

Supplementary materials

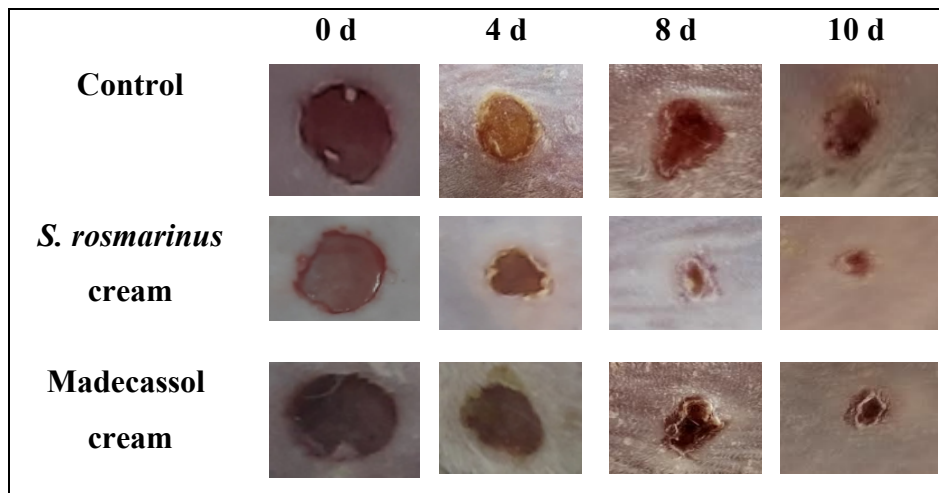


Figure 1S. Photograph of wound area after topical application of essential oil cream of *S. rosmarinus* and Madecassol[®] cream of excision wound model in mice.

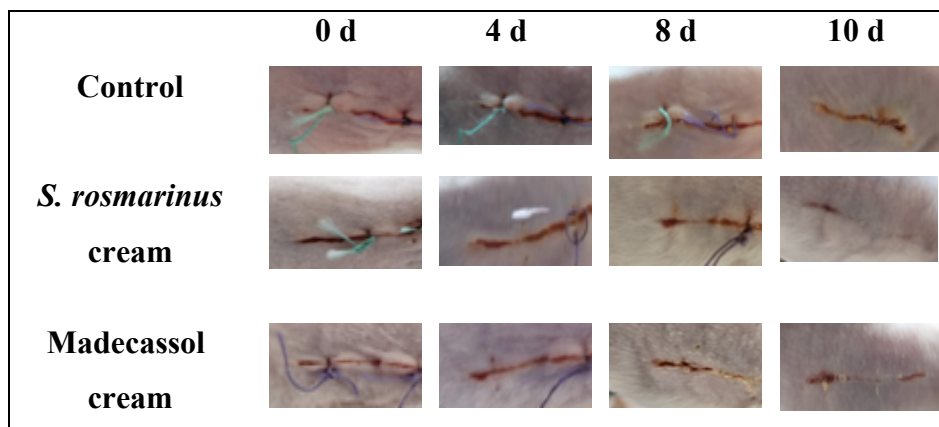


Figure 2S. Photograph of wound area after topical application of essential oil cream of *S. rosmarinus* and Madecassol[®] cream of incision wound model in mice.

