Supplemental information

Experimental Measurements and Thermodynamic Modeling of the Solubilities of Metoprolol Succinate in Organic Solvents at Different Temperatures

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Table S1. Experimental solubilities of metoprolol succinate, $\ln(x_{\text{exp, 298 K}})$, and solvent property values used in QSPR study

Property	Methanol	Ethanol	*n*-Butanol	*n*-Propanol	Isopropanol
$\ln(x_{\text{exp, 298 K}})$	1.5562	−0.1960	−0.9755	−0.9862	−1.8326
Physical properties [a]					
Molecular weight (g/mol)	32.04	46.07	74.12	60.1	60.1
Density at 25 °C (g/mL)	0.792	0.7893	0.81	0.803	0.786
Viscosity at 25 °C (mPa·s)	0.545	1.074	2.573	1.959	1.96
Molar Volume (cm^3/mol)	40.7	58.7	92	75.1	76.9
Dipolar (D)	1.69	1.69	1.66	1.68	1.66
Acidity (p*K*a)	15.5	15.9	16.1	16	16.5
Refractive index	1.3314	1.3611	1.3993	1.3870	1.3776
Melting point (°C)	−98	−114.14	−89	−127	−89.5
Boiling point (°C)	64.7	78.29	117.7	97	82.6
Dielectric Constant	32.6	24.3	17.8	20.1	18.3
Hansen solubility parameters ($MPa^{1/2}$) [b]					
Dispersion	15.14	15.75	15.95	15.95	15.75
Dipolar	12.27	8.8	5.73	6.75	6.14
Acidic	17.18	16.98	13.09	15.34	14.52
Basic	14.52	11.25	9.41	9.82	9.2
Hydrogen Bonding	22.3	19.43	15.75	17.39	16.36

[a] [1] D.R. Lide, CRC Handbook of Chemistry and Physics, Internet Version 2005, CRC Press, Boca Raton, FL, (2005); [2] PubChem: https://pubchem.ncbi.nlm.nih.gov.

[b] A. Jouyban, Handbook of solubility data for pharmaceuticals, CRC Press.

Table S2. The linear correlation coefficient values between solubility ln($x_{exp,\ 298\ K}$) and each physical properties.

	Coefficients
ln($x_{exp,\ 298\ K}$)	1.000
Molecular weight	−0.833
Density at 25 °C (g/mL)	−0.136
Viscosity at 25 °C (mPa·s)	−0.836
Molar Volume	−0.854
Dipolar	0.773
Acidity (pK_a)	−0.960
Refractive index	−0.850
Melting point (°C)	−0.071
Boiling point (°C)	−0.601
Dielectric Constant	0.964
Dispersion	−0.847
Dipolar	0.956
Acidic	0.733
Basic	0.978
Hydrogen Bonding	0.940

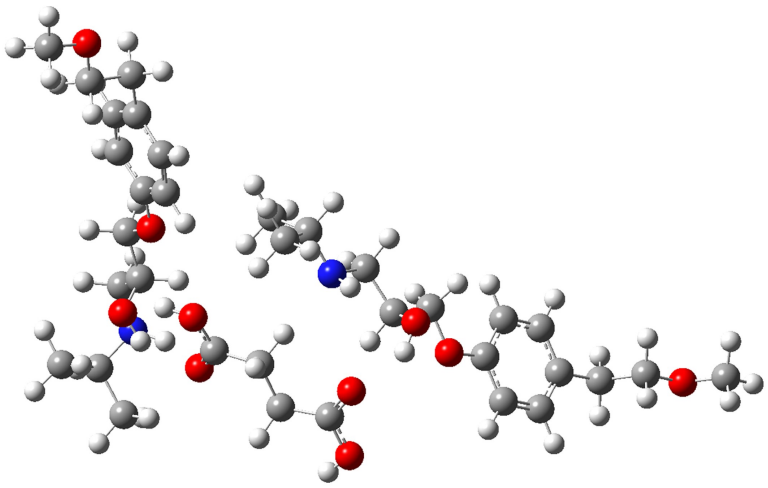

Figure S1. The optimized structure of metoprolol succinate calculated by DFT.

