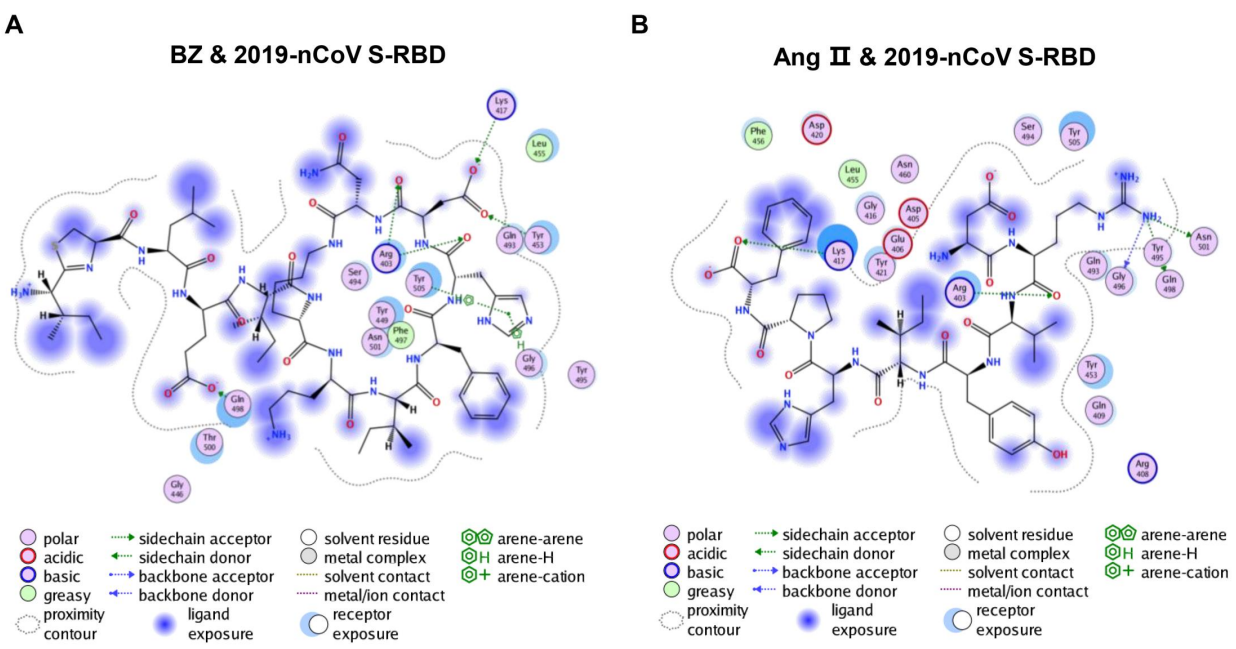
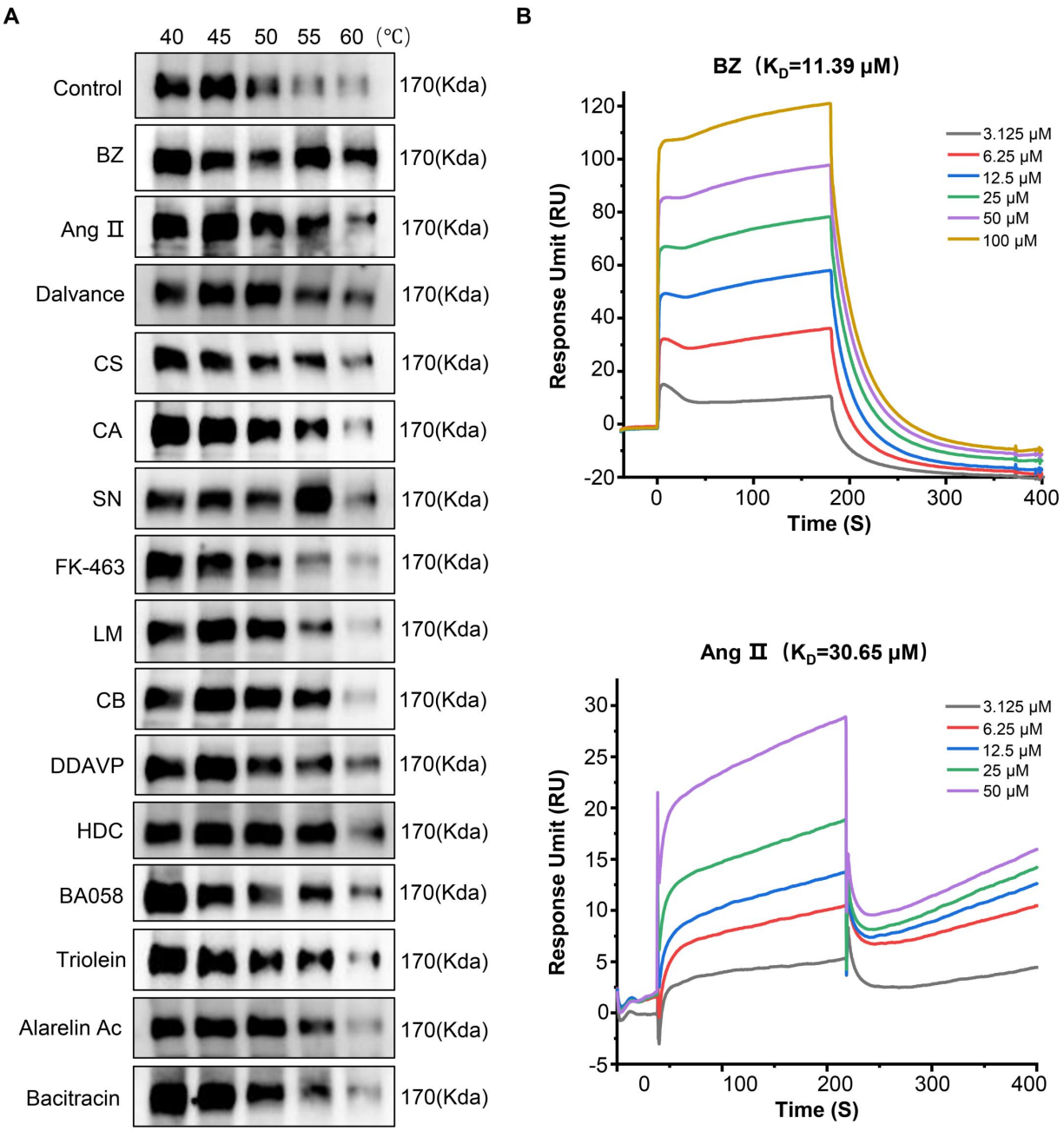
