**Supplementary figure captions and list of abbreviations**



**Fig. S1.** Alignment between the primary amino acid sequences of peptides from the trypsin inhibitor purified from tamarind seeds [model number 56, conformation number 287 (TTIp 56/287)] and peptides derived from plant and bovine lung protease inhibitors. Pep1: Peptide obtained by cleavage with pepsin; Pep2: Peptide obtained by cleavage with pepsin; Tryp1: Peptide obtained by cleavage with trypsin; Tryp2: Peptide obtained by cleavage with trypsin; Chym1: Peptide obtained by cleavage with chymotrypsin; 1H20\_1|Chain: Peptide from potato (*Solanum tuberosum*); 2IT7\_1|Chain: Peptide from cucumber (*Ecballium elaterium*); 1NB1\_1|Chain: Peptide from the *Oldenlandia affinis* plant; 1JXC\_1|Chain: Peptide from mustard (*A. thaliana*); 1TIN\_1|Chain: Peptide from pumpkin (*Cucurbita maxima*); Aprotinin: Peptide from bovine lung.



**Fig. S2.** Alignment between the primary amino acid sequences of peptide analogues to native peptides from the trypsin inhibitor purified from tamarind seeds [model number 56, conformation number 287 (TTIp 56/287)] and peptides derived from plant and bovine lung protease inhibitors. ID 32: Peptide obtained by replacing amino acids in the primary structure of Pep1; ID 76: Peptide obtained by replacing amino acids in the

primary structure of Pep2; ID 63: Peptide obtained by replacing amino acids in the primary structure of Tryp1; ID 336: Peptide obtained by replacing amino acids in the primary structure of Tryp2; ID 101: Peptide obtained by replacing amino acids in the primary structure of Chym1; 1H20\_1|Chain: Peptide from potato (*Solanum tuberosum*); 2IT7\_1|Chain: Peptide from cucumber (*Ecballium elaterium)*; 1NB1\_1|Chain: Peptide from the *Oldenlandia affinis* plant; 1JXC\_1|Chain: Peptide from mustard (*A. thaliana*); 1TIN\_1|Chain: Peptide from pumpkin (*Cucurbita maxima*); Aprotinin: Peptide from bovine lung.



**Fig. S3.** Theoretical model of transmembrane serine protease 2 (TMPRSS2) coupled to the lipid bilayer in 1:1 ratios of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) to 1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-L-serine (POPS).

**1H20\_1|Chain:** Peptide from*Solanum tuberosum*

**1JXC\_1|Chain:** Peptide from*A. thaliana*

**1NB1\_1|Chain:** *Oldenlandia affinis’s* plant peptide

**1TIN\_1|Chain:** Peptide from*Cucurbita maxima*

**2IT7\_1|Chain:** Peptide from*Ecballium elaterium*

**3CL pro :** Protease 3C-like

**ACE-2:** Angiotensin-converting enzyme 2

**CHARMM36:** Chemistry at Harvard Macromolecular Mechanics 36

**CHARMM GUI:** Chemistry at Harvard Macromolecular Mechanics with graphical user interface

**Chym1:** Peptide obtained by cleavage with chymotrypsin at position 57 (TPIDIPIGLG)

**COVID-19:** Coronavirus infectious disease 2019

**DRAMP:** Data Repository of Antimicrobial Peptides

**ExPASy:** Expert Protein Analysis System

**FDA:** Food and Drug Administration

**fs:** femtosecond

**GROMACS:** GROningen MAChine for Chemical Simulations

**ID:** Identification

**ID 32:** Pep1 analogue peptide

**ID 63:** Tryp1 analogue peptide

**ID 76:** Pep2 analogue peptide

**ID 101:** Chym1 analogue peptide

**ID 336:** Tryp2 analogue peptide

**IPE:** Interaction Potential Energy

**IPEi,j:** Energy between a group of atoms i and a group of atoms j

**K:** Kelvin

**kDa:** Kilodaltons

**kJ:** Kilojoules

**LINCS:** LINear Constraints Solver

**MOPAC:** Molecular Orbital PACkage

**Mpro:** Main protease of SARS-CoV-2

**Ni:** Total numbers of atoms in the groups i

**Nj:** Total numbers of atoms in the groups j

**nm:** nanometer

**NPT:** Number of particles, pressure, and temperature

**ns:** nanosecond

**NutriSBioativoS:** Nutrition and Bioactive Substances for Health

**NVT:** Number of particles, volume, and temperature

**PD:** Protease domain

**PDB:** Protein Data Bank

**Pep1:** Peptide obtained by cleavage with pepsin at position 57 (LTVSQTPIDIPIGL)

**Pep2:** Peptide obtained by cleavage with pepsin at position 73 (SSRARISHITTA)

**PME:** Particle-mesh Ewald sum

##### **POPC:** 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine

**POPS:** 1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-L-serine

**ps:** picosecond

**RBD:** Receptor binding domain

**RMSD:** Root-mean-square deviation

**RNA:** Ribonucleic acid

**S:** Spike protein

**SARS-COV-2:** Severe acute respiratory syndrome coronavirus 2

**TIP3P:** Transferable intermolecular potential with 3 points

**TMPRSS2:** Transmembrane serine protease 2

**trRosetta:** Transform-restrained Rosetta

**Tryp1:** Peptide obtained by cleavage with trypsin at position 60 (GGGLGLSNDDDGNCPLTVSQTPIDIPIGLPVR).

**Tryp2:** Peptide obtained by cleavage with trypsin at position 92 (ISHITTALSLNIEFTIAPACAPKPAR).

**TTI:** Trypsin inhibitor from tamarind seeds (Tamarindus indica L.)

**TTIp:** Trypsin inhibitor purified from tamarind seeds

**Velec ():** Electrostatic contributions

**VvdW ():** Van der Waals contributions