International Journal of Scientific Engineering and Applied Science (IJSEAS) – Volume-7, Issue-11, November 2021
ISSN: 2395-3470
www.ijseas.com

Anti-viral properties of carrageenan, a sulphated polysaccharide derived from marine red algae against Covid 19 (SARS-CoV-2) infection- Future prospective

[1] Amruth P., [2]Akshay P., [3] Rosemol Jacob M., [4]R. Anandan, [5]Suseela Mathew

[1,2,3] Reserach scholar, [4,5] Principal Scientist

[1,2,3,4,5,] Biochemistry and Nutrition Division, ICAR-Central Institute of Fisheries Technology, Kochi-682029, Kerala, India

[1,2,3] Faculty of Marine Sciences, Cochin University of Science and Technology Kochi-682022, Kerala

ABSTRACT: The novel coronavirus (nCoV) disease COVID-19, triggered by SARS-CoV-2 is a major threat caused to the public health in the 21th century. Combating the same is a herculean challenge for the scientific world. This is represented as the third corona virus outbreak in preceding 20 years, followed by SARS (2002-2003) and MERS (2012). However, there is no clinically effective drugs against COVID-19 virus infection. For International medical community, development of effective drugs to avoid and cure a viral attack is an urgent requisite during this time. As a consequence, we have piloted an organised review presenting the anti-viral prospective of carrageenan, a sulphated galactan derived from red seaweed. Sulphated polysaccharides are demonstrated as potential antiviral that can intrude the initial stages of viral infections, have wide prospects in anti-corona virus applications. Carrageenan and its oligosaccharides are well reported for its anti-viral properties; chiefly via the obstruction of the attachment stage of virus. The current review presents the survey of antiviral prospective of carrageenan and aims to provide new approach to researchers for exploring seaweed polysaccharides to develop effective therapy against strains of SARS-CoV-2 virus.

Keywords: Anti-viral properties, Carrageenan, COVID-19, SARS-CoV-2, Sulphated polysaccharide

INTRODUCTION

Corona viruses are positive-sense single-stranded enveloped RNA viruses, (Fig.1) that infects vertebrates including animals and human beings causing respiratory and enteric diseases [Weiss *et al.*, 2011; Heald *et al.*, 2012; Anthony *et al.*, 2017]. Corona virus are of four types namely α, β, γ and δ, amongst α- and β-type comprise strains which are human pathogenic [Cui *et al.*, 2019]. The novel strain of COVID-19, from acute respiratory syndrome corona virus 2 (SARS-CoV-2) emerged in 2019 had spread to > 210 countries and caused great threat to global faces. SARS-CoV-2 have infected >8000 people, lead to 774 mortalities in twenty-seven countries [Parvez and Parveen 2017]. It has been reported as the most contagious form and ranked as third recorded escape of virus from animals to humans < 2 decades [Yang *et al.*, 2020] that created severe health implications to humans [Tang *et al.*,2020].

