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Review

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Potential of carrageenans in foods and medical applications

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ABSTRACT

Background: Carrageenans, the polysaccharides obtained by extraction of certain species of red seaweeds (*Rhodophyceae*), have been widely used in both food industry and medical applications because of their excellent physical functional properties that are used as gelling, thickening and stabilizing agent. Several studies showed biological properties of carrageenans such as antiviral, anticoagulant, antitumor, antioxidant, anti-inflammatory and immune-modulatory activity.
Aims: This study is to bring a short overview of the potential of carrageenans in foods and medical applications based on their biological activities.
Methods: This short overview used relevant works and articles examined that collected through several electronic database including PubMed, Science Direct, Springer Link and Google Scholars for the years 1991-2018 with full text in English.
Results: This study is an alternative approach that is necessary in order to present the potential of carrageenans in foods and medical applications.The advantages of carrageenans as a food additive and pharmaceutical formulation lie on their high availability, low cost, and low induction of resistance.
Conclusion: This review suggested that carrageenans are suitable to be applied in many kinds of food products as gelling and thickening agent with their antioxidant potency as well as medical applications such as pharmaceutical formulations in drug delivery and experimental medicine. However, more comprehensive studies on toxicity and side effect of carrageenans are necessary.

INTRODUCTION

Polysaccharides from some seaweeds have been reported to possess biological activity of potential medical value, including carrageenan [1]. Carrageenans are gel forming and viscosifying polysaccharides, which are obtained by extraction of certain species of red seaweeds (*Rhodophyceae*) [2]. Carrageenans are split into six basic forms based on their chemical classification: Kappa (κ)-, Iota (ι)-, Lamda (λ)-, Mu (μ)-, Nu (ν)- and Theta (θ)- [3]. Carrageenans are composed of a linear galactose backbone with a varying degree of sulfatation between 15% and 40% [2]. Carrageenans are formed by alternate units of Ɗ-galactose and 3,6-anhydro-galactose (3,6-AG) joined by α-1,3 and β- 1,4-glycosidic linkage and they have an average relative molecular mass well above 100 kDa [4]. Carrageenans have the EU additive E-number E407 or E407a, which E407a contains amount of cellulose [4]. The Acceptable Daily Intake (ADI) of carrageenan is 0-75 mg/kg bw and the concentration in food products ranges 0.005-2.0% by weight [5].

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Carrageenans have been used both in food and non-food products.

In terms of food industry, carrageenans are used as gelling, thickening and stabilizing agent because of their excellent physical functional properties [3]. Carrageenans are used in yogurt, sauces, jellies, chocolate-milk, frozen desserts, cottage cheese and many other products [2]. Carrageenans have been considered as safe and become a constituent of many food products for many years. It was confirmed in 2001 at the 57th meeting of the Joint Food and Agriculture Organization of the United Nations World Health Organization Expert Committee in Food Additive (JECFA) and only degraded carrageenans were associated to adverse health effects, which should not be consumed [6].

In the non-food industry, carrageenans have been used for cosmetics, pharmaceutical formulations and experimental medicine [4]. Carrageenan has been used for enhancing agent for controlled drug release and prolonged retention in drug delivery [7]. Much research in recent years has focused not only on food applications but also on medical applications. There are several biological properties of carrageenans such as antiviral activity, anticoagulant activity, antitumor activity, antioxidant activity, anti-inflammation and immunomodulatory activity that might bring more benefits in medical applications. Numerous experiments have established that carrageenan has promising potential to be developed as therapeutic agents due to their *in vivo* and *in vivo* activity.

Although there were a lot of study about biological activities of carrageenans, few researchers have addressed the potential of carrageenans in foods and medical applications based on their biological activities. An alternative approach is necessary in order to present the potential of carrageenans in foods and medical applications. Regarding to these widely function, the aim of this review article is to bring a short overview of the potential of carrageenans in foods and medical applications based on their biological activities.

METHODS

The materials of this review were collected on December 2017 to January 2018 through 4 electronic database: PubMed, Science Direct, Springer Link and Google Scholars for the years 1991-2018 with full text in English. There are many biological properties of carrageenans including antiviral activity, anti-coagulant activity, antitumor activity, antioxidant activity, anti-inflammation and immunomodulatory activity, which are the most common effect of carrageenans as food additive or application in medical purpose. Only relevant works and articles examined were included.

THE POTENTIAL OF CARRAGEENANS AS AN ANTIVIRAL

Carrageenans as food additive in many products have beneficial effect including antiviral activity. Carrageenans are considered a good alternative for preventing a wide range of disease, mainly caused by enveloped viruses [8]. The advantages lie on their high availability, low cost and low induction of resistance. The antiviral activity of carrageenan can be influenced using depolymerization [9].

Carrageenans have antiviral activity against human papillomavirus (HPV) [10, 11], herpes simplex and dengue virus [12]. Kappa-, iota- and lambda-carrageenans have a potent inhibitory effect on replication of hepatitis A virus (HAV) in the human hepatoma cell line PLC/PRF/5, which are no cytotoxic effects with concentration up to 200 μg/ml [13]. Another study suggest that carrageenan might serve as an effective topical HPV microbicide [14]. Carrageenan oligosaccharides and its sulphated derivatives present good inhibitory actions on anti-influenza A virus (IAV) *in vitro* and *in vivo* [15].

Iota-carrageenan inhibits a step in virus replication subsequent to viral internalization but prior to the onset of late viral protein synthesis [16]. Another study suggests that iota-carrageenan nasal spray appears to be a promising treatment for safe and effective treatment of early symptoms of common cold caused by virus [17]. Carrageenan nasal spray in virus can be an effective treatment of common cold in children and adults [18].

