Electronic Supplementary Information (ESI)

Molecular Mechanism Behind the Stabilization of Insulin by Choline and Geranate (CAGE) Ionic Liquids - Computational Insights on Oral Insulin Drug Formulation

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[†] Electronic Supplementary Information (ESI) available: The average values of RMSD and Rg, RMSF plots, H-bonding interactions of insulin with CAGE and water, RDF plots of water molecules with choline and geranate, and RDF plots of water molecules with carbonyl and amino groups.

Table S1 The RMSD and radius of gyration values of insulin backbone with different mole fractions of CAGE ILs and water.

No of systems	Mole fractions of CAGE ILs	Backbone RMSD (Å)	Backbone Rg (nm)
1.	0	1.66	1.32
2.	0.05	1.75	1.33
3.	0.10	1.47	1.33
4.	0.30	1.42	1.29
5.	0.50	1.47	1.31
6.	0.80	1.79	1.34
7.	1.00	1.12	1.33

Table S2 The atom types and charges of choline cation.

Atom names	Atom types	Charges
O1	OH	-0.6710
H5	HO	0.4658
C2	CT	0.2646
H3	H1	0.0197
H4	H1	0.0197
C1	CT	-0.0747
H1	HP	0.1496
H2	HP	0.1496
N1	N3	-0.0146
C4	CT	-0.3457
H9	HP	0.1920
H10	HP	0.1920
H11	HP	0.1920
C5	CT	-0.3457
H12	HP	0.1920
H13	HP	0.1920
H14	HP	0.1920
C3	CT	-0.3457
H6	HP	0.1920
H7	HP	0.1920
H8	HP	0.1920

Table S3 The atom types and charges of geranate anion.

Atom names	Atom types	Charges
O1	O2	-0.8338
C10	C	0.9997
O2	O2	-0.8338
C7	CM	-0.5719
H9	HA	0.1774
C3	CM	0.2772
C6	CT	0.0678
H6	HC	-0.0316
H7	HC	-0.0316
H8	HC	-0.0316
C1	CT	-0.0234
H1	HC	-0.0754
H2	HC	-0.0754
C2	CT	0.6023
H3	HC	-0.1493
H4	HC	-0.1493
C4	CM	-0.7484
H5	HA	0.2125
C5	CM	0.4973
C9	CT	-0.6853
H13	HC	0.1820
H14	HC	0.1820
H15	HC	0.1820
C8	CT	-0.6853
H10	HC	0.1820
H11	HC	0.1820
H12	HC	0.1820

