Electronic Supplementary Material (ESI) for RSC Advances.

SUPPLEMENTARY DATA

3,4,3'-Tri-O-methylellagic Acid as an Anticancer Agent: *In Vitro* and *In Silico* Studies

Andika Pramudya Wardana[a,b], Muhammad Ikhlas Abdjan[b], Nanik Siti Aminah[b,c,*], Mochamad Zakki Fahmi[b], Imam Siswanto[b,d], Alfinda Novi Kristanti[b,c], Mirza Ardella Saputra[e], and Yoshiaki Takaya[f]

[a]Ph.D. Student of Mathematics and Natural Sciences, Faculty of Science and Technology, Universitas Airlangga, Surabaya 60115 , Indonesia

[b]Department of Chemistry, Faculty of Science and Technology, Universitas Airlangga, Surabaya 60115, Indonesia

[c]Biotechnology of Tropical Medicinal Plants Research Group, Universitas Airlangga, Indonesia

[d]Bioinformatic Laboratory, UCoE Research Center for Bio-Molecule Engineering, Universitas Airlangga, Surabaya, Indonesia

[e]Nanotechnology Engineering, Faculty of Advanced Technology and Multidiscipline, Universitas Airlangga, Surabaya 60115, Indonesia

[f]Faculty of Pharmacy, Meijo University, Tempaku-468-8502, Nagoya, Japan.

[*]Correspondence: Nanik Siti Aminah

Department of Chemistry, Faculty of Science and Technology, Universitas Airlangga, Surabaya 60115, Indonesia

Tel +62-31-5936501

Fax +62-31-5936502

Email nanik-s-a@fst.unair.ac.id

FIGURES:

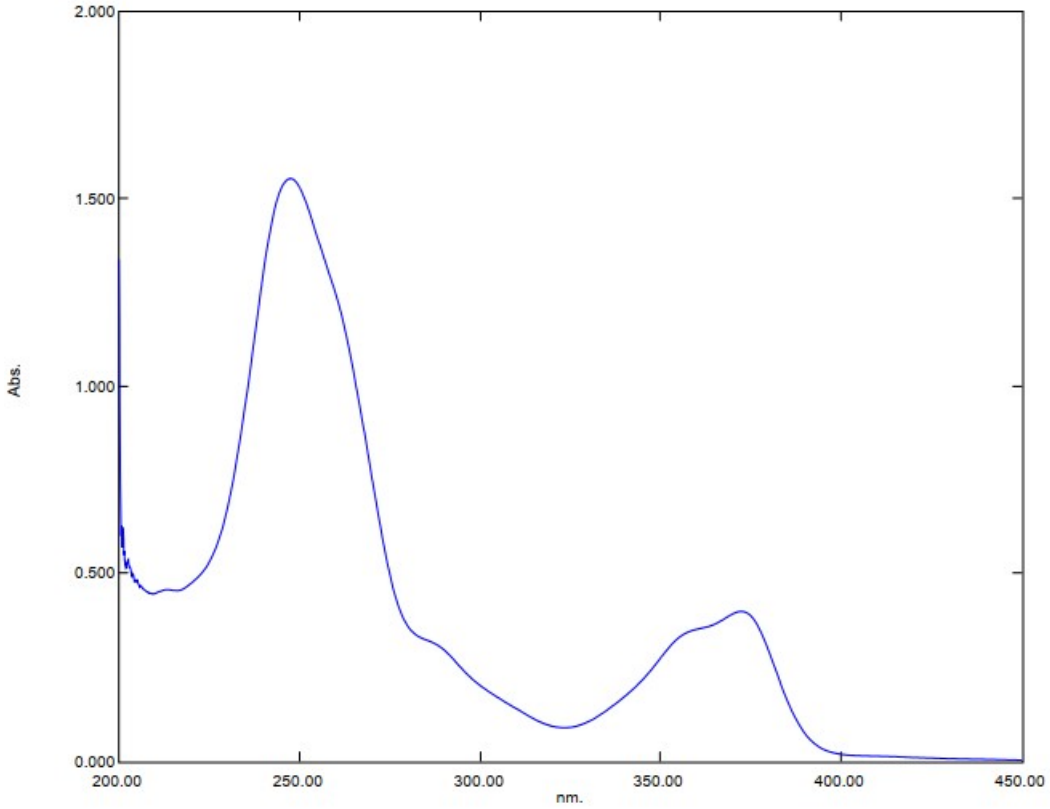

Fig. S1 UV-Vis spectra of T-EA

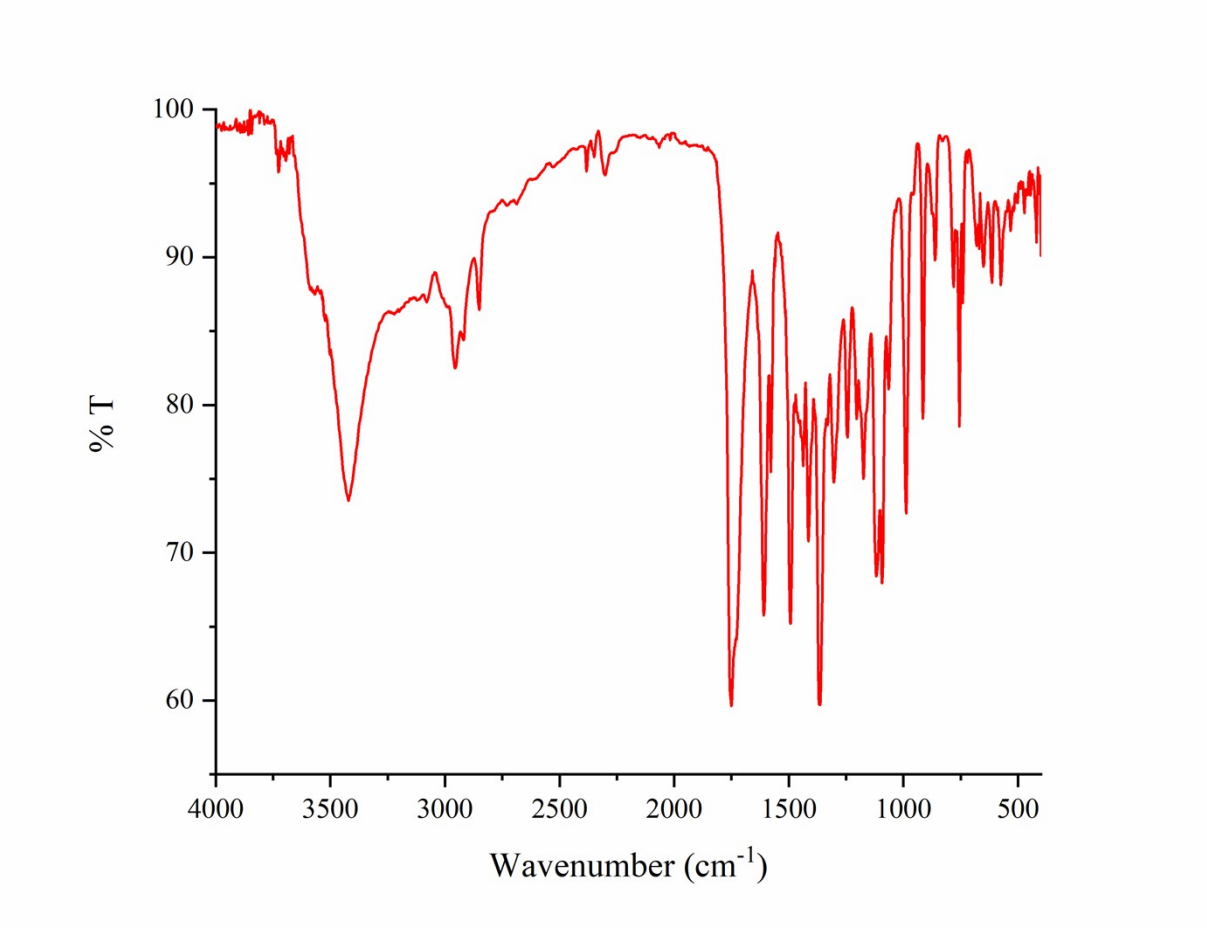

