Supplementary Material

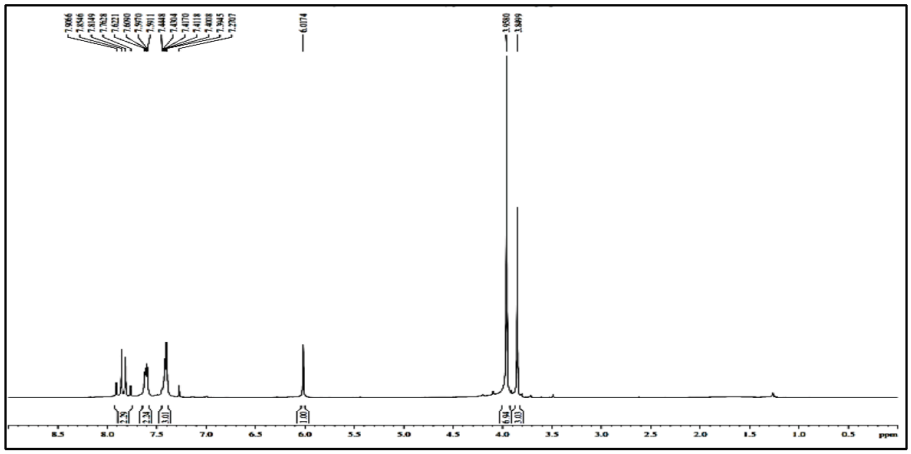

Figure S1: ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of the chalcone (*E*)-1-(2-hydroxy-3,4,6-trimethoxyphenyl)-3-phenylprop-2-en-1-one.

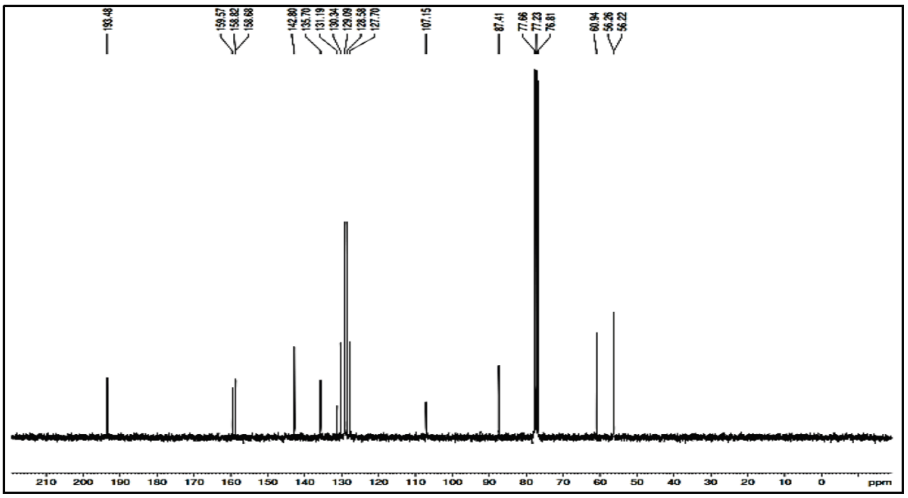

Figure S2: ^{13}C NMR spectrum ($CDCl_3$, 125 MHz) of the chalcone (*E*)-1-(2-hydroxy-3,4,6-trimethoxyphenyl)-3-phenylprop-2-en-1-one.

