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Seaweed sulphated polysaccharide as an inhibitor of calcium oxalate renal stone formation

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ABSTRACT

Sulphated polysaccharides (SPSs) from various seaweeds possess broad spectrum therapeutic and biomedical properties that are known to play a significant inhibitory role in calcium oxalate (CaOx) kidney stones. CaOx stone formation is a multistep process, which includes crystal nucleation, growth, aggregation, and crystal retention. Renal tubular cell injury is one of the determining factors leading to crystal retention and formation of stone in the nidus. In the present review, a comprehensive account was revealed on the therapeutic mechanisms of action of various seaweed SPSs on CaOx renal stone formation. Seaweed SPSs are inhibitor of crystal nucleation, growth, and aggregation. SPSs prevent renal tubular cell damage because of its antioxidant properties, thereby preventing crystal adherence and internalization. Seaweed SPSs are promising molecules because of their role in renal stone prevention. This study contributed much interest for researchers in a wide spectrum.

Contents

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1. Introduction

Renal stone disease has afflicted humans for centuries. Kidney stones affect up to 5% of the population, with about 8%–10% lifetime risk of passing a kidney stone (Asplin, Favus, & Coe, 1996). Although massive progress in kidney stone research exists, the exact mechanism of kidney stone formation and prevention is still unknown. Renal stones are formed from small crystals; however, the crystals are very common and innocuous provided that they are excreted with the urine (Verkoelen, 2006). Crystals in a healthy person and a lithogenic patient are frequently diverse in size and phase (Daudon & Jungers, 2004). Thus, the crystals stay behind the kidneys of stone formers. The supersaturation of urine with poorly soluble calcium salts leads to crystal formation, which in turn may be a result of increased excretion of essential molecules, reduced urine volume, changed urine pH, or a combination of these factors (Coe, Parks, & Asplin, 1992; Ratkalkar & Kleinman, 2011). About 80% of the kidney stones are mainly composed of CaOx crystals (Moe, 2006), the most common of which is calcium oxalate monohydrate (COM) followed by calcium oxalate dihydrate (COD). The lack of urinary inhibitors supported the growth acceleration of the CaOx crystals and permitted crystals to aggregate with each other. The crystals grow large enough to be attached with the renal epithelial cells and retained within the renal tubules, which resulted in stone formation. Small stones are often spontaneously excreted through the urine, but larger stones are generally removed by extracorporeal shock wave lithotripsy and improved surgical procedures. Nevertheless, the recurrence rate of renal stone diseases is high (Aggarwal et al., 2002), which may eventually devastate the kidney. Hence, developing a new drug therapy for the prevention of this disease and its recurrence is a pressing need.

Isolated SPSs from seaweeds are characterized as a source of marine compounds having valuable applications in the field of pharmacology. In the Asian diet, seaweeds have been consumed as food for centuries and are also documented in traditional Chinese medicine to cure diseases for over 1000 years (McLellan & Jurd, 1992). SPSs that are derived from edible marine algae exhibited many biological activities, including anticoagulant (Barahona et al., 2014; Faggio, Pagano, Dottore, Genovese, & Morabito, 2016; Fidelis et al., 2014), antiviral (Mendes et al., 2014; Rabanal, Ponce, Navarro, Gómez, & Stortz, 2014), antitumour (Ropellato et al., 2015; Shao, Pei, Fang, & Sun, 2014; Vishchuk, Ermakova, & Zvyagintseva, 2011), anti-inflammatory (Ribeiro et al., 2014), anti-HIV (Thuy et al., 2015), and antioxidant effects (Rodriguez-Jasso, Mussatto, Pastrana, Aguilar, & Teixeira, 2013; Sellimi et al., 2014; Souza et al., 2012). The molecular structure of each polysaccharide differs according to the algal species (Costa et al., 2010). The biological activity of these polymers was strongly allied to their chemical structure, molecular weight, and content of negatively charged groups, such as sulphate and carboxyl groups (Huang, Zhuo, & Guo, 2008).

Semisynthetic seaweed SPSs, namely, G871 and G872, were studied as inhibitors of CaOx crystallization (Cao et al., 1992) and COM crystal–cell interaction (Verkoelen et al., 1996). Boeve et al. (1994) reviewed the inhibitory effects of urinary SPS, glycosaminoglycans (GAGs), and other semisynthetic polysaccharides on urinary stones. The chemical structure of seaweed polysaccharides is similar to the urinary sulphated GAGs, an inhibitor of CaOx crystallization. Consequently, seaweed SPSs have been shown as powerful exogenous inhibitor of kidney stone diseases. In the present review, the inhibitory activity of various seaweed SPSs on CaOx stones formation was summarized, and an overview on the repair and protective mechanism of seaweed SPSs with different properties against CaOx crystal formation and retention was described. This review is anticipated to provide support for further exploration of new molecules for renal stone healing.

2. Role of SPS in inhibition of CaOx crystallization

CaOx kidney stone formation is the primary result of the supersaturation of CaOx salts in the renal tubular fluid. In this regard, the process of stone formation involved crystal nucleation, growth, and aggregation, which depends on supersaturation and also on crystallization inhibitors and promoters. When urinary supersaturation exceeds the limit of metastability, oxalate and calcium ions start to form spontaneous crystal nucleation (Ratkalkar & Kleinman, 2011). Once a crystal nucleus is accomplished, the overall free energy is decreased with the addition of new ions; this is the beginning of the growth of crystals (Aggarwal, Narula, Kakkar, & Tandon, 2013). Crystal growth is one of the basic mechanisms for kidney stone formation as a crystal cannot become large enough to block the renal tubules; crystals are easily washed out through the urine (Finlayson & Reid, 1978). Accordingly, the growing crystals aggregate with one another to form clusters. The growth of crystals may not be adequate to lodge in the tubules; thus, individual crystals may aggregate to form large crystal clusters that could potentially do so (Worcester, 1994). Although normal urinary environment inhibits the crystallization process, the lack of inhibitory activity or abnormality in the functions of inhibitors and the imbalance between urinary-promoting and urinary-inhibiting factors are proposed to be associated with urinary stone formation (Basavaraj, Biyani, Browning, & Cartledge, 2007). GAGs are polysaccharides that are found in the urine and have an important role in CaOx crystallization (Boeve et al., 1994; Roberts & Resnick, 1986). GAGs seem to be an effective inhibitor of CaOx crystal growth and aggregation and prevent crystal adhesion to renal cell (Dussol & Berland, 1996). However, the concentration of GAGs in the urine is very low to decrease CaOx supersaturation (Basavaraj et al., 2007). The physicochemical properties and molecular structure of seaweed SPSs are composed of repeated disaccharide sugar chain similar to those of GAGs. Thus, the SPS from marine algae acts as a urolith inhibitor in the urine, which could act as a GAG substitute. The inhibitory effects of SPS on CaOx crystallization are explained by directly interacting it with crystals, blocking the growth sites, coating the surface of the growing calcium crystals, or changing the crystal surface property.

Recently, many researchers studied the effect of various isolated seaweed SPSs on CaOx crystallization using diverse crystallization models and various media. Such studies suggested that the SPS could inhibit nucleation, growth and