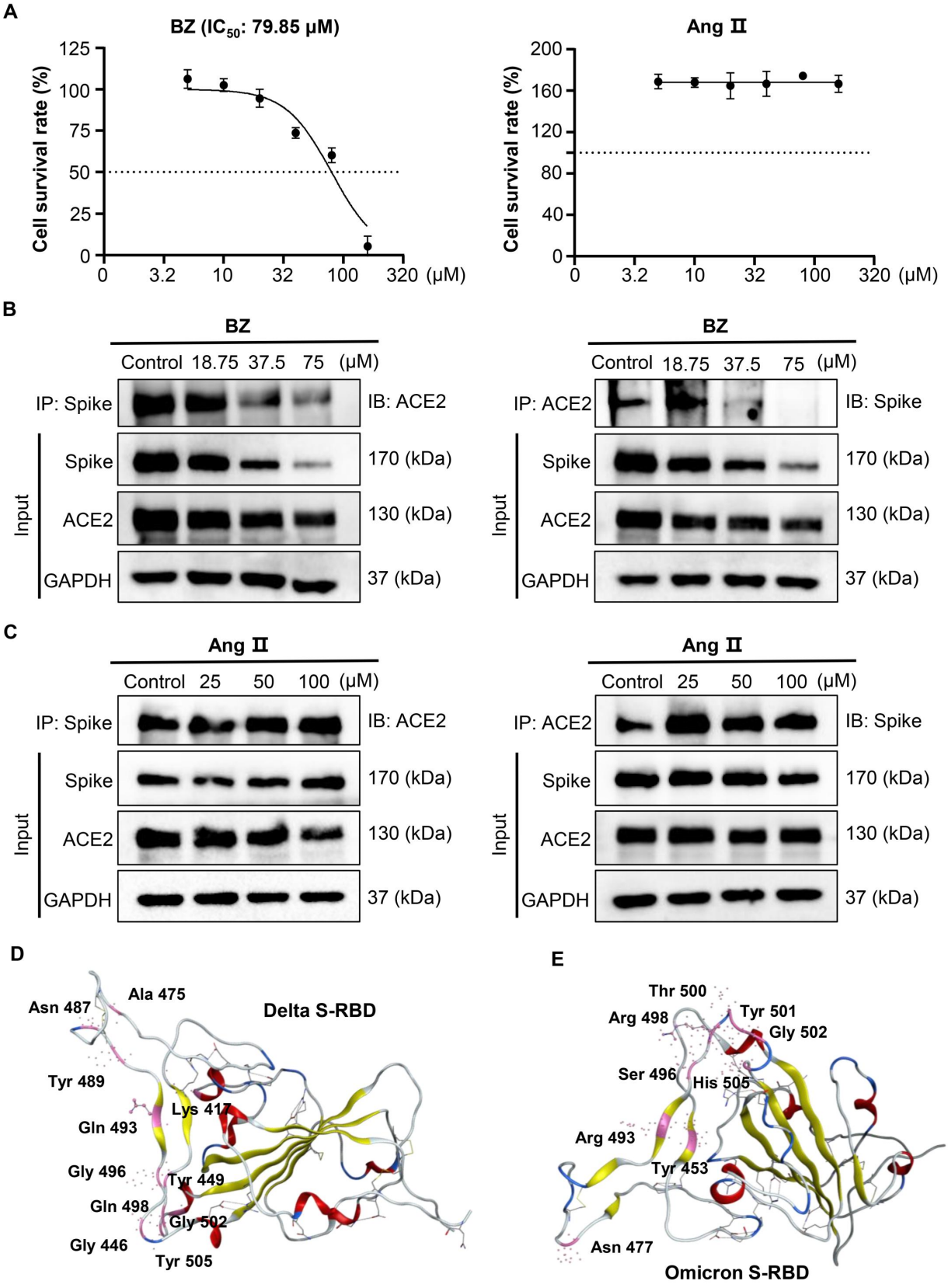