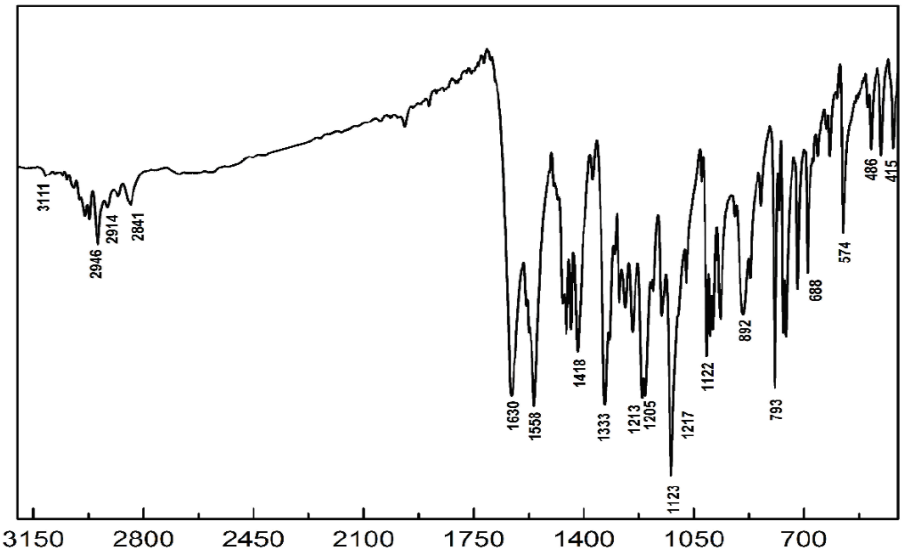

Figure S3: IR spectrum of chalcone (E)-1-(2-hydroxy-3,4,6-trimethoxyphenyl)-3-phenylprop-2-en-1-one.

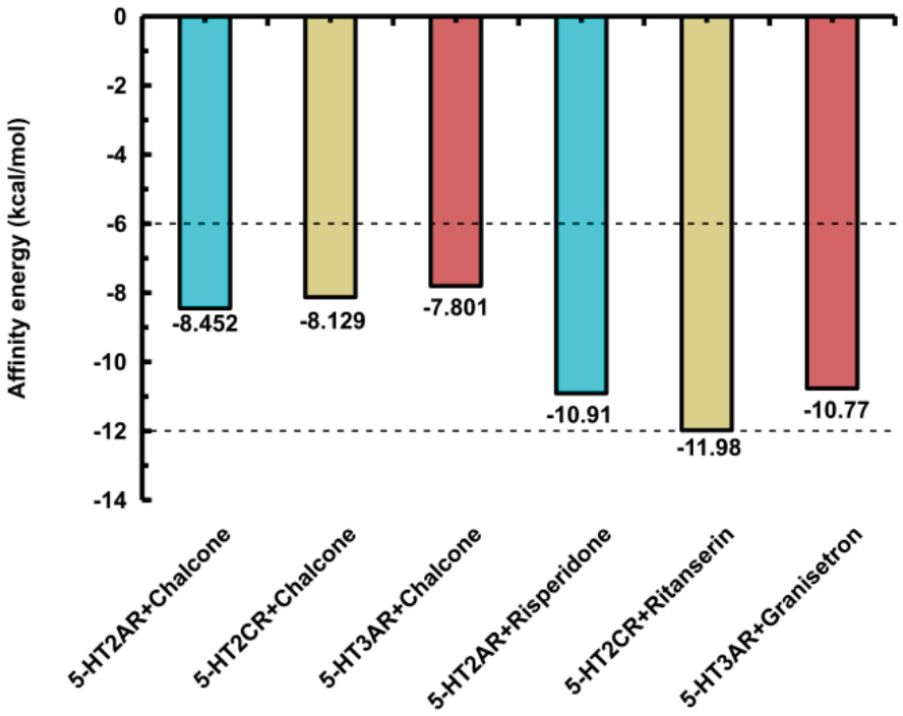

Figure S4: Affinity energy values of ligand-receptor complex formation between chalcone and 5-HT2AR, 5-HT2CR and 5-HT3AR receptors compared to controls risperidone (5-HT2AR antagonist), ritanserin (5-HT2CR agonist) and granisetron (5-HT3AR antagonist), in kcal/mol.

Table S1: ^{1}H NMR and ^{13}C data of the chalcone (*E*)-1-(2-hydroxy-3,4,6-trimethoxyphenyl)-3-phenylprop-2-en-1-one in CDCl3. The chemical shifts in δ_H and δ_C are in ppm

C	δ_C	δ_H
1´	107.1	
2´	158.7	
3´	131.2	
4´	159.5	
5´	87.3	6.01 (s)
6´	158.8	
MeO-3	60.9	3.85 (s)
MeO-4	56.3	3.96 (s)
MeO-6	56.2	3.96 (s)
C=O	193.5	
1	135.7	
2/6	128.6	7.60 (dd, *J* = 7.53; 1.77 Hz)
3/5	129.1	7.43 (m)
4	130.3	7.42 (m)
C_α	127.7	7.79 (d, *J* = 15.60 Hz)
C_β	142.8	7.88 (d, *J* = 15.60 Hz)

Table S2: Chemical descriptors of Global Reactivity Calculated from the Energies of the HOMO and LUMO Frontier Molecular Orbitals

