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Pentosan Polysulfate—A "Better Heparin" as Potential Medication for the Treatment of SARS-CoV-2 Infections?

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With the outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, an extensive search has been initiated to discover further medication to treat viral infections of patients in addition to vaccination strategies. Due to the emergency of the situation, repurposing established drugs has been the major focus of COVID-19 treatment development. While many approaches failed, antiviral activities of heparin were revisited and shed new light on this well-established anticoagulant. It was a breakthrough study by Mycroft-West and colleagues, published in *Thrombosis and Haemostasis* in 2020, which confirmed that heparin could bind to SARS-CoV-2 spike S1-receptor-binding domain (RBD), thus attenuating the interaction with ACE2 and consequently host cell invasion.[1] Highly acknowledged and cited, this study strongly impacted further research bringing fundamental aspects of pathogen–host cell interactions back into focus. As many pathogens, SARS-CoV-2 makes use of cell-surface glycosaminoglycans as co-receptors for host cell invasion. Heparin, as a close structural analogue of heparan sulfates, can interfere with this process. Although heparin nebulization is a current issue as a probable route of administration,[2] bleeding complications remain an issue. This opened the question of whether other, highly negatively charged glycosides could act similarly to impede SARS-CoV-2 infection. This was addressed by Bertini et al[3] in the present issue of this journal. They could show that pentosan polysulfate (PPS), a plant-derived xylan and approved drug for oral treatment of interstitial cystitis, had identical activities to heparin in in vitro approaches for binding S1-RBD and SARS-CoV-2 cell invasion. This was not the only study considering PPS for targeting SARS-CoV-2,[4] but Bertini et al provided a remarkable structural insight into PPS/S1-RBD-binding mode and stoichiometry. An in-depth analysis of size-fractionated PPS composition by nuclear magnetic resonance fingerprinting was correlated with binding analysis using isothermal titration calorimetry, circular dichroism spectroscopy, and molecular docking approaches to complement the in vitro Vero cell invasion studies. The authors suggested that low-anticoagulant-activity PPS, preferably administered via nebulization, could represent a promising antiviral agent for further studies.

Conflict of Interest
None declared.

References

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