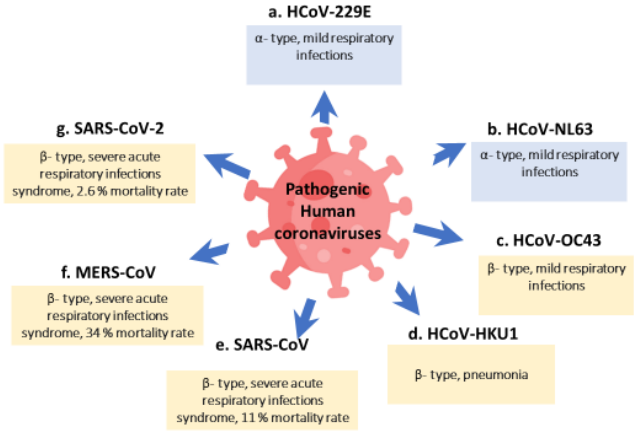

Figure 1: Pathogenic human coronaviruses

The spike glycol-protein (S –protein) of corona virus is considered as the major target for vaccine development. The S protein of corona virus play key role in pathogenesis and induce immune response to the host [Du *et al.*, 2009; Liu *et al.*, 2020]. Till date, there is no effective clinical therapy for COVID-19 infections. Variety of therapies targeted to inhibit virus growth and replication are found to be ineffective as a consequence of mutation and resistance acquired by them against the newly introduced therapies [Chase *et al.*, 2011]. In this regard, there is an important requisite to prepare target specific, high-efficiency, low-toxic drugs against corona virus. Seaweeds owing to their high sulphated polysaccharides content, wide availability, minimum production cost, biodegradability, non-cytotoxic, and biocompatible nature serves as attractive candidates for developing prospective anti-virals [Perez *et al.*, 2016; Hao *et al.*, 2019; Besednova *et al.*, 2019; Chen *et al.*, 2020]. Sulphated polysaccharides mimic heparin sulphate and are demonstrated to inhibit enveloped virus replication [Pereira and Critchley, 2020] by impeding the initial stages of viral replications. This is ascertained by masking the positive charge of viral surface receptors, which restrict them from binding to heparan sulphate proteoglycans on the surface of the host [Witvrouw *et al.*, 1997; Klimyte et al., 2006; Talarico and Damonte, 2007; Hao *et al.*, 2019]. Hence, they are good candidates for developing effective drugs for viruses. In this review, we presents the anti-viral prospective of the commercially important sulphated polysaccharide, carrageenan; their mechanism of anti-viral actions in brief to deliver a novel methods for the formulation of clinically effective therapy against corona virus. In traditional Chinese medicine, polysaccharides serve as a major ingredient, gained potential application prospect in the prevention and cure of corona virus due to their pronounced anti-viral functionality and remarkable anti-viral mode of action. Carbohydrate attaching agents are having the efficacy to inhibit porcine reproductive and respiratory syndrome virus (PRRSV), mouse hepatitis virus (MHV), feline corona

viruses I and II serotypes, infectious bronchitis virus (IBV), transmissible gastroenteritis virus and corona virus [Ghosh et al.,2009].

Carrageenan remains as a linear, anionic, sulphated polysaccharide derived from marine red seaweed [Manuhara *et al.*, 2015]. It is structurally composed of D-galactose and 3, 6-anhydro-galactose units with α-1,3 and β-1,4 glycosidic linkage [Rees, 1972; Necas and Bartosikova, 2013]. Carrageenan based on the number and position of sulfate groups of 3, 6 anhydro-galactose (3, 6 AG) are classified into various forms such as κ, λ, ι, ε, μ. The number and position of sulphate residues of 3, 6 AG influence primarily its structural characteristic. Structurally, κ-carrageenan constitutes a 3, 6 AG bridge with single sulphate ester group, ascertains low hydrophilicity, λ-carrageenan pose no hydrophobic 3, 6 AG bridge and constitute three hydrophilic sulphate ester groups, ascertaining greatest hydrophilicity at almost all conditions. While, i-carrageenan poses a 3, 6 AG bridge with two sulfate ester groups [Distantina and Fahrurrozi 2011]. Carrageenan is well noted for its pronounced activities such as anti-viral [Marchetti et al., 1995; Carlucci et al., 1999; Campo et al., 2009], immunomodulatory [Zhou et al., 2004] and numerous others. The chemical structure of carrageenan is depicted in fig. 2.

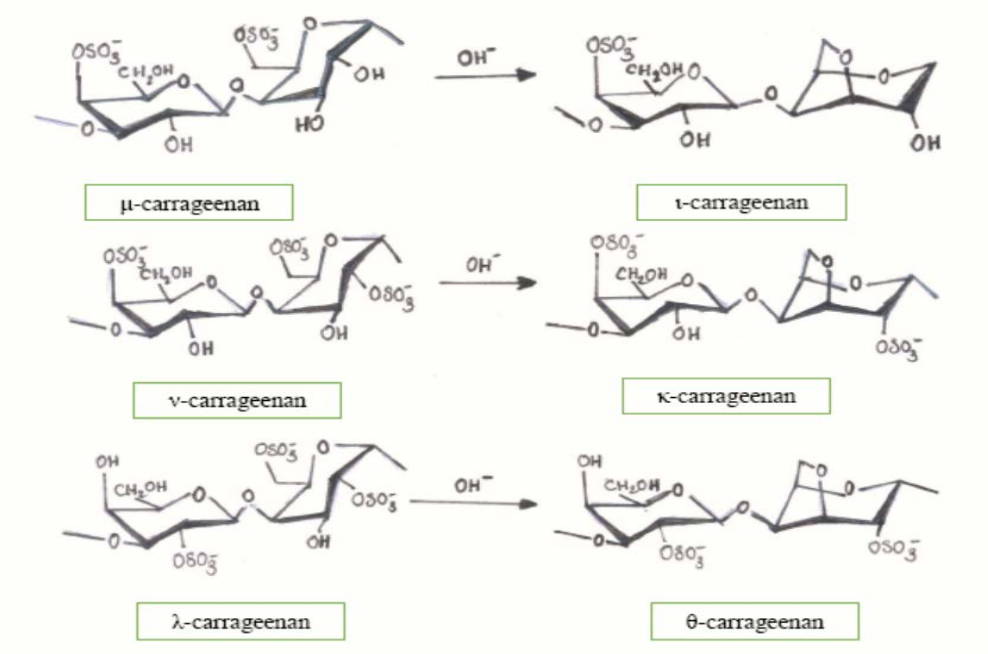

Figure 2: Chemical structure of carrageenan

Carrageenan, a potential anti-viral candidate for COVID-19 research

Although, carrageenan is described to have a direct virucidal effect against different enveloped viruses [Chen and Huang, 2018], there are only few studies tested for virucidal efficacy of sulphated polysaccharide, especially carrageenan. Studies conducted by Harden and co-workers (2009) reported the antiviral activity against herpes simplex virus-2 of carrageenan extracted from *Gigartina atropurpurea*. Antiherpetic activity of λ-carrageenan

