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Interaction of SARS-CoV-2 Spike protein with phycocyanobilin

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Algae have been consumed as food and medicine for centuries. Their benefits are so pronounced, due to high concentrations of vitamins, minerals, antioxidants and proteins that they are commonly referred to as superfoods. Phycocyanobilin (PCB) is a bioactive compound of microalga *Spirulina platensis*. It is a blue tetrapyrrole chromophore of C-phycocyanin (C-PC), the major chromoprotein of this microalga. It is covalently attached to cysteine residues of C-PC via thioether bond. The outbreak of Coronavirus Disease 2019 (COVID-19) has posed a serious threat to global public health, calling for the development of safe and effective prophylactics and therapeutics against infection of its causative agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The SARS-CoV-2 spike (S) protein plays the most important roles in viral attachment, fusion and entry, and it serves as a target for development of antibodies, entry inhibitors and vaccines. It mediates viral entry into host cells by first binding to a host angiotensin-converting enzyme 2 (ACE2) receptor through the receptor-binding domain (RBD) and then fusing the viral and host membranes. This study aimed to investigate interaction of bioactive PCB with S protein and RBD respectively.

Combination of electrophoretic techniques and fluorescence spectroscopy was employed in order to examine interactions of PCB and S protein, as well as interactions of PCB and RBD, while the effects of PCB binding on RBD structure were studied by CD spectroscopy.

SDS-PAGE with Zn^{2+} staining has revealed that PCB covalently binds to both S protein and RBD, via free cysteine residues. Binding constants determined by fluorescence quenching method were: 2.1×10^7 M^{-1} for PCB and S protein, and 8.4×10^4 M^{-1} for PCB and RBD. Far-UV circular dichroism spectra showed that PCB influences RBD structure.

Our results support the importance of further research on covalent binding of PCB to S protein and RBD and its implications. Due to its interaction with S protein and RBD, PCB may exert one of its many bioactive effects via impact on S protein binding to ACE2 receptor.

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