Descriptors	DMSO	Water
HOMO energy (E_{HOMO}, eV)	-6.1199	-6.1218
LUMO energy (E_{LUMO}, eV)	-2.5056	-2.5086
Energy gap (ΔE_{gap}, eV)	3.6143	3.6132
Ionization potential (I, eV)	6.1199	6.1218
Electron affinity (A, eV)	2.5056	2.5086
Electronegativity (χ, eV)	4.3128	4.3152
Global chemical hardness (η, eV)	1.8072	1.8066
Global chemical softness (S, eV^{-1})	0.5534	0.5535
Global electrophilicity index (ω, eV)	5.1462	5.1536
Global nucleophilicity index (ϵ, eV^{-1})	0.1943	0.1940

Table S3: Data from Molecular Docking Simulations Expressed in Statistical Parameterization of RMSD and Ligand-Receotor Interactions

Target (PDB)	Compound	RMSD	Ligand-receptor interactions		
			Type	Residue	Distance
5-HT_{2A}R (6A93)	Chalcone	1.199 Å	Hydrophobic	Pro209	3.92
			Hydrophobic	Ile210	3.65
			Hydrophobic	Leu229	3.39
			Hydrophobic	Phe234	3.73
			H-bond	Ser159	2.81
	Risperidone	1.626 Å	Hydrophobic	Trp151	3.47
			Hydrophobic	Phe332	3.75
			Hydrophobic	Trp336	3.54
			Hydrophobic	Phe339	3.89
			Hydrophobic	Leu362	3.58
			H-bond	Tyr370	3.41
			π-Stacking	Trp336	4.64
			π-Stacking	Trp336	5.04
			π-Stacking	Phe340	4.75
			Salt Bridges	Asp155	3.09
5-HT_{2C}R (6BQH)	Chalcone	1.426 Å	Hydrophobic	Ile142	3.94
			Hydrophobic	Phe223	3.58
			Hydrophobic	Phe328	3.95

			H-bond	Asp134	2.26
			π-Stacking	Trp324	4.83
			π-Stacking	Phe327	5.20
			π-Stacking	Phe328	4.95
	Ritanserin*	1.14 Å	Hydrophobic	Trp130	3.69
			Hydrophobic	Ile142	3.75
			Hydrophobic	Ala222	3.87
			Hydrophobic	Phe223	3.75
			Hydrophobic	Phe328	3.34
			Hydrophobic	Tyr358	3.92
			π-Stacking	Trp324	4.89
			Halogen bond	Phe214	3.74
			Salt Bridges	Asp134	3.07
5-HT_{3A}R (6NP0)	Chalcone	1.309 Å	Hydrophobic	Ile44	3.65
			Hydrophobic	Trp63	3.91
			Hydrophobic	Phe199	3.70
			Hydrophobic	Phe199	3.80
			Hydrophobic	Tyr207	3.78
			H-bond	Arg65	3.23
			H-bond	Arg169	2.73
			H-bond	Arg169	3.21
			π-Stacking	Tyr207	4.14
	Granisetron*	1.647 Å	Hydrophobic	Ile44	3.66
			Hydrophobic	Trp63	3.60
			Hydrophobic	Arg65	3.78
			Hydrophobic	Trp156	3.66
			Hydrophobic	Phe199	3.53
			Hydrophobic	Tyr207	3.55
			π-Cation	Arg65	4.43
			π-Cation	Arg65	4.26

*Ligands co-crystallized in the three-dimensional structure of the receptors.

Table S4: Physicochemical Properties Calculated and Applied to the Pfizer, Inc. Biopharmaceutical Classification System

Property	Value	T0
ClogP	3.76	0.62
ClogD at pH 7.4	3.75	0.13
MW	314.34 g/mol	1.00
TPSA	64.99 Å²	1.00
HBD	1	0.75
pKa	-4.44	1.00
MPO score	4.50	-
Pfizer rule	Alert	ClogP > 3 and TPSA < 75 Å²
Golden Triangle rule	Accepted	-

Table S5: Pharmacokinetic Properties Predicted from the ADME Consensus Test between the ADMETlab 2.0 and pkCSM Platforms Related to MPO Analyses

Property	ADMETlab 2.0	pkCSM
P_{app} [a]	1.5×10^{-5} cm/s	1.24 ($\log P_{app}$ in cm/s)
P-gp substrate	0.67	No
HIA	>30%	96.67%
Fu	3.85%	0.03
$CL_{int,u}$	8.90 mL/min/kg	0.28 ($\log CL_{int,u}$ in mL/min/kg)
DILI	0.54	No
Mutagenicity	0.07	No

a: Estimated P_{app} value for the MDCK (ADMETlab 2.0) and Caco-2 (pkCSM) cell lines.