

Exploring the Potential and Mechanisms of Natural Proteins and Synthetic Drugs Against SARS-CoV-2

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Outline

1. Introduction
2. Remdesivir Metabolite GS-441524 Effectively Inhibits SARS-CoV-2 Infection in Mouse Models
3. Bovine lactoferrin inhibits SARS-CoV-2 and SARS-CoV-1 by targeting the RdRp complex and alleviates viral infection in the hamster model
4. Conclusion

Abstract

SARS-CoV-2 has caused the global COVID-19 pandemic. Although remdesivir was the first antiviral approved for clinical use, its therapeutic efficacy remains controversial, prompting further investigation of its primary active antiviral component. In addition, SARS-CoV-2 RNA has been detected in the breast milk of infected mothers, but infectious virus particles have never been isolated, suggesting that there may be antiviral components in breast milk. These two studies respectively examined the antiviral potential of GS-441524-the parent nucleoside of remdesivir and the naturally occurring milk protein bovine lactoferrin (bLf) derived from milk against SARS-CoV-2, as well as their possible mechanisms.

In cell experiments and animal models, GS-441524 can effectively inhibit SARS-CoV-2 activity and reduce tissue damage, while its production cost and efficacy are also lower compared to remdesivir. This study also developed the first SARS-CoV-2 animal model in AAV-hACE2 mice using GS-441524. The second study shows that bLf and milk fat globule membrane (MFGM) are identified as the main antiviral components in breast milk. Among them, bLf can block the interaction between the spike protein and ACE2, inhibit viral RNA replication, and has been shown to directly inhibit the RNA polymerase (RdRp) of SARS-CoV-2.

1 Overall, these studies show that GS-441524 and bLf can combat SARS-CoV-2 by
2 inhibiting viral replication. These findings support the antiviral potential of both synthetic
3 nucleoside analogs and natural proteins against coronaviruses.

4 **Reference**

5 Li, Y., Cao, L., Li, G., Cong, F., Li, Y., Sun, J., et al. (2021). Remdesivir Metabolite GS-
6 441524 Effectively Inhibits SARS-CoV-2 Infection in Mouse Models. *Journal of*
7 *Medicinal Chemistry*, 65(4), 2785–2793.

8 He, S.-T., Qin, H., Guan, L., Liu, K., Hong, B., Zhang, X., et al. (2022). Bovine lactoferrin
9 inhibits SARS-CoV-2 and SARS-CoV-1 by targeting the RdRp complex and alleviates
10 viral infection in the hamster model. *Journal of Medical Virology*, 95(1), e28281.