derived from *G. skottsbergii*, has been conducted with suid herpesvirus-1 and bovine herpesvirus-1 which are animal herpes viruses [Diogo *et al.*, 2015]. In addition, Gomaa and Elshoubaky [2016] have reported the inactivation of herpes simplex virus-1 and Rift valley fever virus by using carrageenan extracted from *Hydroclathrus cathralus* and *Acanthophora specifira*. It was observed that varicella zoster virus infectivity was inhibited ≈ 85% when treated with ι-carrageenan's [Abu- Galiyun *et al.*, 2019].

Antiviral mechanism of action of carrageenan

Carrageenan and their derivates are prospective antivirals that are effective to impede the growth and replication of enveloped viruses. The members of Herpesviridae family constituting herpes simplex virus types 1 and 2 [Talarico *et al.*,2004; De *et al.*,2006; Harden *et al.*,2009;], cytomegalovirus [Baba *et al.*,1988], varicella-zoster virus [Abu- Galiyun *et al.*,2019], equid herpesvirus 3 [Vissani *et al.*,2016], suid herpes virus type 1 and bovine herpesvirus type 1 [Diogo *et al.*,2015] remain as the most studied forms. Other enveloped viruses affected by carrageenan include dengue virus type 2 [De *et al.*,2006; Talarico *et al.*,2007], human immunodeficiency virus [Yamamnda *et al.*,2000], Sindbis virus [Baba et al.,1988], Influenza virus [Besednova *et al.*,2019], human metapneumovirus [Klimyte *et al.*,2016], porcine reproductive and respiratory syndrome virus [Guo *et al.*,2019], rabies virus [Luo *et a*l.,2015], Rift Valley fever virus [Goma et al.,2016], vaccinia virus [Gonzalex et al.,1987; Baba et al.,1988], Semliki forest virus, swine fever virus and hantaviruses [Pavliga et al.,2016].

Moreover, in a recent study, it is established that ι and λ carrageenan have a strong inhibitory action against SARS-CoV2 [Bansal *et al.*,2020; Jang *et al.*,2021, Morokutti-Kurz *et al.*,2021], and other sulphated polysaccharide have been assumed as good candidates for treatment of COVID-19 infection [Andrew and Jayaraman, 2021]. There are also few relevant studies reported the antiviral functionality against human rhinovirus (non-enveloped virus) [Grassauer et al., 2008], enterovirus 71 [Chiu *et al.*, 2012], and papillomavirus type 16 [Buck *et al.*, 2006]. A schematic illustration of antiviral action of carrageenan is summarized in Fig. 3

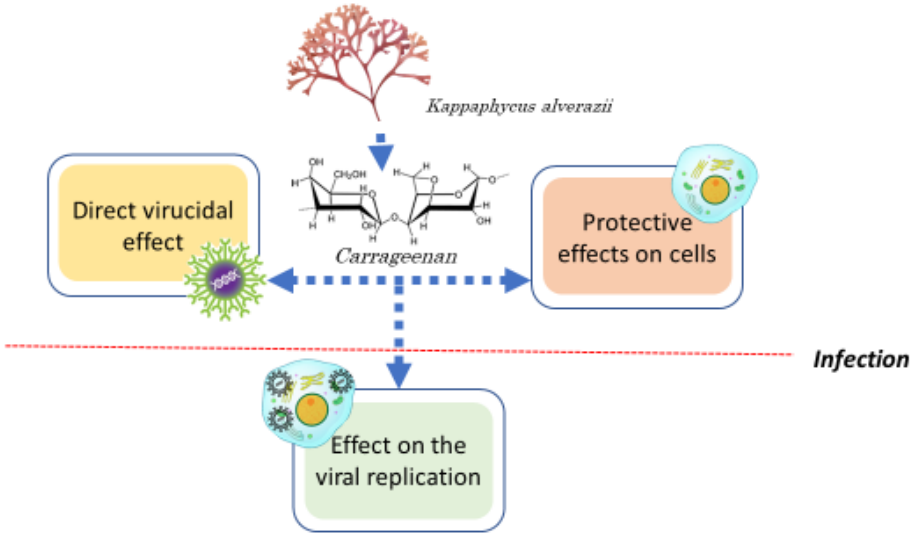

Figure 3: Schematic illustration of antiviral action of carrageenan extracted from red seaweeds

Effect of anti-viral property of carrageenan on viral replication

The inhibitory activity of carrageenan against viral replication is depicted in the fig. 4. Cell attachment (1), entry (2), uncoating (3), synthesis (4) Viral genome replication, translation and assembly (5), and release (6) are the six consecutive steps regulating the viral replication.

