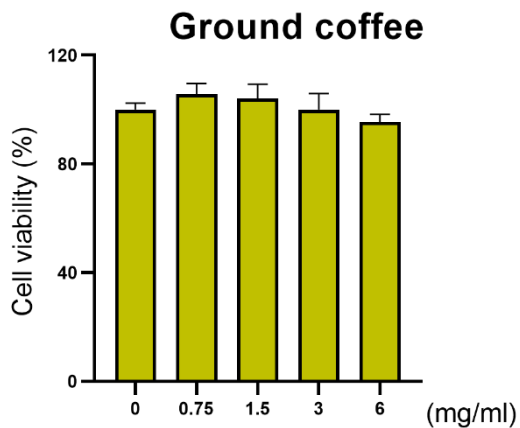
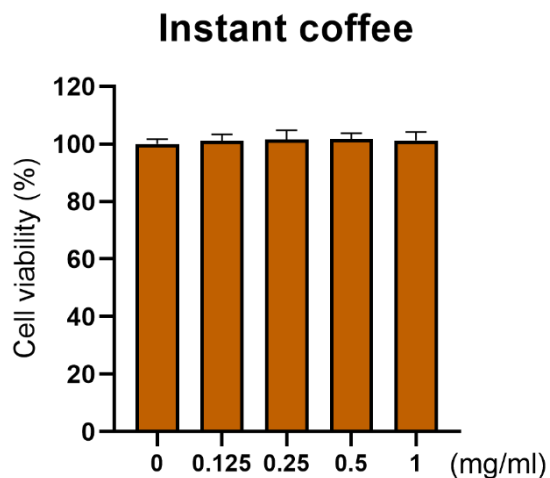


## S1 Fig

a



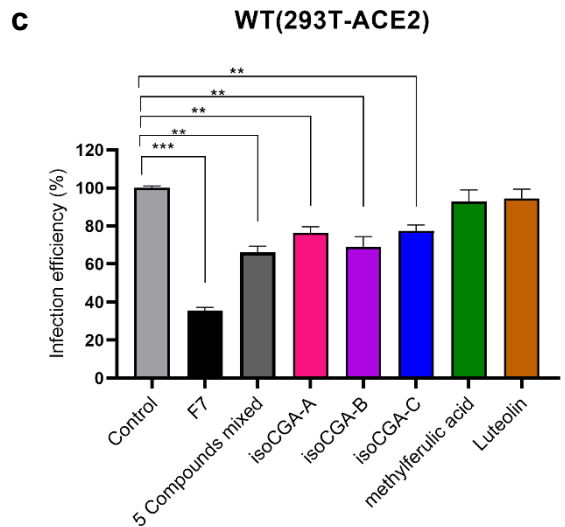
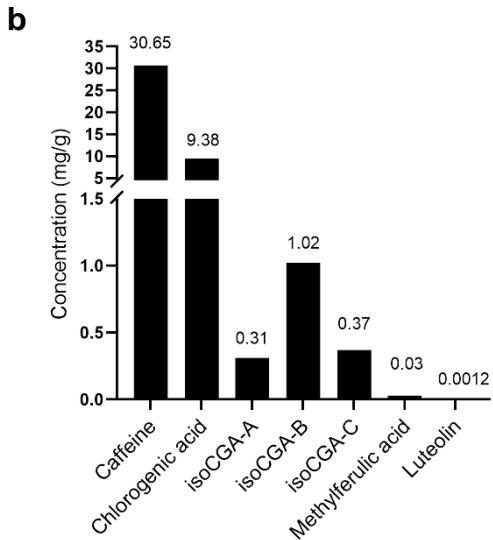
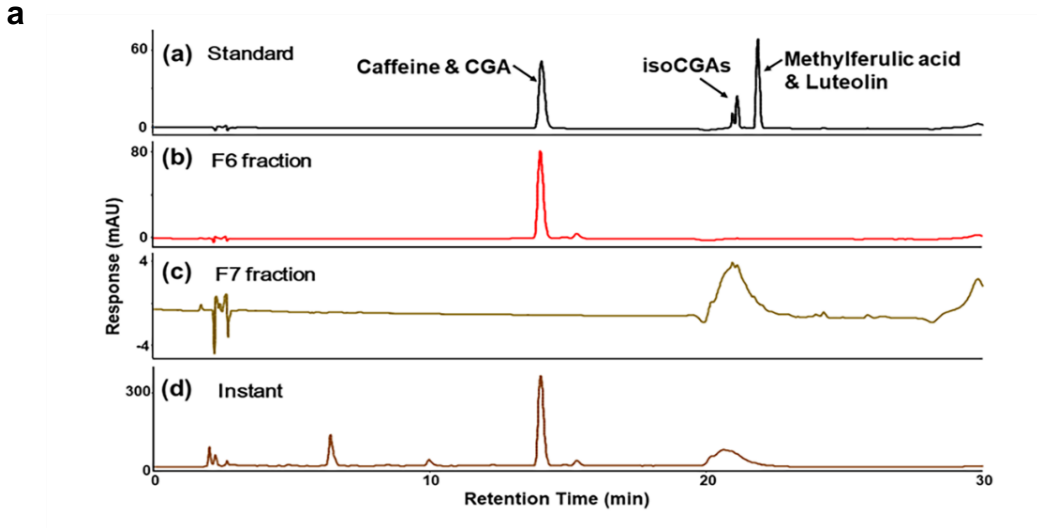
b