Fig. S2 FTIR spectra of T-EA

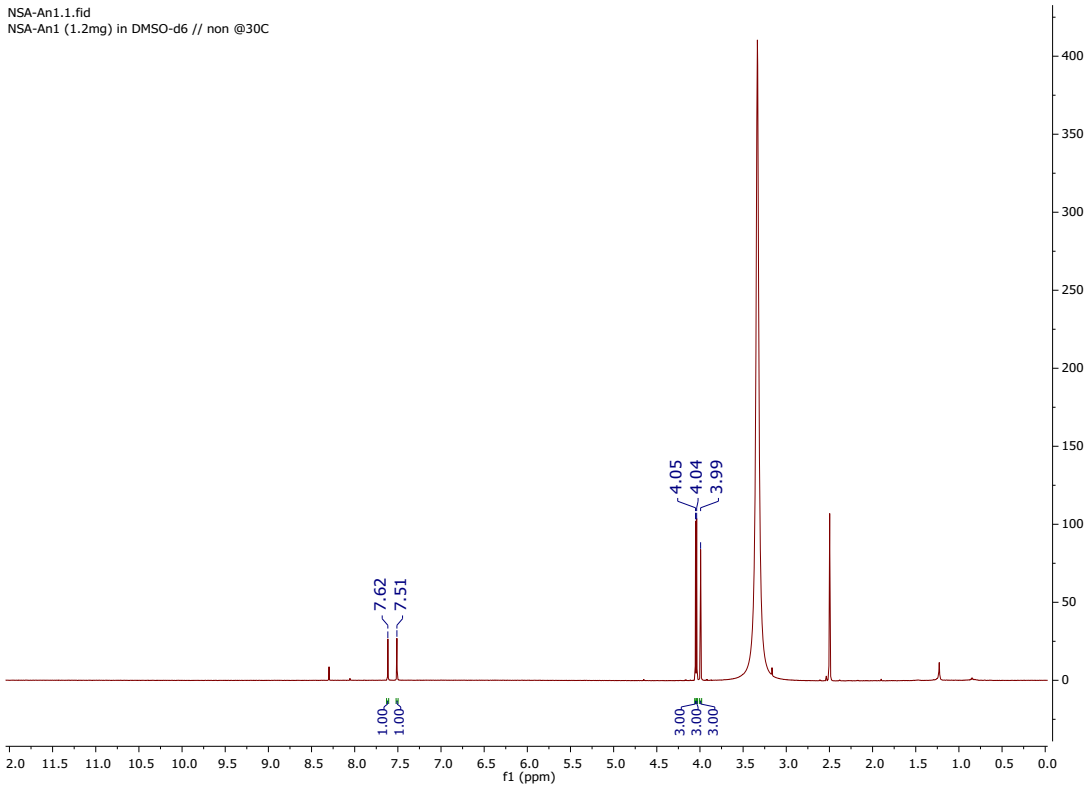