Supplementary Fig. 1. Molecular docking of two compounds with 2019-nCoV S-RBD. Two-dimensional diagram illustrates the interactions between (**A**) Bacitracin Zinc (BZ) and (**B**) Angiotensin IIHuman Acetate (Ang II) with the 2019-nCoV S-RBD.



Supplementary Fig. 2. Compounds bind to 2019-nCoV S-RBD.
CETSA analysis of the 2019-nCoV S protein was performed using HEK293T cell lysates. The lysates were then incubated with **(A)** 100 μM 15 compounds and subsequently analyzed by Western blotting. The 2019-nCoV S-RBD was immobilized on a CM5 sensor chip using the Biacore 8K instrument. The association and dissociation curves for **(B)** two compounds are shown. The compounds were tested at various concentrations, and the K_D values were determined by fitting the data to a 1:1 binding model using Biacore Insight Evaluation Software. K_D represents the equilibrium dissociation constant.



Supplementary Fig. 3.

The cytotoxicity of **(A)** BZ or Ang II was assessed in HEK293T cells, with IC_{50} values measured at 24 hours. Co-immunoprecipitation (Co-IP) assays were performed to investigate the interaction between SARS-CoV-2 Spike protein and hACE2 in HEK293T cells. Cells were treated with **(B)** BZ or **(C)** Ang II for 24 hours. Immunoprecipitation was carried out using anti-hACE2 or anti-Spike antibodies, followed by immunoblotting with antibodies against hACE2, Spike, and GAPDH. Crystal structure of the **(D)** Delta S-RBD and **(E)** Omicron S-RBD. The binding sites of S-RBD with hACE2 are shown in pink.

Supplementary table1. Report on residues involved in the interaction of two compounds

Compound	Ligand	Receptor (S-RBD)	Interaction	E (kcal/mol)
BZ	-COOH	Gln 498	H-acceptor	-0.7
	-CONH-	Arg 403	H-acceptor	-3.3
	-COOH	Lys 417	H-acceptor	-0.5
	-COOH	Tyr 453	H-acceptor	-2.6
	-C3H4N2	Gly 496	П-H	-2.0
	-C3H4N2	Tyr 505	П-H	-1.3
Ang Ⅱ	-NHC (=NH) NH_2	Gly 496	H-donor	-1.4
	-NHC (=NH) NH_2	Gln 498	H-donor	-2.6
	-NHC (=NH) NH_2	Asn 501	H-donor	-1.5
	-COOH	Lys 417	H-acceptor	-1.0
	-CONH-	Arg 403	H-acceptor	-3.3

Supplementary table2. Report on molecular docking scores and interacting residues for 5 compounds

Compound	Docking score (s)	Receptor		Interaction
ATOP	-7.23	Delta	Gly 496	H-acceptor
	-7.70	Omicron	Ser 496	H-acceptor
			Arg 498	H-acceptor
			Tyr 501	П-H
			His 505	П-H
CTM-HCl	-7.52	Delta	Asn 501	H-donor
			Tyr 505	H-donor
			Thr 500	H-donor
			Asp 405	Ionic
			Gly 502	П-H
			Tyr 505	П-H
	-7.39	Omicron	Arg 403	П-H
			Tyr 501	П-H
Melittin	-12.13	Delta	Lys 478	H-acceptor
			Asn 481	H-acceptor
			Phe 486	H-acceptor
			Cys 488	H-donor
			Gln 498	H-donor
			Thr 500	H-donor
	-15.76	Omicron	Leu 455	H-donor
			Asn 477	H-donor
			Gly 476	H-donor
			Ser 496	H-acceptor
			His 505	П-H
TEC	-8.62	Delta	Tyr 449	П-H
			Leu 455	П-H
			Asn 501	H-donor
	-9.14	Omicron	Arg 403	H-donor
			Tyr 449	H-acceptor
			Ser 496	H-acceptor
			His 505	П-H