### S1 Fig. *Identification of cell viability.*

The cell viability was tested to verify the safety of ground coffee (a) and instant coffee (b).

## S2 Fig

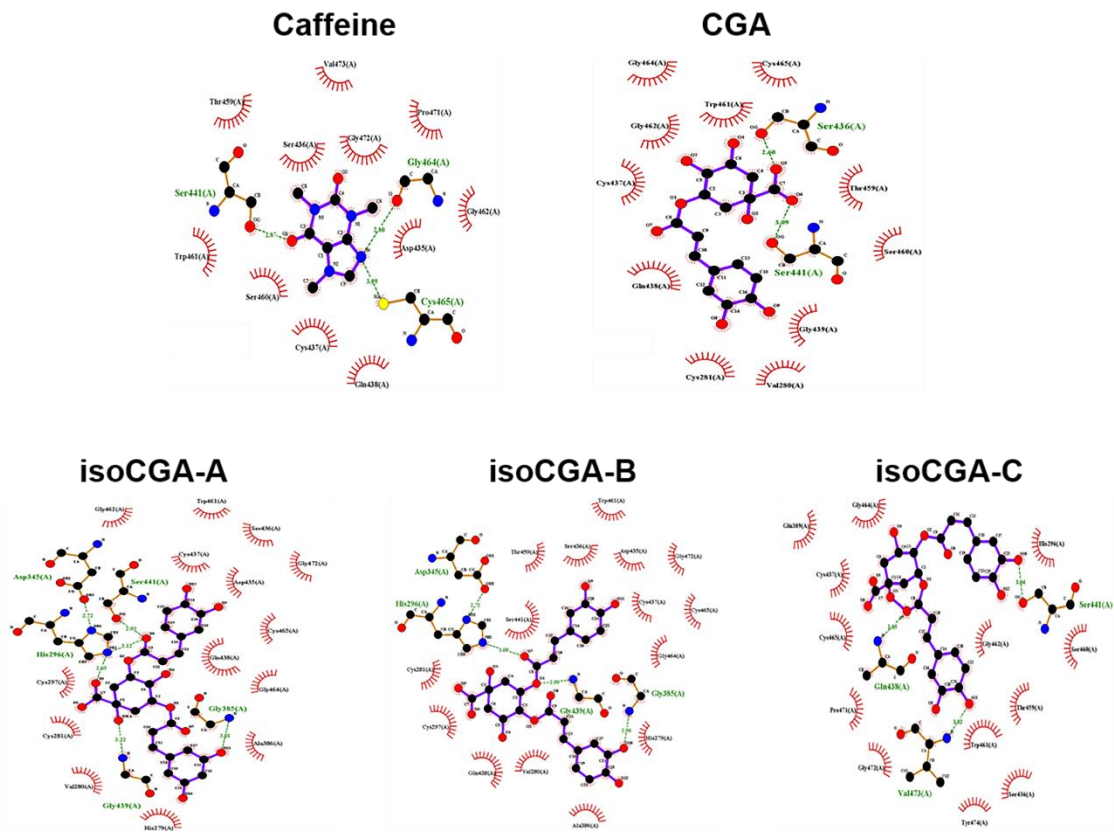


### S2 Fig. Evaluation of the content of compounds in coffee and the inhibiting efficacy against SARS-CoV-2 entry.

(a) Compared with the standard of pure compounds, caffeine and chlorogenic acid (CGA) exist in fraction 6, as well as isochlorogenic acid A (isoCGA-A), isochlorogenic acid B (isoCGA-B), isochlorogenic acid C (isoCGA-C), methylferulic acid, and luteolin exist in fraction 7. (b) Analysis the content of compounds in instant coffee by UHPLC-HRMS. (c) According to the content of compounds in coffee, comparing the effect of caffeoylquinic acid derivatives alone, mixed, and fraction 7 on inhibiting SARS-CoV-2 entry by VPP assay.