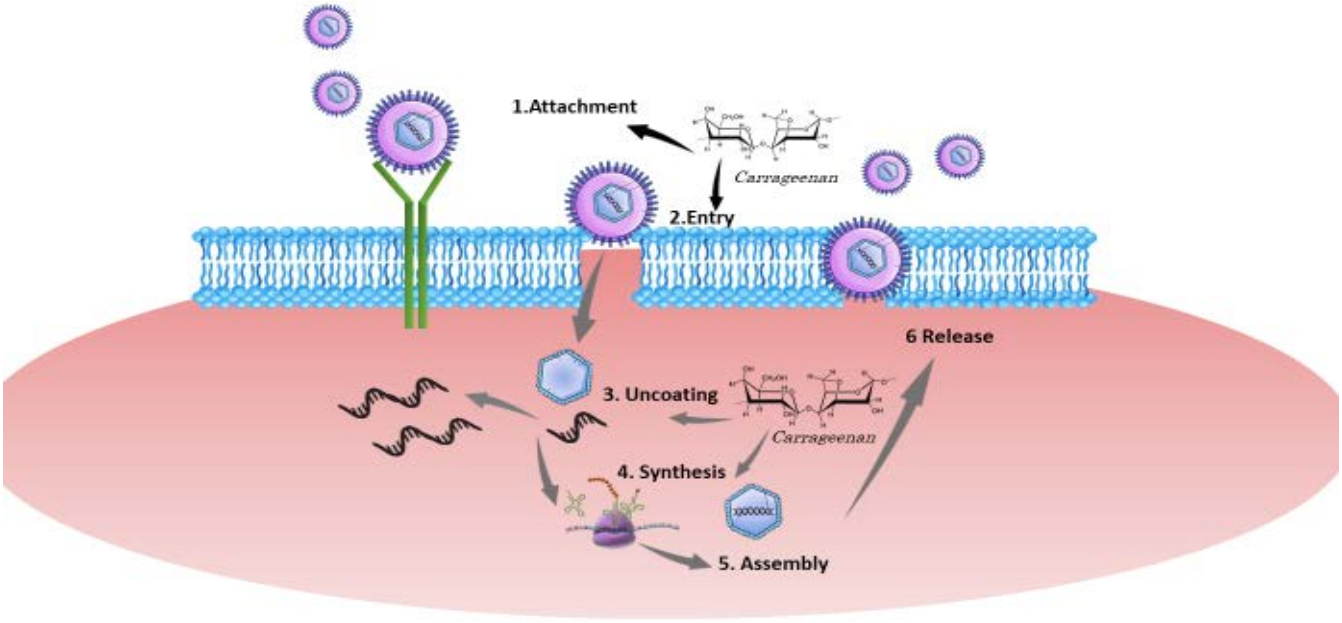

Figure 4: Schematic representation of the proposed model depicting the process of viral infection and ant-viral effect of carrageenan on virus replication (Adapted from Shi et al., 2017)

Inhibition of viral attachment

In several studies, carrageenan has demonstrated the potential to block the interaction amongst glycosaminogylcans, chiefly heparin sulphate and various enveloped (membrane) and non-enveloped (non-membrane) virus [Abu-Galiyun *et al.*,2019; Klimtye *et al.*,2016; Shao *et al.*, 2009]. In enveloped virus, carrageenan has the efficacy to bind with the proteins like glycoproteins of herpes simplex and hemaglutinin of influenza, restricting the entry of virus particles thereby preventing virus attachment to GAGs [Carlucci *et al.*, 1997]. The mechanism of restricting the contact between the capsid of virus and cell surface receptors, is assumed as an activity against non-enveloped viruses [Buck *et al.*, 2006].

Inhibition of Viral Internalization/Entry

Viral proteins undergo change in conformation when attached to cell surface. As a consequence, signaling cascades are activated and membrane of the cell destabilizes, resulting internalization of the virus [Sobhy *et al.*, 2017]. There is very scant information reported on the study of carrageenan against virus entry since the demonstration require more sophisticated techniques. However, the study of Talarico and Damonte [2007], λ-carrageenan can inhibit DENV-2 nucleocapsid internalization. It is reported that these compounds serve as effective inhibitor of primary dengue virus infection in human myeloid K562 and U937 cells. [Piccini *et al.*, 2020].

Likewise, rabies virus (RABV) internalization was affected by λ-carrageenan P32 [Luo *et al.*, 2015]. Herpes simplex virus type-1 internalization were blocked by ι-carrageenan, with the aid of radiolabeled viral particles

[Gonzalex *et al*., 1987]. These compounds are assumed to have inhibitory post attachment effect against human papilloma virus and human rhino virus by impeding essential conformational changes in the viral particle and by blocking virion surfaces involved in binding to specific receptors [Grassauer *et al*, 2008].