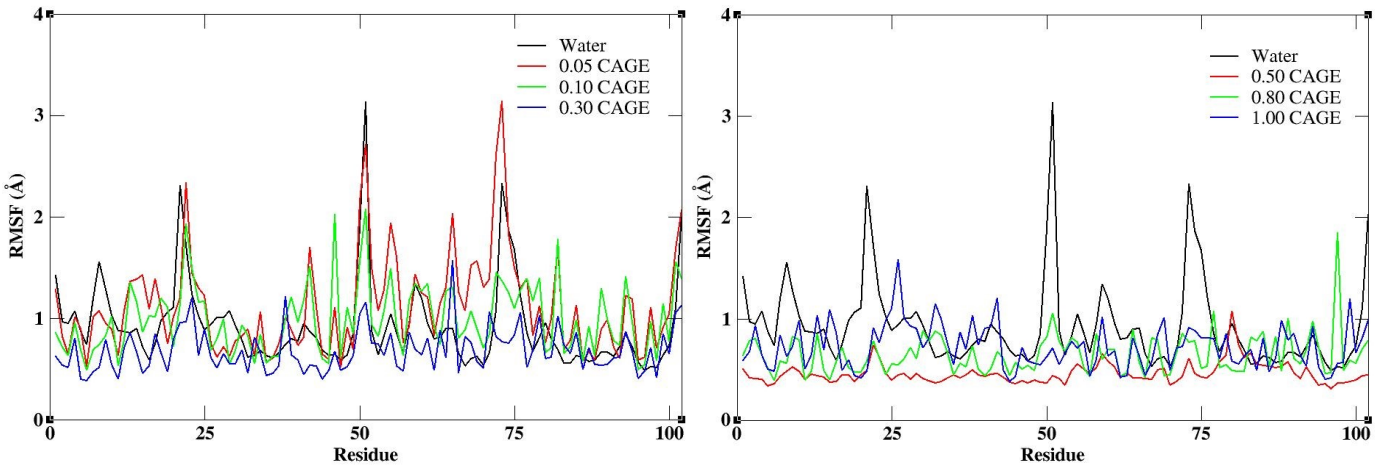

Fig. S1 The RMSF plots of insulin backbone with water and different mole fraction of CAGE ILs.