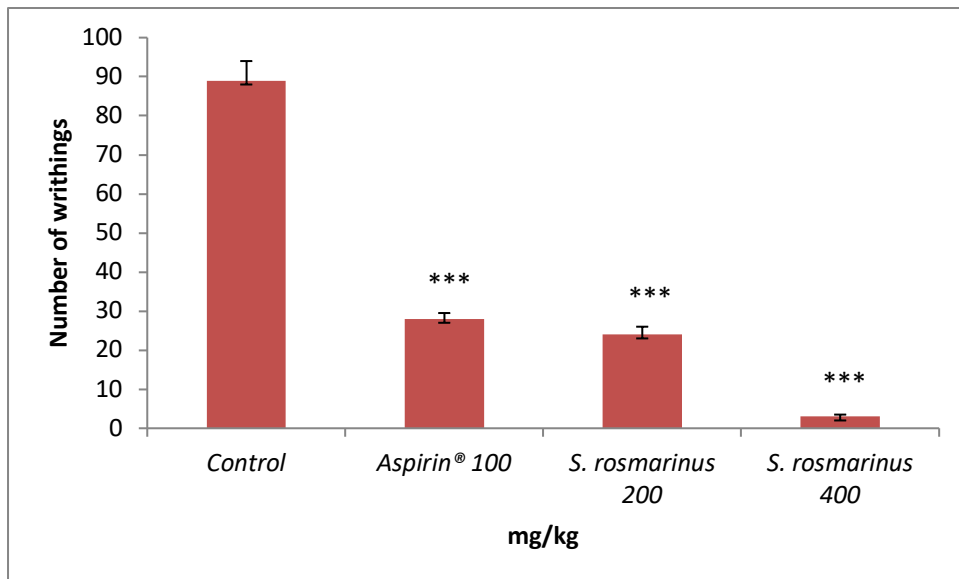


Figure 3S. Effect of *S. rosmarinus* on acetic acid-induced writhing in mice.

* $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$ are considered significant, compared to the control.

