Aeration-by-sea used in combating airborne viruses in ventilation systems

Antiviral activity of carrageenan

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1. Literature review

The carrageenans (CNGs) are a family of linear sulfated polysaccharides extracted from red edible seaweed. The diverse chemical structure and the degree of sulfation divides CGNs into three major polysaccharide groups, kappa (κ)-, iota (ι)- and lambda (λ)-CGNs, which contain one, two, and three negatively charged sulfate ester groups per disaccharide repeating unit, respectively. Due to their physiochemical properties, including gelling, thickening, and stabilizing, CGNs are widely used in the food industry, especially in dairy and meat products because of their strong binding to food proteins. As biomolecules, CGNs have various biological activities, including anti-tumor (Liu et al., 2019), anti-oxidation (Cristiane et al., 2007), anti-inflammation (Davydova et al., 2020) as well as strong anti-microbial properties (Zhu et al., 2017).

Numerous *in vitro* and *in vivo* studies reported anti-viral properties of CGNs particularly against such enveloped viruses as enterovirus 71 (Chiu et al., 2012), human immunodeficiency virus (HIV), herpes simplex virus (HSV; Kolender et al., 1998), human cytomegalovirus (HCMV; Hamasuna et al., 1993), dengue virus (Talarico & Damonte, 2016) and respiratory syncytial virus (RSV), African swine fever virus (ASFV), influenza A, B virus (Wang et al., 2011) and coronavirus (Jang et al., 2021) but also against non-enveloped viruses including rhinovirus (Grassauer et al., 2008). Research suggests that carrageenan affects viruses in direct and indirect ways. Indirect virucidal effect is associated with the inhibition of virus replication in the host cell, interference of virus adsorption and binding to the cell, as well as uncoating. Thus, the indirect antiviral activity of CGN lies in the inhibition of the initial virus infection process. However, these studies showed that the antiviral activities of CGN are associated with the molecular weight and the sulfated fraction as the antiviral activity only applies if CGN can penetrate the tissue to protect the host cells from the infecting virus. On the other hand, the direct virucidal effect is attributed to the negative charge of CGN which enables the polysaccharide to bind to enveloped viruses (such as Influenza virus and Coronavirus) and form virus-carrageenan complexes, rendering the envelope unavailable for attachment to the host cell (Wang et al., 2012).

Influenza virus and coronavirus are major causes of human respiratory diseases. Although, therapeutic antivirals and preventive vaccines against influenza virus have been successfully developed, emerging

drug-resistant strains and mismatch-derived inefficacy of vaccines still result in an estimated annual mortality burden of 290,000 to 650,000 deaths. Moreover, despite the formidable circulation of recently emerging coronaviruses such as SARSCoV (first identified in 2003), MERS-CoV (identified in 2012), and currently circulating SARS-CoV-2 still there are no coronavirus-specific antivirals (Jang et al., 2021). Since, the symptoms and transmission routes of these two respiratory viruses are very similar, a broad-spectrum antiviral agent such as CGN would be an advantageous strategy incombating these pathogens.

2. Studies on the antiviral activities of carrageenan performed by Avecom

The antiviral activity of κ-CGN (the polysaccharide used as an active compound in the developed filter coating) against coronavirus was tested by Rega Institute (KU Leuven, Belgium). **The results confirmed that the tested κ-CGN solution had an antiviral activity against the human coronavirus OC43 with EC50 values in the range of 20-100 µg/mL**. Interestingly, comparable results were also obtained when antiviral activity of κ-CGN was tested against Influenza A virus. In this study Wang et.al. reported that the EC50 value of κ-CGN against Influenza A virus is 32.1 µg/mL (Wang et al., 2011). Moreover, intranasal administration of ι-CGN showed therapeutic effects in an influenza A virus-infected mouse model (Leibbrandt et al., 2010). Notably, a randomized double-blind study in volunteers with early symptoms of the common cold confirmed the efficacy and safety of an antiviral ι-CGN nasal spray (Eccles et al., 2010).

Since the filter coating applied in the "SEA AERATION'' system developed by TakeAirLabs and Avecom consists of two layers: product P and κ-CGN, the antiviral activity of κ-CGN suspended in product P was also examined. In this study, the porcine reproductive and respiratory syndrome virus (PRRSV) developed by Prof. Hans Nauwynck the head of the Virology laboratory at the Faculty of Veterinary Medicine (Ghent University) together with a group from Department of Infectious and Parasitic Diseases, FARAH Research Centre, Faculty of Veterinary Medicine (Liege University) as a surrogate for SARS-CoV-2 (COVID19) virus was used. Because the utilization, concentration, and cultivation of infectious SARS-CoV-2 necessary for analyses investigating its inactivation pose obvious problems in terms of the availability and equipping of BSL3 facilities, the use of conservative surrogates is justified and crucial to gain an as accurate as possible insight into SARS-CoV-2 survival in the air ventilation system. While PRCV, which infects the respiratory tract of swine, is not in the same genus as SARS-CoV-2, the two members of the subfamily Coronavirinae in the family Coronaviridae show sufficient similarities as to genome length and virion structure (notwithstanding differences in envelope glycoproteins), for them to be expected to behave similarly outside their hosts. **The incubation of PRCV with the carrageenan/product P emulsion resulted in 98 % reduction of the virus titer.** These results confirm the antiviral potential of the developed filter coating against coronaviruses and that its effect can probably be extended to other enveloped viruses as it most likely follows the direct mode of virus inactivation described above.

3. Bibliography

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