Fig. S3 ^{1}H-NMR spectra of T-EA

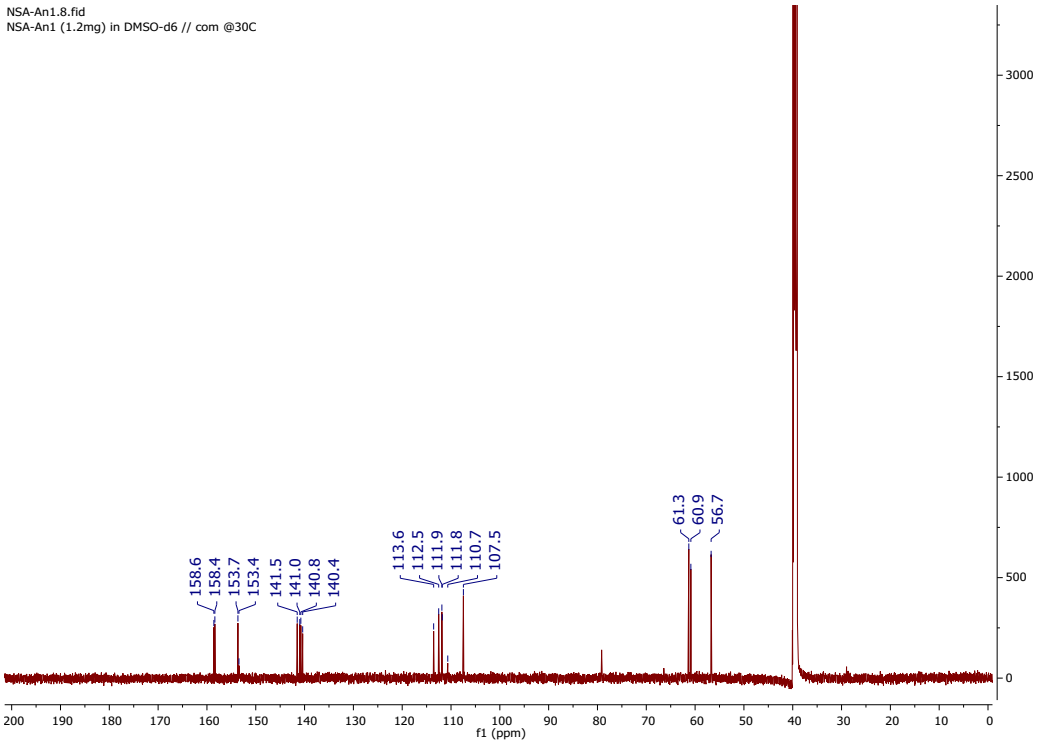

Fig. S4 ^{13}C-NMR spectra of T-EA.