Inhibition of Uncoating

The study carried out by Talarico and Damonte [2007] demonstrated that dengue virus-2 internalization is blocked by λ-carrageenan. It is anticipated that virions that invade the cells are unable to undergo uncoating and are expelled from the endosomes. The work of Luo et al. [2015] revealed that λ-carrageenan P32 have the efficacy to prevent the conformational changes of RABV glycoprotein. As a consequence, cellular fusion is restricted, leading to inhibition of virus uncoating.

Inhibition of Synthesis

The effect of carrageenan polysaccharides on the synthesis of protein and enzymatic actions of avian mieloblastosis virus and herpes simplex virus-1 were reported. [Nakashima *et al*., 1987]. In the presence of carrageenan, the viral protein synthesis was declined for herpes simplex virus [Gonzalez *et al*., 1987]. It has been reported that reverse transcriptase activity of alpha mosaic virus were inhibited in the presence of λ-carrageenan derived from *Schizymeniapacifica* [Nakashima *et al*., 1987]. The effect of carrageenan on intracellular replication has been systematically evaluated in influenza A virus [Wang *et al*., 2011]. In Vero-infected cells, k form of carrageenan demonstrated the suppression of EV 71 mRNA synthesis [Chiu *et al*., 2012]. The assumed effect of ι-carrageenan in dengue virus and varicella-zoster virus intracellular replication steps has been observed. In Vero cells, seventy five percent inhibition of VZV intracellular replication and in C6/36 HT mosquito-derived cell line, the inhibition of replication of DENV were reported. [Abu-Galiyum *et al*., 2019, Talarico *et al*., 2011].

Protective Effect on Cells

Carrageenan exerts its antiviral role by binding to the viruses and inhibiting them from adsorbing to cell cultures. Hence the prophylactic action of carrageenan has not been explored. In the study of Chiu *et al*. [2012], Vero cells pre-treated with κ-carrageenan demonstrated that these molecule can bind to both surface of virus and the receptor of the cell and when C6/36HT mosquito cells were pretreated with ι-carrageenan, it resulted in a decline in the virus yield at post infection and the EC50 value remained comparable to the value ascertained on incubation of carrageenan and virus for the entire infection [Talarico *et al*., 2011].In Vero E6 cells, pretreatment with λ-,κ-and ι-carrageenan, reduced the titer of hantavirus PM-95 [Pavliga et al.,2016].

CONCLUSION AND FUTURE PROSPECTS

Polysaccharides gained significance for several decades due to the active ingredients present in them. In traditional Chinese medicine, carrageenan and their derivatives pose broad spectrum of antiviral activities and serve as a major ingredient. Carrageenan possess boundless application prospects in anti-corona virus due to their potential to exert anti-viral property by interfering with the life cycle of virus with their unique mechanisms. We speculate that carrageenan and its derivatives will exert anti-SARS-CoV-2 effects by the mechanisms as presented in Fig.4. This review may provide an innovative idea for the formulation of drugs against COVID-19

and effective therapies by understanding the anti-viral mechanism of action of carrageenan at various stages of viral replication.

Acknowledgement

The authors acknowledge Director, ICAR-Central Institute of Fisheries Technology (ICAR-CIFT), Cochin, Kerala, India for granting permission to publish the data acquired from the study. The authors would like to express their sincere gratitude to Cochin University of Science and Technology (CUSAT) and ICAR-Seaweed project

REFERENCES

[1] Abu-Galiyun E., Huleihel M, and Levy-Ontman O. Antiviral bioactivity of renewable polysaccharides against Varicella Zoster. *Cell Cycle.*18(24), 2019, 3540-3549.

[2] Andrew, M., and Jayaraman, G. Marine Sulfated Polysaccharides as potential antiviral drug candidates to treat Corona Virus disease (COVID-19). *Carbohydrate Research*. 2021, 108326.

[3] Anthony, S.J., Johnson, C.K., Greig, D.J., Kramer, S., Che, X., Wells, H., Hicks, A.L., Joly, D.O., Wolfe, N.D., Daszak, P. and Karesh, W. Global patterns in coronavirus diversity. *Virus evolution*. *3*(1), 2017, vex012.

[4] Baba, M., Snoeck, R., Pauwels, R., & De Clercq, E. Sulfated polysaccharides are potent and selective inhibitors of various enveloped viruses, including herpes simplex virus, cytomegalovirus, vesicular stomatitis virus, and human immunodeficiency virus. *Antimicrobial agents and chemotherapy*. 32(11), 1988, 1742-1745.