Inhibition of viral cytopathology and antigen expression was also detached to the presence of the carrageenans [19]. On another case, κ/β-carrageenan extracted from *Tichocarpus crinitus* possesses antiviral activity against Tobacco mosaic virus (TMV), which inhibits TMV infection in detached tobacco leaves at early stages [20]. Carrageenan, especially κ/β-carrageenan extracted from *Tichocarpus crinitus*, may be regarded as a promising preparation for plant protection against viruses [21]. The κ/β-carrageenan from *Tichocarpus crinitus* has another antiviral activity against potato virus X (PVX) infection in the leaves of *Datura stramonium* L, that shows the potential of carrageenans as antiviral [22].

BIOLOGICAL ACTIVITY OF CARRAGEENANS IN EDEMA STUDY

Some carrageenans showed a reduced anticoagulant activity only at concentration that were considerably higher than the IC_{50} [23]. A study about quantitative evaluation of inflammation demonstrated that iota and lambda carrageenans have higher inflammatory potential than do kappa-carrageenans [24]. This study induced paw edema using kappa, iota and lamda-carrageenans in saline solution into the hind paw male Wistar rats.

The histological analysis in paw edema suggests that lamda and iota carrageenans showed major cellular infiltration in relation to kappa-carrageenan [24]. Kappa/iota carrageenan possessed for the potential anticoagulant activity, which was extremely strong in low concentration [25]. Anticoagulant activity of carrageenans depends on the monosaccharide composition of polysaccharides, number, position and distribution of sulphate groups along galactan chain [25].

The study by Yermak et al. (2012) showed hybrid kappa/beta-carrageenan has fairly high activity independent on concentration. Position of sulfate groups shows the biggest impact on both the anticoagulant activity and the cell proliferation [26]. Sulfation at C2 of 3,6-anhydro-α-Ɗ-Gal*p* and C6 of β-Ɗ-Gal*p* increased the anticoagulant activity [27]. Another theory suggests that the ability to influence on the cytokine production by human cells is greatly dependent on concentration and structure of polysaccharides [25].

Carrageenan has been used on some *in vivo* studies. The study by Matsumoto et al. (2015) demonstrated the anti-inflammatory activity of linezolid and other anti-MRSA agents using the carrageenan-induced rat paw edema model. However, further studies are needed on the molecular mechanisms underlaying these anti-inflammatory activities [28]. Another studies suggest that kappa-carrageenan oligo-saccharide may have some biological activity for preventing the process of some central nervous system disease [29].

The study by Yermak et al. (2012) suggest that all types of carrageenans induced the secretion of anti-inflammatory IL-10 in dose-dependent manner. The immunomodulation activity of carrageenans depends on the composition of polysaccharides including their position, number and distribution of sulphate groups along galactan chain [25]. Another factor that might be the key factor is the basic structure of the carrageenan [30].

THE POTENTIAL OF CARRAGEENANS AS ANTITUMOR

Carrageenans as a food additive have some benefits such as antitumor activity. Carrageenan has effect to cancer cells that could possibly be developed into a tumor cell-specific anticancer agent [31]. Antitumor mechanism of carrageenans were relevant to their inhibitory activity of tumor cells directly and activating immunocompetence of the body. However, the exact mechanisms should be achieved through more other experiments [32].

Chemical modification of carbohydrate can lead to differences in their biological activities where sul-fation of carrageenan oligosaccharides will enhance the antitumor effect and boost the antitumor immunity [33]. Carrageenan oligosaccharides exert its antitumor effect by promoting the immune system [30]. The degraded λ-carrageenan could add the antitumor activities and improve the immune-competence damages [32].

Molecular weight of carrageenans had notable effect on the activities [34]. Another studies suggest that the antitumor activity of carrageenan oligosaccharides may be due to their recognition or interaction with the tumor-specific molecules [35]. The anti-tumor activity of the sulfonated oligosaccharide is related to its antioxidant activity, immunological regulation and inhibition of tumor metastasis [36]. Furthermore, there needs further investigation in term of anti-tumor mechanism, relationship between structure and biological activity remain to be elucidated and the exact correlation between molecular weight and antitumor activity.

CARRAGEENANS AS A FOOD ADDITIVE WITH ANTIOXIDANT ACTIVITY

Carrageenans have potential as an antioxidant which is widely used in the food industry [1] as gelling and stabilizing agent [37]. Algal polysaccharides have beneficial effect as antioxidant with respect to the inhibition of superoxide radical formation [1]. The inclusion of antioxidant-rich polysaccharides, especially carrageenan, or other fractions will probably prevent the oxidative deterioration of food.

Current studies about application of carrageenan on food suggest that carrageenans have antioxidant activity. Kappa-carrageenan oligosaccharides were applied to increase shelf-life of frozen shrimps during 120 days of frozen storage and their antioxidant affected on myofibrillar protein in peeled shrimp (*Litopenaeus vannamei*) [38]. As an antioxidant, carrageenan has potential application as a photoprotective agent in addition to just being used as an excipient [39]. The antioxidant activity of carrageenans depend on their structural composition and the extraction method used [40].

CONCLUSION

Some studies showed biological properties of carrageenans including antiviral, anticoagulant, antitumor, anti-inflammatory and immunomodulatory activity that can be appropriate in medical applications. The advantages lie on their high availability, low cost and low induction of resistance. It is suggested that carrageenans are suitable to be applied in many kinds of food products as gelling and thickening agent with their antioxidant potency as well as medical applications such as pharmaceutical formulation in drug delivery and experimental medicine. However, all of these potentials need to be approved by further studies that focused on the each biological activity of carrageenans after applied in food products or medicines. Moreover, comprehensive studies on toxicity and side effect of carrageenans are necessary.

CONFLICT OF INTERESTS

The author declares that the author has no conflicts of interest.

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