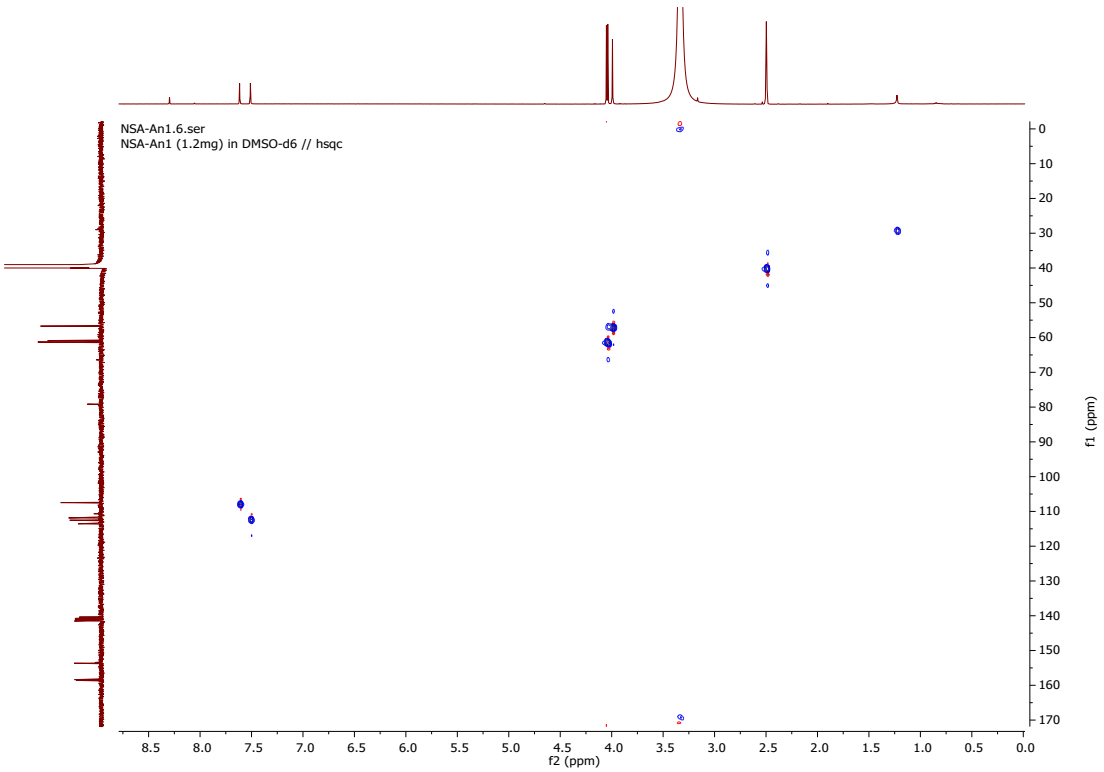

Fig. S5 HSQC spectra of T-EA.

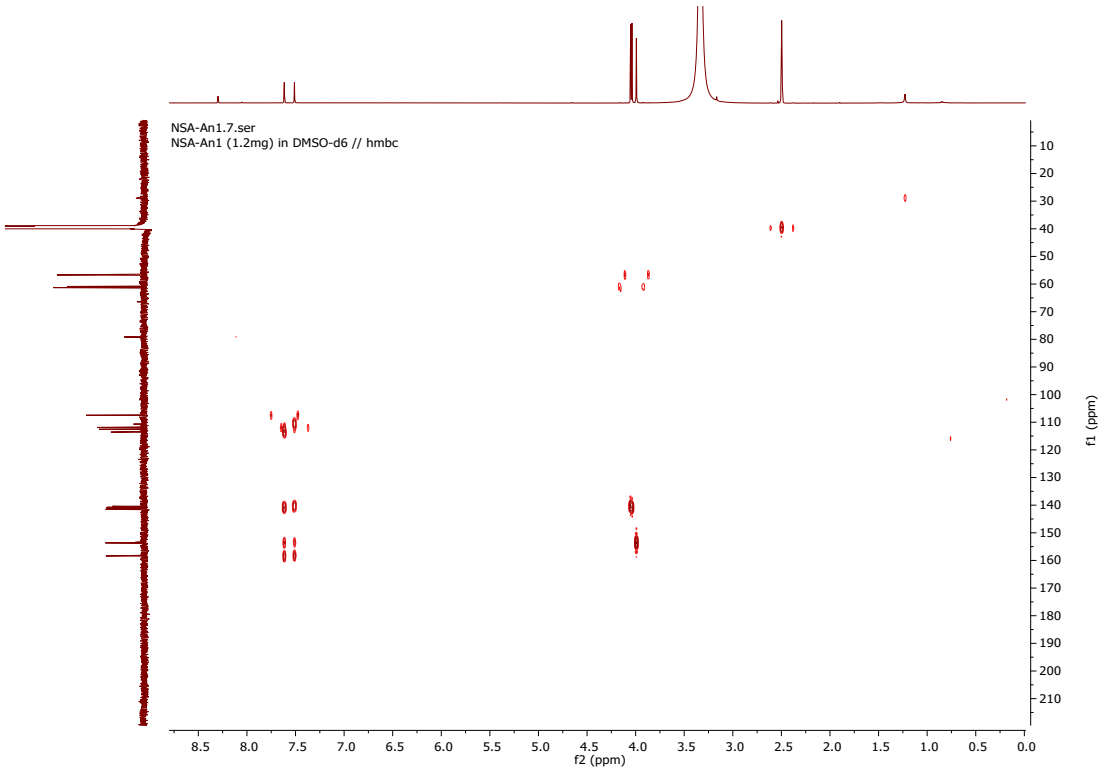

Fig. S6 HMBC spectra of T-EA.