[5] Bansal, S., Jonsson, C. B., Taylor, S. L., Manuel Figueroa, J., Vanesa, A., Palacios, C., & César Vega, J. Iota-carrageenan and xylitol inhibit SARS-CoV-2 in cell culture 2020. *bioRxiv 2020*.

[6] Besednova, N.N., Zvyagintseva, T.N., Kuznetsova, T.A., Makarenkova, I.D., Smolina, T.P., Fedyanina, L.N., Kryzhanovsky, S.P. and Zaporozhets, T.S. Marine algae metabolites as promising therapeutics for the prevention and treatment of HIV/AIDS. *Metabolites*. 9(5), 2019, 87.

[7] Buck, C.B., Thompson, C.D., Roberts, J.N., Müller, M., Lowy, D.R. and Schiller, J.T. Carrageenan is a potent inhibitor of papillomavirus infection. *PLoS pathogens*. 2(7), 2006, 69.

[8] Campo, V. L., Kawano, D. F., da Silva Jr, D. B., and Carvalho, I. Carrageenans: Biological properties, chemical modifications and structural analysis–A review. *Carbohydrate polymers*. 77(2), 2009, 167-180

[9] Carlucci, M. J., Scolaro, L. A., and Damonte, E. B. Inhibitory action of natural carrageenans on Herpes simplex virus infection of mouse astrocytes. *Chemotherapy*, 45(6), 1999, 429-436.

[10] Carlucci, M. J., Pujol, C. A., Ciancia, M., Noseda, M. D., Matulewicz, M. C., Damonte, E. B., & Cerezo, A. S. Antiherpetic and anticoagulant properties of carrageenans from the red seaweed Gigartina skottsbergii and their cyclized derivatives: correlation between structure and biological activity. *International Journal of Biological Macromolecules*. 20(2), 1997, 97-105.

[11] Chase, G., Wunderlich, K., Reuther, P., and Schwemmle, M. Identification of influenza virus inhibitors which disrupt of viral polymerase protein–protein interactions. *Methods*. *55*(2), 2011, 188-191.

[12] Chen, L. and Huang, G. The antiviral activity of polysaccharides and their derivatives. *International journal of biological macromolecules*, 115, 2018, 77-82.

[13] Chen, X., Han, W., Wang, G. and Zhao, X. Application prospect of polysaccharides in the development of anti-novel coronavirus drugs and vaccines. *International journal of biological macromolecules*. 164, 2020, 331-343

[14] Chiu, Y.H., Chan, Y.L., Tsai, L.W., Li, T.L. and Wu, C.J. Prevention of human enterovirus 71 infection by kappa carrageenan. *Antiviral research*, 95(2), 2012, 128-134.

[15] Cui, J., Li, F. and Shi, Z.L. Origin and evolution of pathogenic coronaviruses. *Nature Reviews Microbiology*. 17(3), 2019, 181-192.

[14] De Sf-Tischer, P.C., Talarico, L.B., Noseda, M.D., Guimarães, S.M.P.B., Damonte, E.B. and Duarte, M.E.R. Chemical structure and antiviral activity of carrageenans from Meristiella gelidium against herpes simplex and dengue virus. *Carbohydrate polymers*. 63(4), 2006, 459-465.

[15] Diogo, J.V., Novo, S.G., González, M.J., Ciancia, M. and Bratanich, A.C. Antiviral activity of lambda-carrageenan prepared from red seaweed (Gigartina skottsbergii) against BoHV-1 and SuHV-1. *Research in veterinary science*. 98, 2015, 142-144.

[16] Distantina, S. and Fahrurrozi, M. Carrageenan properties extracted from Eucheuma cottonii, Indonesia. *International Journal of Chemical and Molecular Engineering*. 5(6), 2011, 487-491.

[17] Du, L., He, Y., Zhou, Y., Liu, S., Zheng, B.J. and Jiang, S. The spike protein of SARS-CoV — a target for vaccine and therapeutic development. *Nature Reviews Microbiology*. 7(3), 2009, 226-236.

[18] Ghosh, T., Chattopadhyay, K., Marschall, M., Karmakar, P., Mandal, P., and Ray, B. Focus on antivirally active sulfated polysaccharides: from structure–activity analysis to clinical evaluation. *Glycobiology*. *19*(1), 2009, 2-15.

[19] Girond, S., Crance, J. M., Van Cuyck-Gandre, H., Renaudet, J.,and Deloince, R. Antiviral activity of carrageenan on hepatitis A virus replication in cell culture. *Research in virology*. 142(4), 1991, 261-270

[20] Gomaa, H.H. and Elshoubaky, G.A. Antiviral activity of sulfated polysaccharides carrageenan from some marine seaweeds. *International Journal of Current Pharmaceutical Review and Research*. 7(1), 2016, 34-42.

[21] Gonzalez, M.E., Alarcón, B. and Carrasco, L. Polysaccharides as antiviral agents: antiviral activity of carrageenan. *Antimicrobial agents and chemotherapy*. 31(9), 1987, 1388-1393.