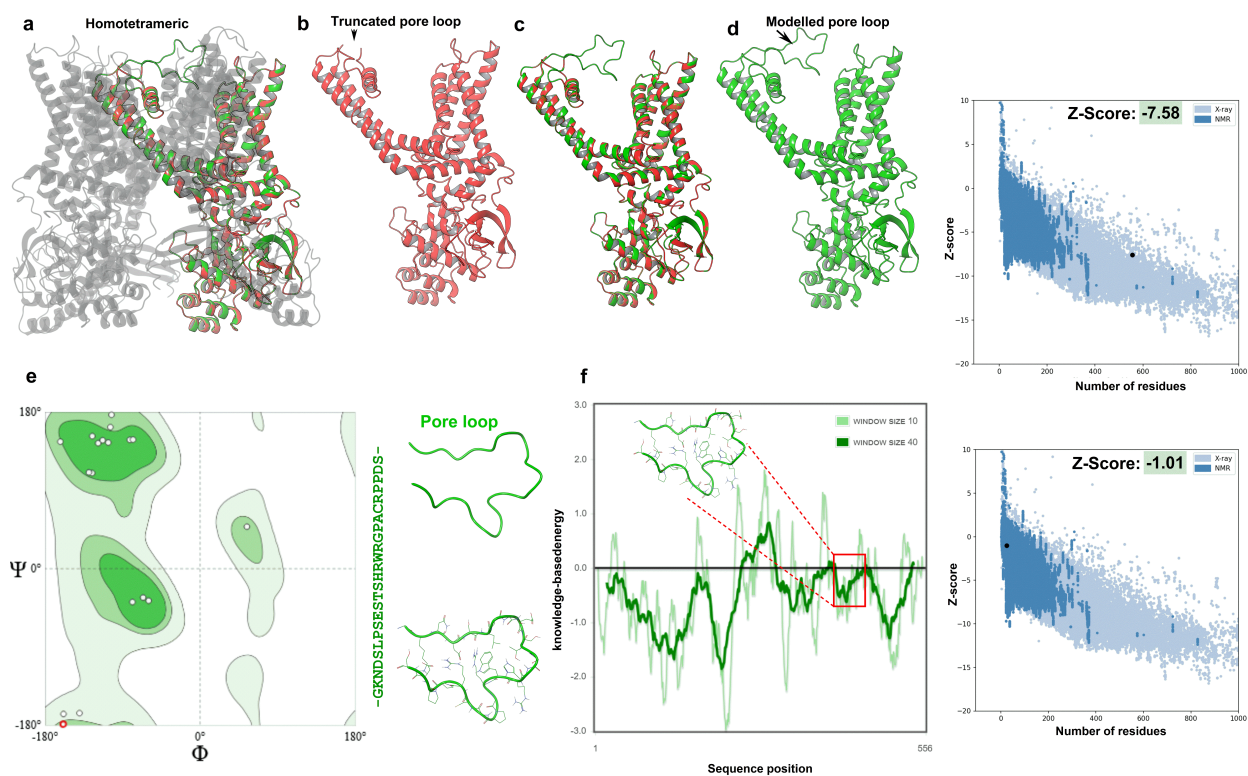


Figure 4S. Pore loop 3D modeling and validation include: (a) superposition of the modeled subunit (in green color) with one subunit of the tetrameric structure, (b) subunit of hTRPV1 with truncated pore loop (red color), (c) superposition of the two subunits of hTRPV1 with

truncated pore loop and modeled pore loop, and (d) subunit of hTRPV1 with modeled loop (in green color).

Validation: (e) ProSA-web, with a Z score of -7.58 for one subunit included the modeled Pore loop and Z score of -1.01 for the modeled Pore loop, as well as the local model quality by plotting energies as a function of amino acid sequence position (Pore loop region is bordered in red) (f) Ramachandran plot analysis showing in favored (dark green) and allowed (light green), regions of protein residues.

hTRPV1: human Transient receptor potential vanilloid1

Table 1S. Docking binding affinity of the screened compounds against hCOX-2 and hTRPV1.

Inflammation		Pain	
hCOX-2		hTRPV1	
Ligand	Binding affinity (kcal/mol)	Ligand	Binding affinity (kcal/mol)
α -Calacorene	-8	β -Bisabolene	-6.3