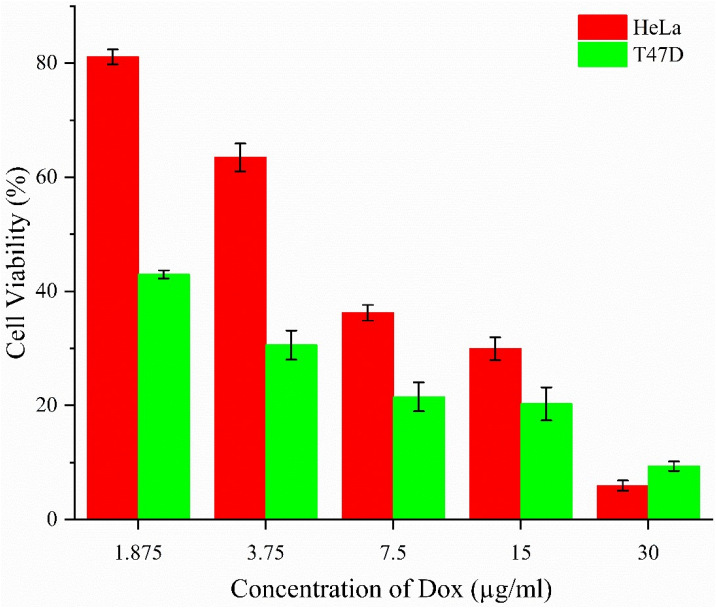

Fig. S7 The doxorubicin concentration-effect: The percentage of cell viability on HeLa and T47D cell line.

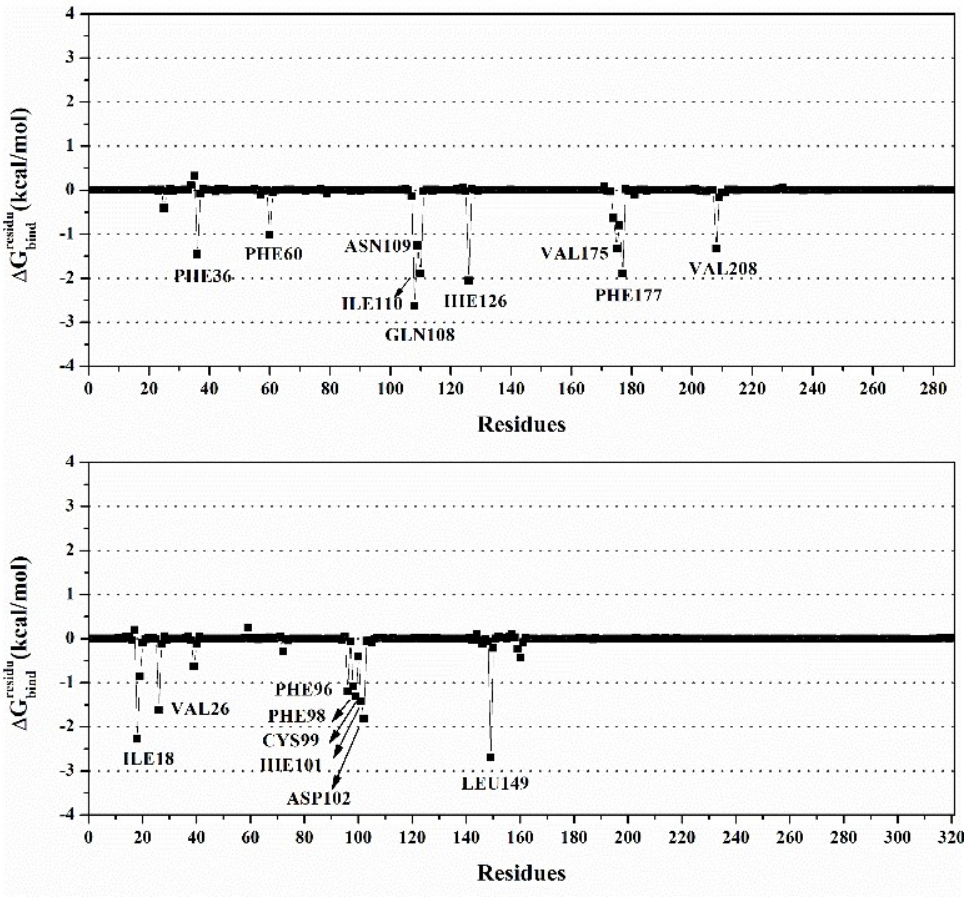

Fig. S8 The residual energy decomposition was plotted along with the simulation over the last 20 ns using the MM-GBSA approach: T-EA-4I5I (top) and T-EA-3TNH (bottom).