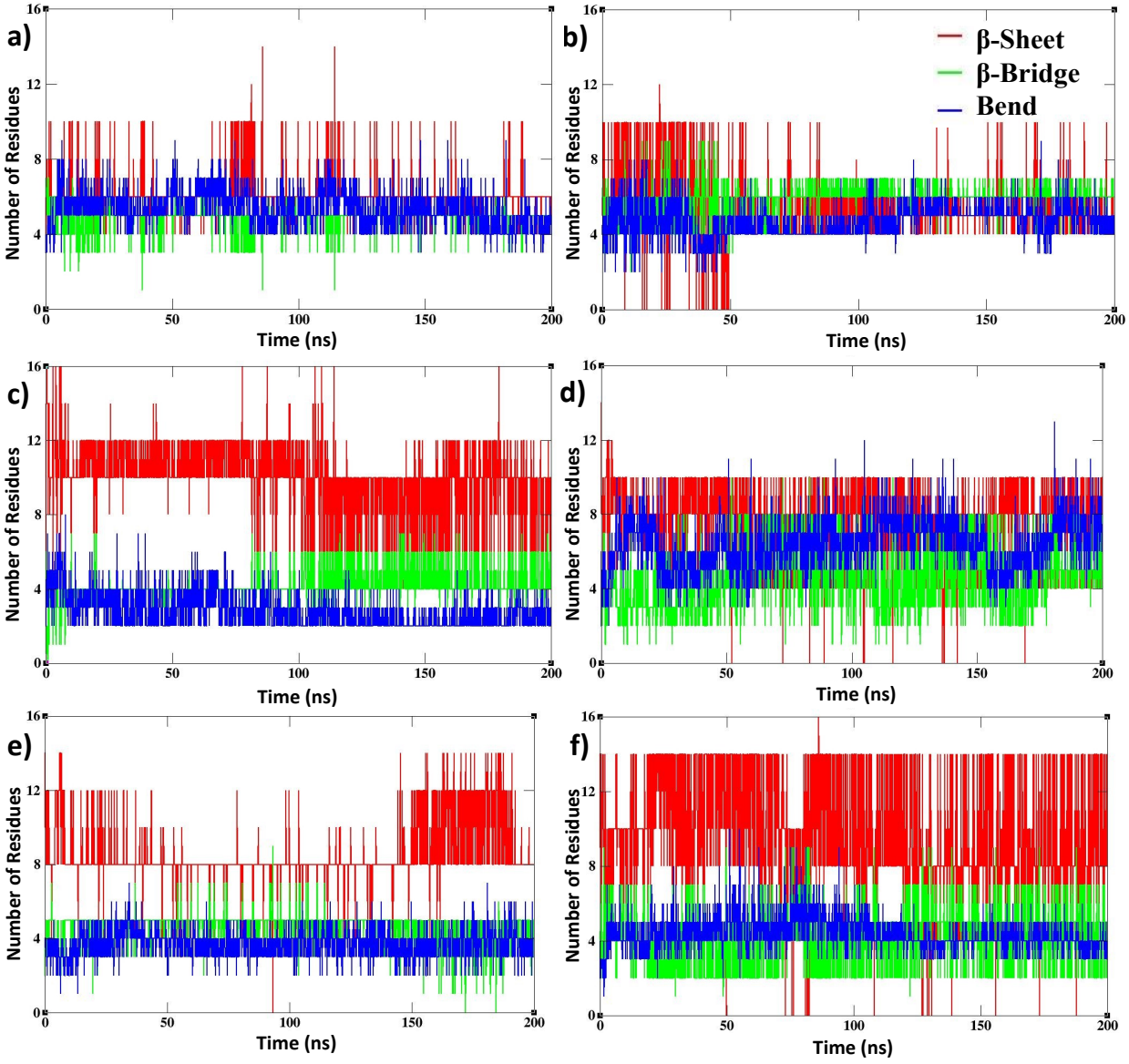

Fig. S2 The secondary structure of β-Sheet, β-Bridge and Bend are calculated for a) 0.05 b) 0.10 c) 0.30 d) 0.50 e) 0.80 f) 1.00 mole fraction of CAGE ILs.

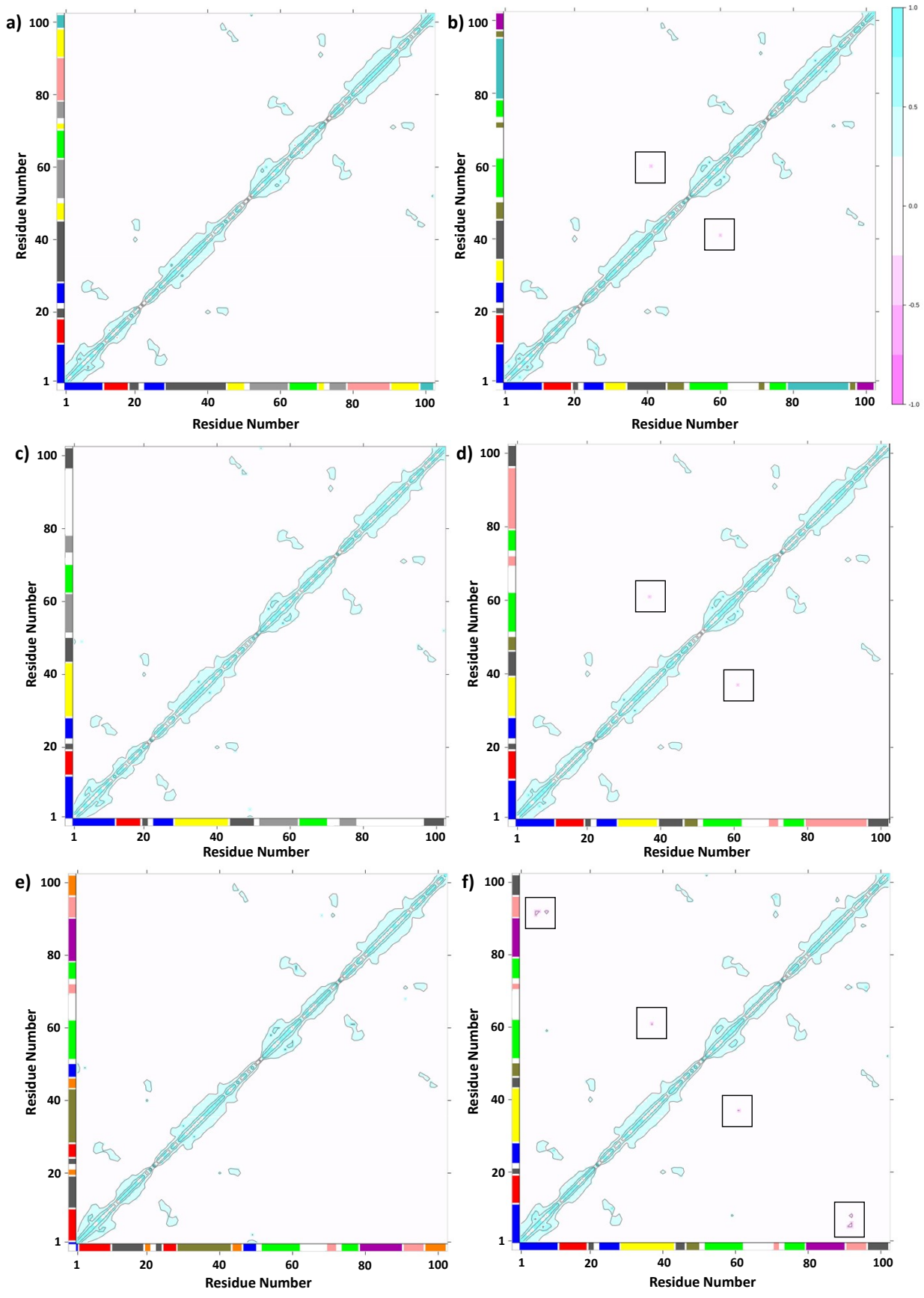
a)
b)
c)
d)
e)
f)
Residue Number
1
20
40
60
80
100
1.0
0.5
0.0
-0.5
-1.0