[22] Grassauer, A., Weinmuellner, R., Meier, C., Pretsch, A., Prieschl-Grassauer, E. and Unger, H. Iota-Carrageenan is a potent inhibitor of rhinovirus infection. *Virology journal*. 5(1), 2008, 1-13.

[23] Guo, C., Zhu, Z., Yu, P., Zhang, X., Dong, W., Wang, X., Chen, Y. and Liu, X. Inhibitory effect of iota-carrageenan on porcine reproductive and respiratory syndrome virus in vitro. *Antiviral therapy*. 24(4), 2019, 261-270.

[24] Hao, C., Yu, G., He, Y., Xu, C., Zhang, L. and Wang, W. Marine glycan–based antiviral agents in clinical or preclinical trials. *Reviews in medical virology*. 29(3), 2019, e2043.

[25] Harden, E.A., Falshaw, R., Carnachan, S.M., Kern, E.R. and Prichard, M.N. Virucidal activity of polysaccharide extracts from four algal species against herpes simplex virus. *Antiviral research*. 83(3), 2009, 282-289.

[26] Heald-Sargent, T. and Gallagher, T. Ready, set, fuse! The coronavirus spike protein and acquisition of fusion competence. *Viruses*. 4(4), 2012, 557-580.

[27] Jang, Y., Shin, H., Lee, M.K., Kwon, O.S., Shin, J.S., Kim, Y.I., Kim, C.W., Lee, H.R. and Kim, M.,. Antiviral activity of lambda-carrageenan against influenza viruses and severe acute respiratory syndrome coronavirus 2. *Scientific reports*. 11(1), 2021, 1-12.

[28] Klimyte, E.M., Smith, S.E., Oreste, P., Lembo, D. and Dutch, R.E. Inhibition of human metapneumovirus binding to heparan sulfate blocks infection in human lung cells and airway tissues. *Journal of virology*. 90(20), 2016, 9237-9250.

[29] Liu, C., Zhou, Q., Li, Y., Garner, L.V., Watkins, S.P., Carter, L.J., Smoot, J., Gregg, A.C., Daniels, A.D., Jervey, S. and Albaiu, D. Research and development on therapeutic agents and vaccines for COVID-19 and related human coronavirus diseases. *ACS Central Science*. 6 (3), 2020, 315-331

[30] Luo, Z., Tian, D., Zhou, M., Xiao, W., Zhang, Y., Li, M., Sui, B., Wang, W., Guan, H., Chen, H. and Fu, Z.F. λ-carrageenan P32 is a potent inhibitor of rabies virus infection. *PLoS One*. 10(10), 2015, e0140586.

[31] Manuhara, G.J., Praseptiangga, D. and Riyanto, R.A. Extraction and characterization of refined K-carrageenan of red algae [Kappaphycus Alvarezii (Doty ex PC Silva, 1996)] originated from Karimun Jawa Islands. *Aquatic Procedia*. 7, 2016, 106-111.

[32] Marchetti, M., Pisani, S., Pietropaolo, V., Seganti, L., Nicoletti, R. and Orsi, N. Inhibition of herpes simplex virus infection by negatively charged and neutral carbohydrate polymers. *Journal of chemotherapy*. 7(2), 1995, 90-96.

[33] Milewska, A., Zarebski, M., Nowak, P., Stozek, K., Potempa, J. and Pyrc, K. Human coronavirus NL63 utilizes heparan sulfate proteoglycans for attachment to target cells. *Journal of virology*. 88(22), 2014, 13221-13230.

[34] Morokutti-Kurz, M., Fröba, M., Graf, P., Große, M., Grassauer, A., Auth, J., Schubert, U. and Prieschl-Grassauer, E. Iota-carrageenan neutralizes SARS-CoV-2 and inhibits viral replication in vitro. *PloS one*. 16(2), 2021, e0237480.

[35] Nakashima, H.Y.N.Y.M.N., Kido, Y., Kobayashi, N., Motoki, Y., Neushul, M. and Yamamoto, N. Purification and characterization of an avian myeloblastosis and human immunodeficiency virus reverse transcriptase inhibitor, sulfated polysaccharides extracted from sea algae. *Antimicrobial agents and chemotherapy*. 31(10), 1987, 1524-1528.

[36] Necas J and Bartosikova L. Carrageenan: a review. *Veterinarnimedicina*. 58(4), 2013, 187–205

[37] Parvez, M. K., and Parveen, S. Evolution and emergence of pathogenic viruses: past, present, and future. *Intervirology*. *60*(1-2), 2017, 1-7.

[38] Pavliga, S.N., Kompanets, G.G. and Tsygankov, V.Y. The experimental research (in vitro) of carrageenans and fucoidans to decrease activity of Hantavirus. *Food and environmental virology*. 8(2), 2016,120-124.