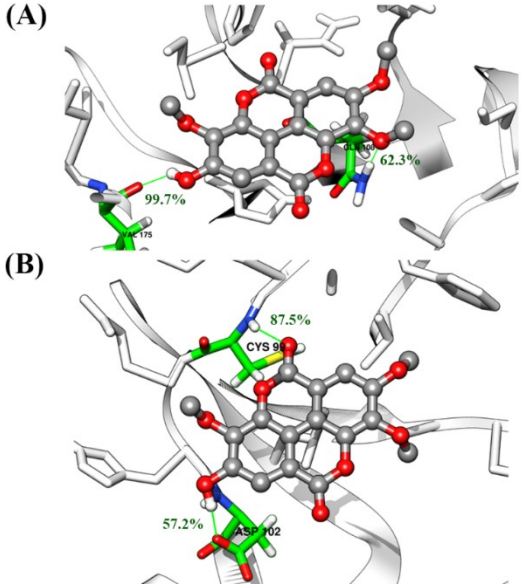

Fig. S9 H-bond analysis of each complex during the simulation over the last 20 ns.

Tables:

Table S1 Molecular docking validation of native ligand.

Reference Ligand	RMSD (Å)	H-bond (Å)	Grid score (kcal/mol)	E_{VDW} (kcal/mol)	E_{Elec} (kcal/mol)	E_{Int} (kcal/mol)
4I5	0.449	4I5:HN2-Gln108:O (2.70) Ile110:H-4I5:O1 (2.06) 4I5:H11-Asp111:OD2 (1.84) Asp111:H-4I5:O1 (2.35)	-59.10	-53.30	-5.80	1.77
F18	0.519	F18:H161-Ile18:O (2.91) Lys41:HZ2-F18:O3 (2.00) F18:H3-Glu59:OE2 (1.77) F18:H182-Asp97:O (2.35) Cys99:H-F18:N17 (2.05) F18:H20-Cys99:O (2.66)	-49.10	-40.56	-8.53	8.60

Table S2 Molecular docking result of candidate-receptor.

Energy Component (Kcal/mol)	T-EA-4I5I	T-EA-3TNH
Grid score	-59.59	-55.90
E_{VDW}	-58.71	-53.08
E_{Elec}	-0.88	-2.81
E_{Elec}	4.86	4.97

Table S3 Physicochemical properties, lipophilicity, water-solubility, drug-likeness, and pharmacokinetics.

Classification	Parameters	T-EA
Physicochemical Properties	Formula	$C_{17}H_{12}O_8$
	MW (g/mol)	344.27
	Num. Atoms	37
	Number of Carbon	17
	Number of Heteroatoms	3
	Number of Rings	4
	Number of Rotatable bonds	3
	Fraction Csp3	0.18
	∑ HBD	1
	∑ O+N	8
	TPSA ($Å^2$)	88.72
	Molar Refractivity	108.34
Lipophilicity	Log $P_{o/w}$ (X LogP3)	2.08
	Log $P_{o/w}$ (W LogP)	2.22
	Log $P_{o/w}$ (M LogP)	0.89
Water-solubility	Log S (ESOL)	-3.56
	ESOL Class	Soluble
Drug-likeness	Lipinski	0/Yes
	Ghose	0/Yes
	Veber	0/Yes
	Egan	0/Yes
	Muegge	0/Yes
	Total Valiations/n	0
	Bioavailibility Score	0.55
Pharmacokinetics	GI Absorption	High
	BBB Permanent	No
	CYP2C19 Inhibitor	No
	CYP2D6 Inhibitor	No