Fig. S3 The DCCM plots of insulin at a) 0.05 b) 0.10 c) 0.30 d) 0.50 e) 0.80 f) 1.00 mole fraction of CAGE ILs.

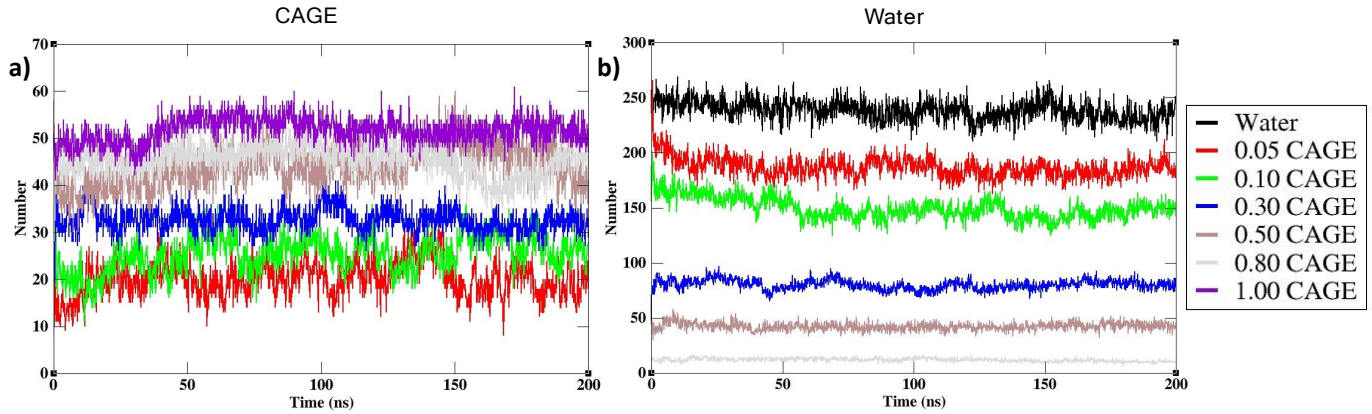

Fig. S4 The H-bonding interactions of insulin with a) CAGE and b) Water.