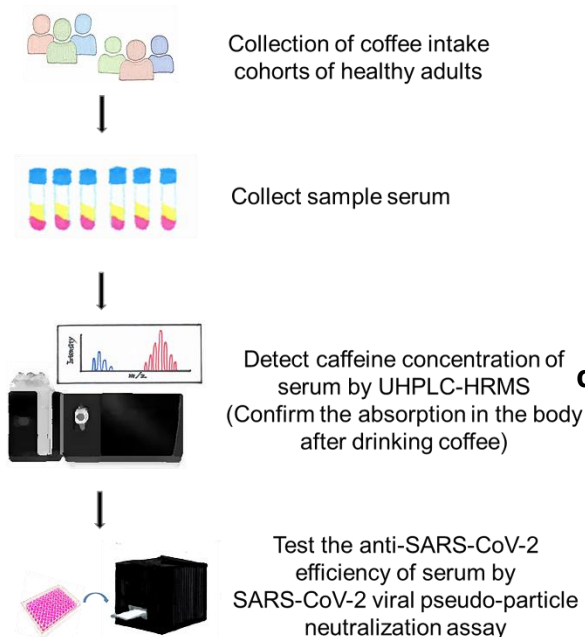
S4 Fig



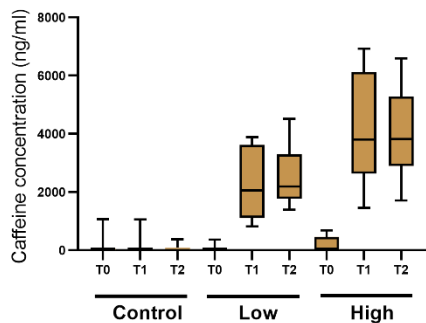
**S4 Fig.** Ligplot+ shows the interactions between Caffeine, CGA, isoCGA-A, isoCGA-B and isoCGA-C with TMPRSS2 amino acids. Hydrogen bonds are shown as green dashed lines. Hydrophobic contacts are represented as spline curves.

## S5 Fig

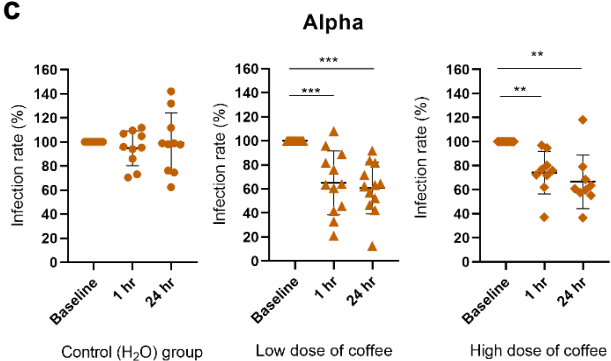
**a**



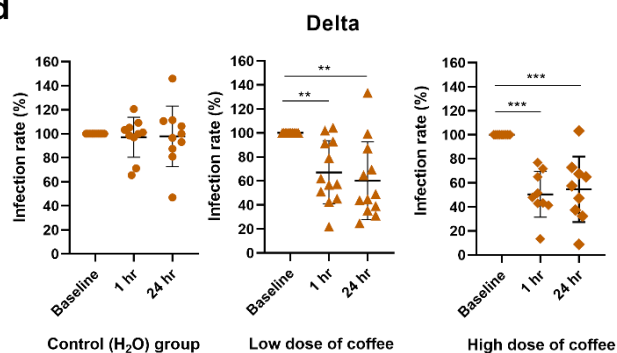
**b**



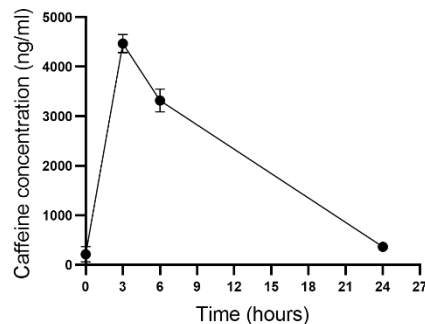
**c**



**d**



**e**



### S5 Fig. *Drinking coffee has the ability against SARS-CoV-2 in the cohort study.*

(a) Experimental flow chart of the cohort study. (b) Validation of caffeine metabolic concentrations in the serum of coffee-drinking groups by HPLC analysis. (c) Examination of the serum in drinking coffee with different concentrations against the Alpha variant by Vpp. (d) The efficacy of the serum in drinking coffee with different concentrations against the Delta variant was tested by Vpp. (e) Time course of caffeine metabolism in serum after drinking coffee by HPLC. Statistical significance was concerned as \*,  $P < 0.05$ , \*\*,  $P < 0.01$  or \*\*\*,  $P < 0.001$ .