[39] Pereira, L. and Critchley, A.T. The COVID 19 novel coronavirus pandemic 2020: seaweeds to the rescue? Why does substantial, supporting research about the antiviral properties of seaweed polysaccharides seem to go

unrecognized by the pharmaceutical community in these desperate times?. *Journal of Applied Phycology*. 32, 2020, 1875-1877.

[**40**] Pérez, L.R., Vera, M.Á., Díaz, L.F.M., Iglesias, O.V. and del Barrio Alonso, G. Preliminary evaluation of the antiviral activity of Laurencia obtuse extract against herpesvirus and dengue virus. *Revista Cubana de Farmacia*. 50(1), 2016, 106-116.

[**41**] Piccini, L.E., Carro, A.C., Quintana, V.M. and Damonte, E.B. Antibody-Independent and dependent infection of human myeloid cells with dengue virus is inhibited by carrageenan. *Virus Research*. 290, 2020, 198150.

[**42**] Rees, D. A. Polysaccharide gels: a molecular view. *Chem. Ind*. 630, 1972

[**43**] Shao, Q., Guo, Q., Xu, W.P., Li, Z. and Zhao, T.T. Specific inhibitory effect of κ-carrageenan polysaccharide on swine pandemic 2009 H1N1 influenza virus. *PloS one*. 10(5), 2015, p.e0126577.

[**44**] Shi, Q., Wang, A., Lu, Z., Qin, C., Hu, J. and Yin, J. Overview on the antiviral activities and mechanisms of marine polysaccharides from seaweeds. *Carbohydrate research*. 453, 2017, 1-9.

[**45**] Sobhy, H. A comparative review of viral entry and attachment during large and giant dsDNA virus infections. *Archives of virology*. 162(12), 2017, 3567-3585.

[**46**] Talarico, L.B., Zibetti, R.G., Faria, P.C., Scolaro, L.A., Duarte, M.E., Noseda, M.D., Pujol, C.A. and Damonte, E.B. Anti-herpes simplex virus activity of sulfated galactans from the red seaweeds Gymnogongrus griffithsiae and Cryptonemia crenulata. *International Journal of Biological Macromolecules*. 34(1-2), 2004, 63-71.

[**47**] Talarico, L.B. and Damonte, E.B. Interference in dengue virus adsorption and uncoating by carrageenans. *Virology*. 363(2), 2007, 473-485.

[**48**] Talarico, L.B., Noseda, M.D., Ducatti, D.R., Duarte, M.E. and Damonte, E.B. Differential inhibition of dengue virus infection in mammalian and mosquito cells by iota-carrageenan. *Journal of General Virology*. 92(6), 2011, 1332-1342.

[**49**] Tang, B., Bragazzi, N.L., Li, Q., Tang, S., Xiao, Y. and Wu, J. An updated estimation of the risk of transmission of the novel coronavirus (2019-nCov). *Infectious disease modelling*. 5, 2020, 248-255.

[**50**] Vissani, A., Galdo Novo, S., Ciancia, M., Zabal, O.A., Thiry, E., Bratanich, A.C. and Barrandeguy, M.E. Effects of lambda-carrageenan on equid herpesvirus 3 in vitro. *Journal of Equine Veterinary Science*. 39, 2016, S56-S65

[**51**] Wang, W., Zhang, P., Hao, C., Zhang, X.E., Cui, Z.Q. and Guan, H.S. In vitro inhibitory effect of carrageenan oligosaccharide on influenza A H1N1 virus. *Antiviral research*. 92(2), 2011, 237-246.

[**52**] Weiss, S.R. and Leibowitz, J.L. Coronavirus pathogenesis. *Advances in virus research*. 81, 2011, 85-164.

[**53**] Witvrouw, M. and De Clercq, E. Sulfated polysaccharides extracted from sea algae as potential antiviral drugs. General Pharmacology: *The Vascular System*. 29(4), 1997, 497-511.

[54] Yamada, T., Ogamo, A., Saito, T., Uchiyama, H. and Nakagawa, Y. Preparation of O-acylated low-molecular-weight carrageenans with potent anti-HIV activity and low anticoagulant effect. *Carbohydrate Polymers*. 41(2), 2000, 115-120.

[55] Yang, Y., Peng, F., Wang, R., Guan, K., Jiang, T., Xu, G., Sun, J. and Chang, C. The deadly coronaviruses: The 2003 SARS pandemic and the 2020 novel coronavirus epidemic in China. *Journal of autoimmunity*. 109, 2020, 102434.

[56] Zhou, G., Sun, Y., Xin, H., Zhang, Y., Li, Z. and Xu, Z. In vivo antitumor and immunomodulation activities of different molecular weight lambda-carrageenans from Chondrus ocellatus. *Pharmacological research*. 50(1), 2004, 47-53.