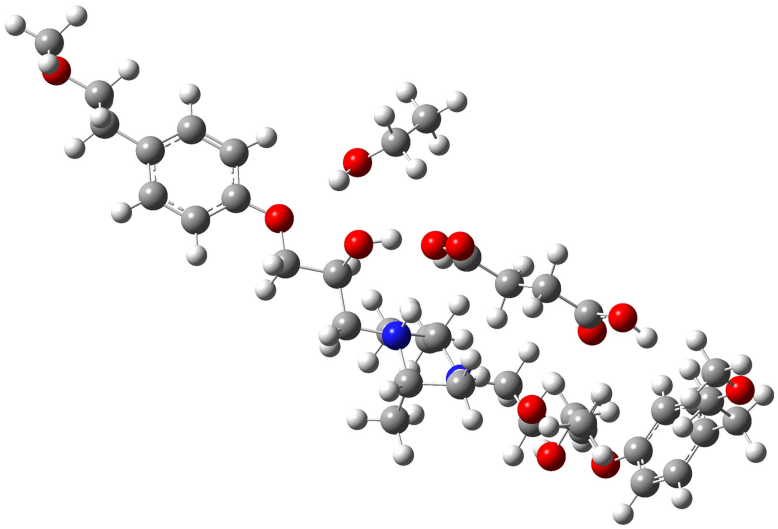

Figure S2. The optimized structure of metoprolol succinate with ethanol calculated by DFT.

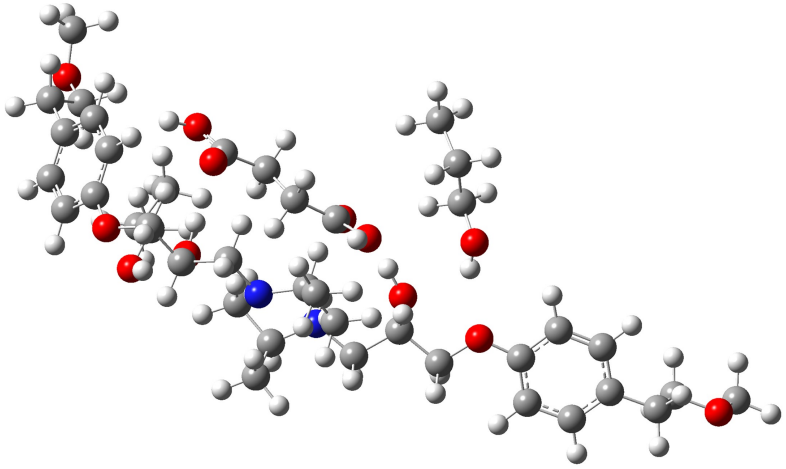

Figure S3. The optimized structure of metoprolol succinate with *n*-propanol calculated by DFT.

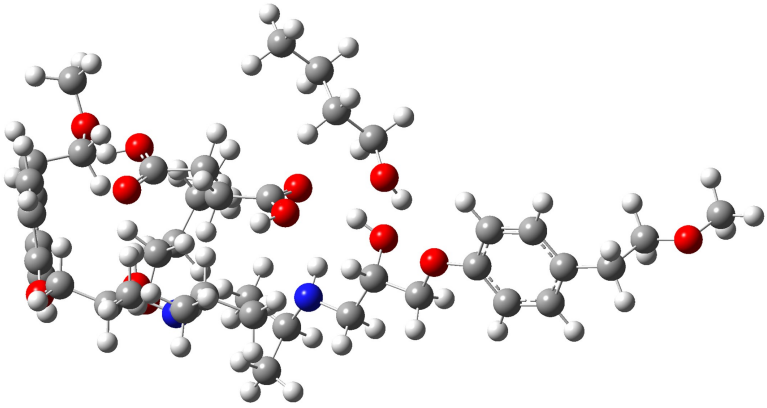

Figure S4. The optimized structure of metoprolol succinate with *n*-butanol calculated by DFT.

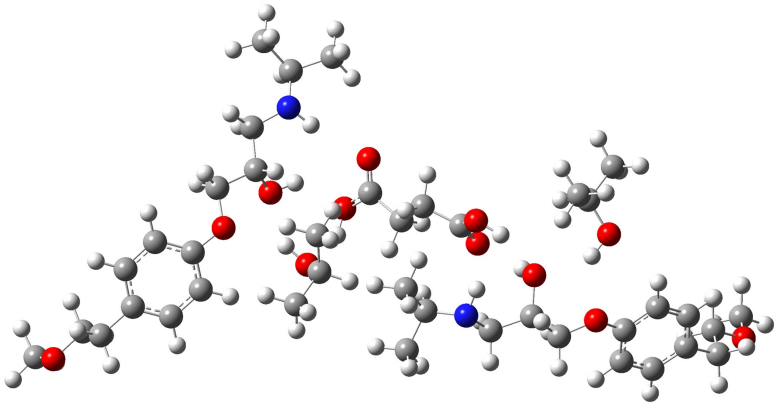

Figure S5. The optimized structure of metoprolol succinate with isopropanol calculated by DFT.