Antioxidants: Biochemistry and Clinical Applications, Birkhauser, Basel. 274–294.

13. Khan SR, Kok DJ (2004) Modulators of urinary stone formation. Front Biosci 9: 1450-1482.

14. Wang Kai, Ping Shun, Huang Shuai, Hu Lin, Xuan Hongzhuang, et al. (2013) Molecular Mechanisms Underlying the In V itro Anti-Inflammatory Effects of a Flavonoid Rich Ethanol Extract from Chinese Propolis (Poplar Type). Evidence-Based Complementary and Alternative Medicine 2013.

15. Park Eun-Hee, Kim Sun-Hee, Park Soo-Sun (1996) Anti-inflammatory activity of propolis. Archives of Pharmacal Research 19: 337-341.

16. Borrelli F, Maffia P, Pinto L, Ianaro A, Russo A, et al. (2002) Phytochemical compounds involved in the anti-inflammatory effect of propolis extract. Fitoterapia 73 Suppl 1: S53-63.

17. Khayyal MT, el-Ghazaly MA, El-Khatib AS (1993) Mechanisms involved in the antiinflammatory effect of propolis extract. Drugs Exp Clin Res 19: 197-203.

18. Mo SF, Zhou F, Lv YZ, Hu QH, Zhang DM, et al. (2007) Hypouricemic action of selected flavonoids in mice: structure-activity relationships. Biol Pharm Bull 30: 1551-1556.

19. Sanhuerza J, Valdes J, Campos R, Garrido A, Valenzuela A (1992) Changes in the xanthine dehydrogenase/xanthine oxidase ratio in the rat kidney subjected to ischemia-reperfusion stress: preventive effect of some flavonoids. Res Commun Chem Pathol Pharmacol 78: 211-218.

20. Yoshizumi K, Nishioka N, Tsuji T (2005) [Xanthine oxidase inhibitory activity and hypouricemia effect of propolis in rats]. Yakugaku Zasshi 125: 315-321.

21. Bichler KH, Eipper E, Naber K, Braun V, Zimmermann R, et al. (2002) Urinary infection stones. Int J Antimicrob Agents 19: 488-498.

22. Lavigne Jean-Philippe, Vitrac Xavier, Bernard Louis, Bruyère Franck, Sotto Albert (2011) Propolis can potentialise the anti-adhesion activity of proanthocyanidins on uropathogenic Escherichia coli in the prevention of recurrent urinary tract infections. BMC Research Notes 4:322

23. Kolankaya D, Selmanoglu G, Sorkun K, Salih B (2002) "Protective effects of Turkish propolis on alcohol-induced serum lipid changes and liver injury in male rats,". Food Chemistry 78: 213–217.

24. Krishna Ramaswamy, Ojas Shah (2014) Metabolic syndrome and nephrolithiasis. The Translational Andrology and Urology 3: 285-295.

25. Holoch PA, Tracy CR (2011) Antioxidants and self-reported history of kidney stones: the National Health and Nutrition Examination Survey. J Endourol 25: 1903-1908.

26. Ozyurt H, Irmak MK, Akyol O, Sogut S (2001) Caffeic acid phenethyl ester changes the indices of oxidative stress in serum of rats with renal ischaemia-reperfusion injury. Cell Biochem Funct 19: 259-263.

27. Ozen S, Akyol O, Iraz M, Sogut S, Ozugurlu F, et al. (2004) Role of caffeic acid phenethyl ester, an active component of propolis, against cisplatin-induced nephrotoxicity in rats. J Appl Toxicol 24: 27-35.

28. Zhu Wei, Chen Minli, Shou Qiyang, Li Yinghua, Hu Fuliang (2011) Biological Activities of Chinese Propolis and Brazilian Propolis on Streptozotocin-Induced Type 1 Diabetes Mellitus in Rats. Evidence-Based Complementary and Alternative Medicine 2011.

29. Borihi L, Meschi T, Guerra A, Briganti A, Schianchi T, et al. (1999) Essential arterial hypertension and stone disease. Kidney Int 55: 2397-2406.

30. Aoi Wataru, Niisato Naomi, Miyazaki Hiroaki, Marunaka Yoshinori (2004) Flavonoid-induced reduction of ENaC expression in the kidney of Dahl salt-sensitive hypertensive rat. Biochemical and Biophysical Research Communications 315: 892-896.