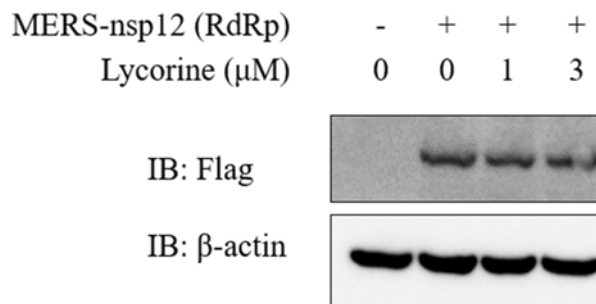
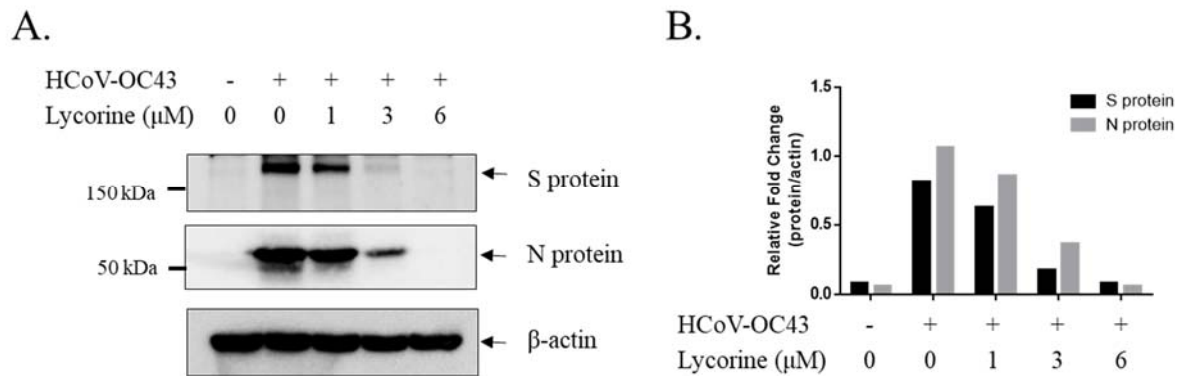


Supplementary Fig. 1



Supplementary Fig. 1. Consistent MERS-CoV RdRp expression during the cell based MERS-CoV RdRp reporter assay with lycorine treatment. HEK293T cells were seeded and transfected with Flag-tagged MERS-CoV nsp12 (RdRp) expressing plasmid. After 6 hr, cells was treated with the indicated concentrations of lycorine. Cells were harvested after 16 hours and lysed in Glo lysis buffer (Promega). Lysates were separated on the 8% SDS-PAGE gel and transferred to nitrocellulose membrane (Bio-Rad). Transferred membranes were incubated with 5% skim milk in TBST for 30 min at room temperature. The membranes were rinsed with TBST and incubated with anti-Flag antibody (Abcam) or anti- β -actin (Cell signaling Technology) antibodies at 4°C for overnight. HRP-conjugated secondary antibodies (Abcam) were incubated for 1 hour at RT, and the membranes were detected with ECL solution (Thermo) using Chemidoc Touch Imaging System (Bio-Rad).

Supplementary Fig. 2



Supplementary Fig. 2. Dose-dependent inhibition of Human Coronavirus OC43 (HCoV-OC43) spike protein and nucleoprotein expression in MRC-5 cells by Lycorine. (A) MRC-5 cells (ATCC) were infected with $10^{3.5}$ TCID₅₀ HCoV-OC43 (ATCC), treated with Lycorine at indicated concentrations, and incubated at 33°C. After 2 days post infection, cells were lysed. Lysates were separated on the 8% SDS-PAGE gel and transferred to nitrocellulose membranes (Bio-Rad Lab.). The membranes were blocked with 5% skim milk contained in TBST for 30 min at RT, then rinsed with TBST and incubated with anti-Spike (S) protein (CusaBio), anti-Nucleocapsid (N) protein (Merck) or anti- β -actin (Cell signaling Technology) specific antibodies at 4°C for overnight. HRP-conjugated secondary antibodies (Abcam) were incubated for 1 hour at RT, and the membranes were detected with ECL solution (Thermo) using Chemidoc Touch Imaging System (Bio-Rad). (B) The protein band intensities of Spike (S) protein and Nucleocapsid (N) protein were quantified.

Supplementary Table 1.

Supplementary Table 1. List of the inhibitory concentration (IC₅₀), cytotoxic concentration (CC₅₀), and selectivity index (CC₅₀/IC₅₀, SI) values of lycorine against CoV infection. Data are presented as mean ± SEM of duplicate experiments.

CoV _s	Lycorine		Remdesivir	
	(CC ₅₀ >50μM)		(CC ₅₀ >50μM)	
	IC ₅₀ (μM)	SI	IC ₅₀ (μM)	SI
MERS-CoV	2.123 ± 0.053	>23.55	7.407 ± 0.216	>6.75
SARS-CoV	1.021 ± 0.025	>48.97	4.084 ± 0.248	>12.24
SARS-CoV-2	0.878 ± 0.022	>56.95	6.499 ± 0.256	>7.69