

**Thermodynamic solubility profile of temozolomide in different commonly used
pharmaceutical solvents**

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Materials

TMZ was purchased from “Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan)”. DMSO and 1-BuOH were bought from “BDH Laboratory Supplies (Poole, UK)”. EA was acquired from “Winlab Ltd. (Leicestershire, UK)”. EG and PG were obtained from “Anova Chem (Hurden, Switzerland)”. EtOH was bought from “Sigma-Aldrich (St. Louis, MO, USA)”. IPA was obtained from “Panreac Química, S.A.U. (Barcelona, Spain)”. Milli-Q H₂O was obtained from a “Millipore system (Millipore SAS, Molsheim, France)”. PEG-400 was obtained from “Merck Schuchardt (Munchen, Germany)”. TC was purchased from “Sigma-Aldrich (St. Louis, MO, USA)” (Table S1).

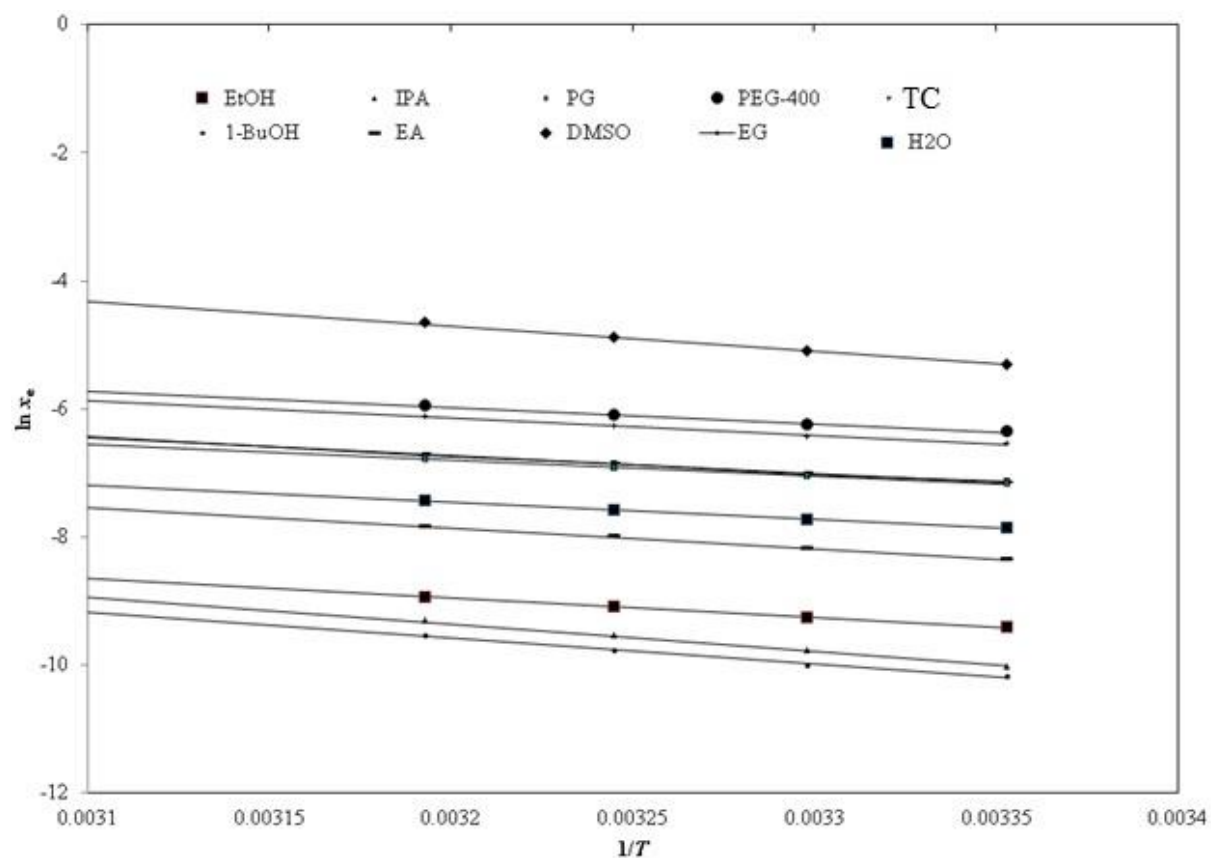


Figure S1: Correlation of $\ln x_e$ values of TMZ with “Van’t Hoff model” in various neat solvents as a function of $1/T$; symbols represent the experimental solubilities of TMZ and solid lines represent the solubilities of TMZ estimated by “Van’t Hoff model”.