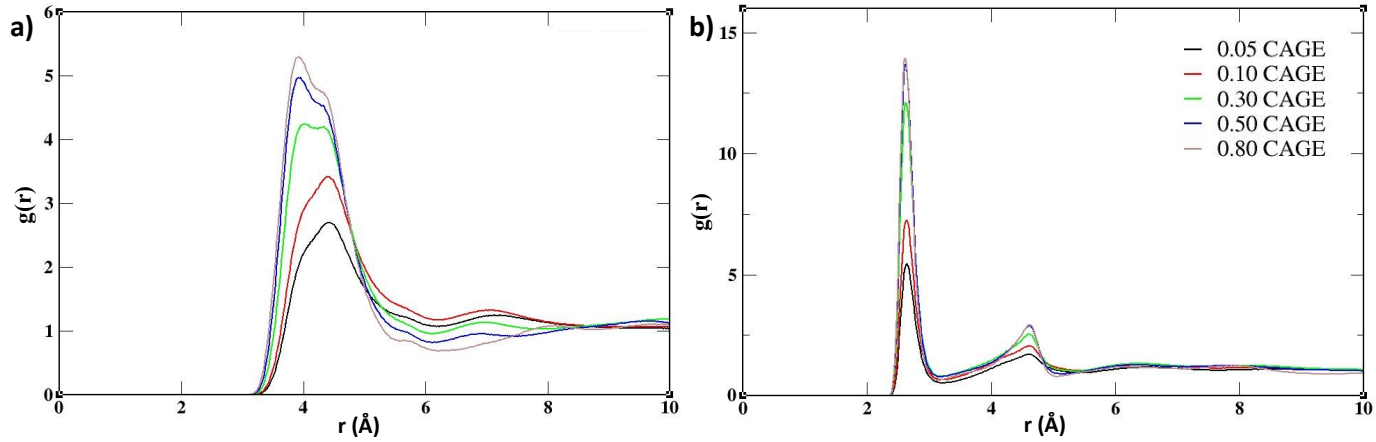

Fig. S5 The RDF plots of a) choline and b) geranate with water molecules.

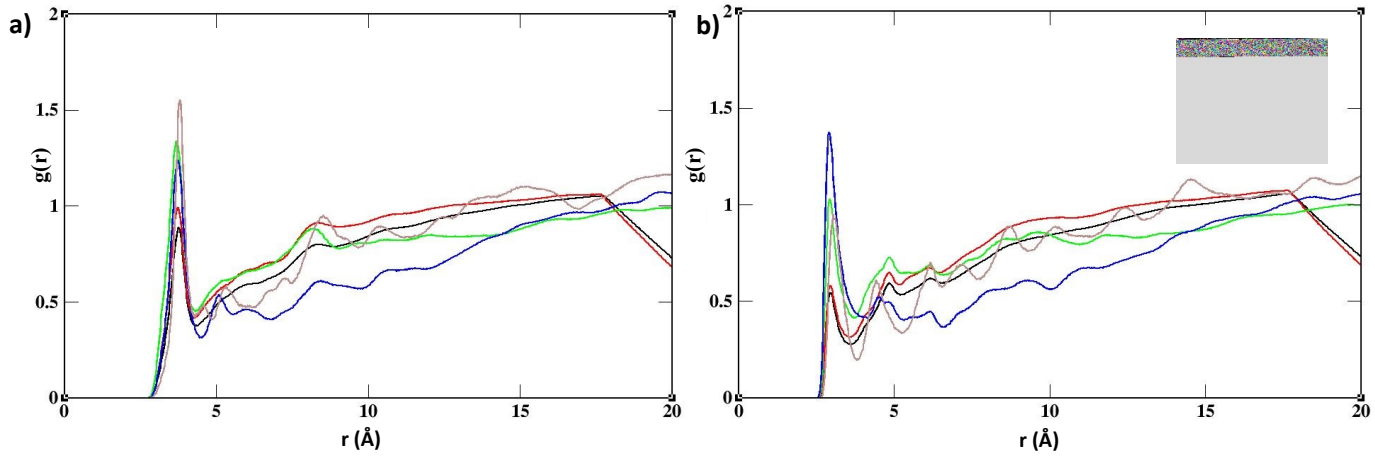

Fig. S6 The RDF plots of a) carbonyl and b) amino groups of insulin with water molecules.