hCOX-2: Human Cyclooxygenase 2

hTRPV1: Human Transient Receptor Potential Vanilloid type 1

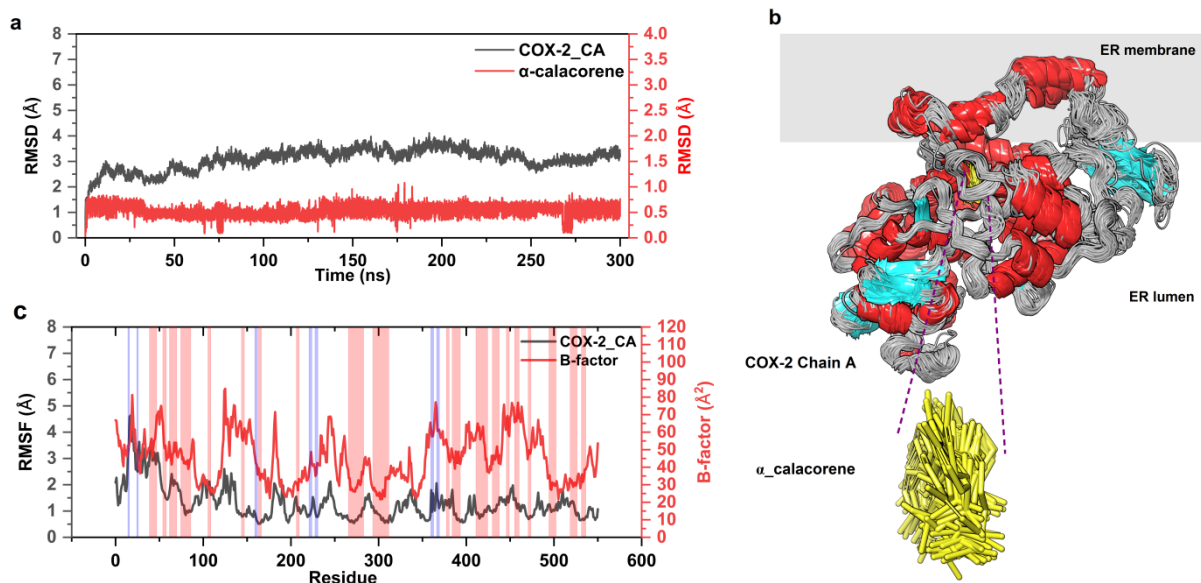


Figure 5S. Analysis of the RMSD for the (a) COX2/ α -calacorene complex throughout 300ns; COX2-C α and α -calacorene RMSD are colored in black and red respectively, (b) supported by view of superposition of 41 binding poses of the COX-2/ α -calacorene complex, (ligand is shown in yellow). (c) Root mean square fluctuations RMSF of the COX-2 C α atoms compared with the temperature factor (B factor) for 300ns trajectory. The regions corresponding to alpha-helix and beta-sheet structures are indicated by red and blue backgrounds, respectively.

RMSD: Root Mean Square Deviation

COX-2: Cyclooxygenase 2

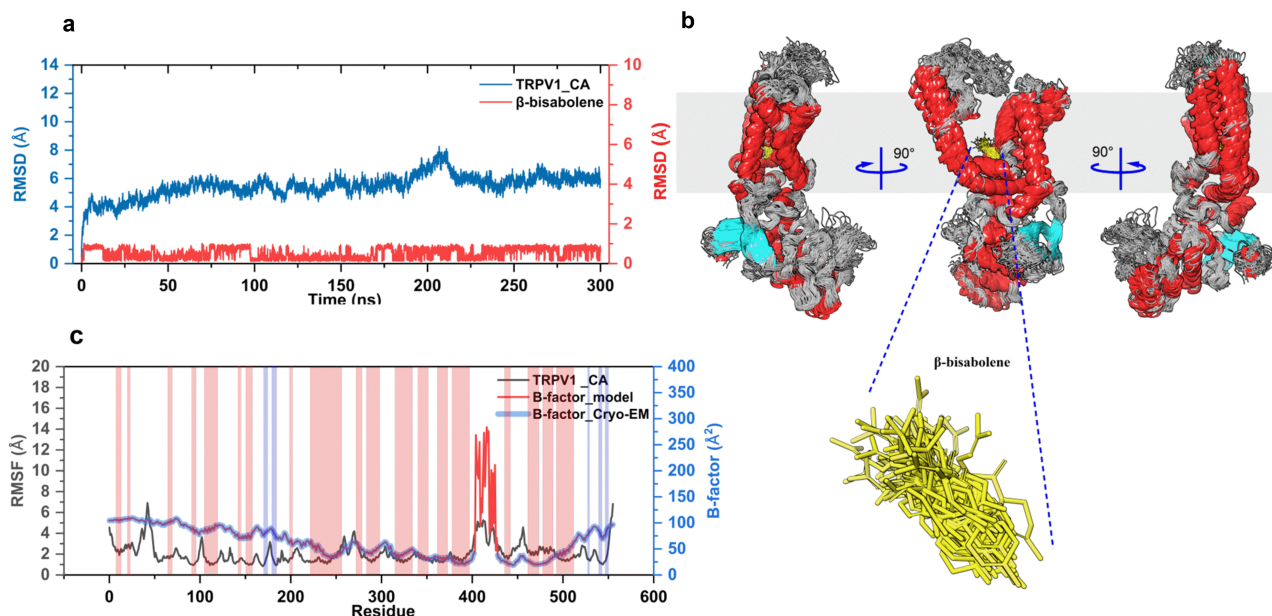


Figure 6S. Analysis of the RMSD for the (a) hTRPV1/ β -bisabolene complex throughout 300ns; TRPV1-C α and β -bisabolene RMSD are colored in blue and red respectively, (b) supported by view of superposition of 41 binding poses of the β -bisabolene complex, (ligand is shown in yellow). (c) Root mean square fluctuations (RMSF) of the TRPV1C α atoms compared with the temperature factor (B-factor) for 300ns trajectory. The modeled Pore loop B-factor is shown in red, alpha-helix and beta-sheet regions are highlighted in red and blue backgrounds, respectively.

RMSD: Root Mean Square Deviation

hTRPV1: human Transient receptor potential vanilloid1