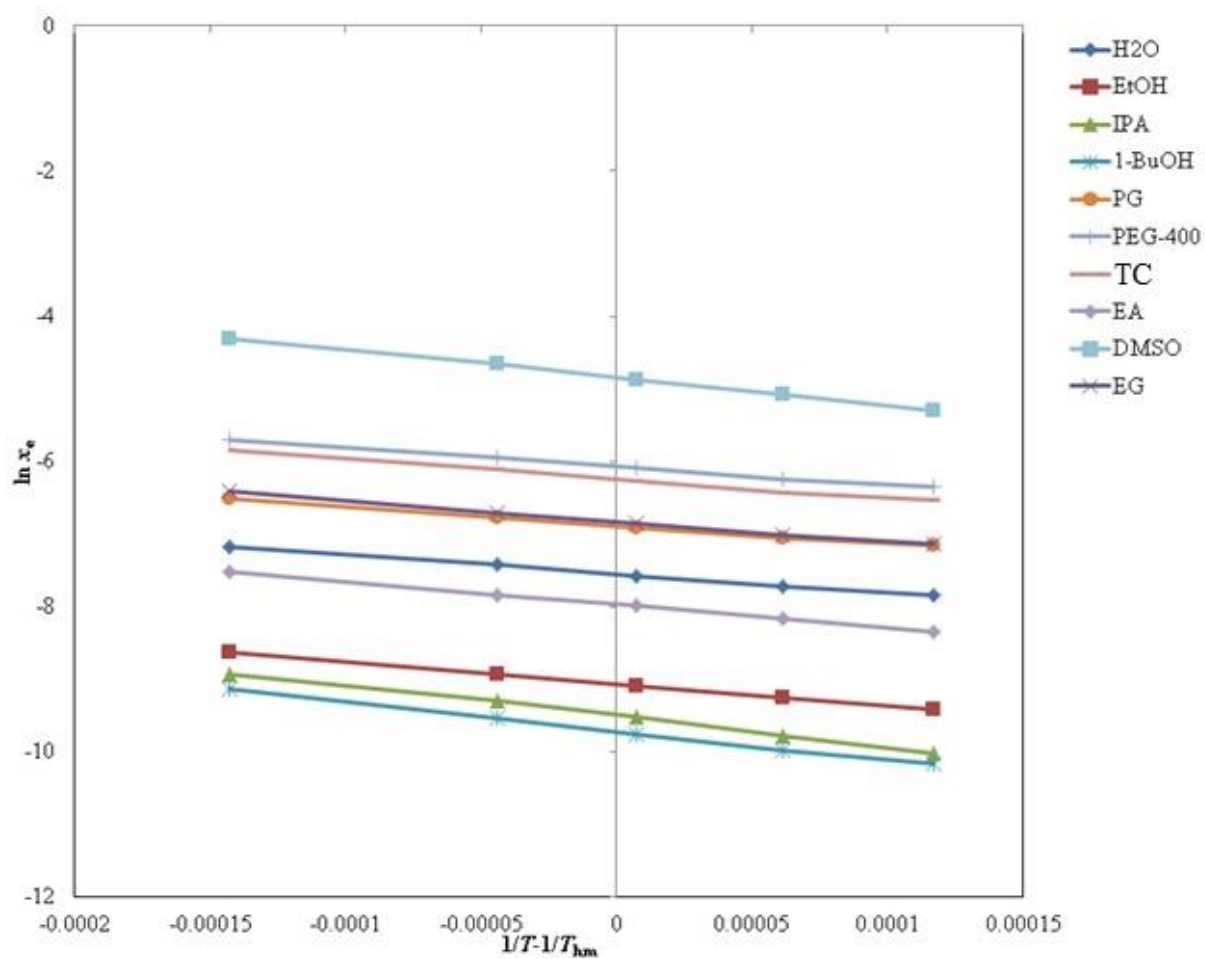


Figure S2: Van't Hoff plots for TMZ plotted between $\ln x_e$ and $1/T - 1/T_{hm}$ in various examined solvents.

Table S1. A sample table for materials.

Material	Molecular formula	Molar mass (g mol ⁻¹)	CAS Registry no.	Purification method	Mass fraction purity	Source
TMZ	C ₆ H ₆ N ₆ O ₂	194.15	85622-93-1	None	0.980	Tokyo Chemical Industry
EtOH	C ₂ H ₅ OH	46.07	64-17-5	None	0.995	Sigma-Aldrich
EG	C ₂ H ₆ O ₂	62.07	107-21-1	None	0.996	Annova Chem
TC	C ₆ H ₁₄ O ₃	134.17	111-90-0	None	0.999	Gattefosse
PG	C ₃ H ₈ O ₂	76.09	57-55-6	None	0.995	Annova Chem
PEG-400	H(OCH ₂ CH ₂) _n OH	400	25322-68-3	None	0.999	Merck Schuchardt
IPA	C ₃ H ₈ O	60.10	67-63-0	None	0.997	Panreac Química
1-BuOH	C ₄ H ₁₀ O	74.12	71-36-3	None	0.998	BDH Laboratory

						Supplies
DMSO	C ₂ H ₆ OS	78.13	67-68-5	None	0.990	BDH Laboratory Supplies
EA	C ₄ H ₈ O ₂	88.11	141-78-6	None	0.998	Winlab limited
H ₂ O	H ₂ O	18.07	7732-18-5	None	-	Milli-Q

Table S2. Hansen solubility parameters of TMZ and various neat solvents at $T = 298.2$ K.

Components	Hansen solubility parameters			
	$\delta_d/\text{MPa}^{1/2}$	$\delta_p/\text{MPa}^{1/2}$	$\delta_h/\text{MPa}^{1/2}$	$\delta/\text{MPa}^{1/2}$
TMZ	17.80	20.50	13.40	30.30
H ₂ O	15.50	16.00	42.30	47.80
EtOH	16.20	8.40	17.60	25.40
EG	18.00	11.10	23.40	31.60
PG	17.40	9.10	21.70	29.20
PEG-400	14.60	7.50	9.40	18.90
TC	16.30	7.20	11.90	21.40
IPA	15.80	6.60	14.30	22.30
1-BuOH	15.90	6.30	15.20	22.90
EA	15.70	5.60	7.00	18.10
DMSO	17.40	14.20	7.30	23.60