Supporting Information

Solubility of Tolbutamide and Chlorpropamide in Supercritical Carbon Dioxide

*Luigi Manna, Mauro Banchero**

Dipartimento Scienza Applicata e Tecnologia, Politecnico di Torino, Corso Duca degli Abruzzi, 24, Torino, Italy

**Corresponding author*. Tel: +39 011 0904703 *E-mail*: mauro.banchero@polito.it

Table S1. Model equations, regression parameters and *AARD%* of the density-based models used to fit the experimental solubility of chlorpropamide[a]

model	equation	parameters	*AARD%*[b]
Chrastil (1982)[28]	$y_2 = \rho^{\alpha} exp\left(\beta_0 + \frac{\beta_1}{T}\right)$	α=6.0076, β_0=-31.557, β_1=-6.2973·10^3	4.4%
Adachi and Lu (1983)[29]	$y_2 = \rho^{(\alpha_0+\alpha_1\rho+\alpha_2\rho^2)} \exp\left(\beta_0 + \frac{\beta_1}{T}\right)$	α_0=4.4777, α_1=6.7815·10^{-4}, α_2=-2.8836·10^{-7}, β_0=-23.729, β_1=-6.2943·10^3	4.5%
Del Valle and Aguilera (1988)[30]	$y_2 = \rho^{\alpha} \exp\left(\beta_0 + \frac{\beta_1}{T} + \frac{\beta_2}{T^2}\right)$	α=6.0956, β_0=-6.2393, β_1=-2.3352·10^4, β_2=2.8014·10^6	3.9%
Kumar and Johnston (1988)[38]	$y_2 = \exp\left(\alpha_0 + \frac{\alpha_1}{T} + \alpha_2\rho\right)$	α_0=1.0294, α_1=-6.1064·10^{-3}, α_2=8.7136·10^{-3}	13.3%
Bartle (1991)[39]	$y_2 = \frac{P_{ref}}{P} \exp\left[\alpha_0 + \frac{\alpha_1}{T} + \alpha_2(\rho - \rho_{ref})\right]$	α_0=19.552,	6.6%

		α_1=-8.4854·10^3, α_2=1.1937·10^{-2}	
Yu (1994)[43]	$y_2 = \alpha_0 + \alpha_1 P + \alpha_2 P^2 + \alpha_3 T + \alpha_4 T^2 + \alpha_5 PT(1 - y_2)$	α_0=3.4647·10^{-4}, α_1=-1.9601·10^{-5}, α_2=-1.7566·10^{-8}, α_3=-1.1213·10^{-6}, α_4=-8.018·10^{-11}, α_5=6.7913·10^{-8}	9.4%
Gordillo (1999)[44]	$y_2 = \exp(\alpha_0 + \alpha_1 P + \alpha_2 P^2 + \alpha_3 T + \alpha_4 T^2 + \alpha_5 PT)$	α_0=-28.26, α_1=-7.9857·10^{-1}, α_2=-8.3951·10^{-3}, α_3=1.4141·10^{-1}, α_4=3.3081·10^{-4}, α_5=3.9232·10^{-3}	9.8%
Méndez-Santiago and Teja (1999)[27]	$Tln(Py_2) = \alpha_0 + \alpha_1 \rho + \alpha_2 T$	α_0=-11.442·10^4, α_1=3.9109, α_2=17.86	11.6%
Sung and Shim (1999)[31]	$y_2 = \rho^{\left(\alpha_0 + \frac{\alpha_1}{T}\right)} \exp\left(\beta_0 + \frac{\beta_1}{T}\right)$	α_0=5.8669, α_1=48.573, β_0=-30.597, β_1=-6.6283·10^3	4.5%
Jouyban (2002)[32]	$y_2 = \rho^{\alpha} \exp\left(\beta_0 + \beta_1 P + \beta_2 P^2 + \beta_3 PT + \beta_4 \frac{T}{P}\right)$	α=3.8789, β_0=-39.271, β_1=-3.5796·10^{-1}, β_2=-3.5857·10^{-3}, β_3=1.7058·10^{-3}, β_4=-2.6047·10^{-3}	4.4%
Sparks with five parameters (2008)[25]	$y_2 = \rho^{(\alpha_0 + \alpha_1 \rho)} exp\left(\beta_0 + \frac{\beta_1}{T} + \frac{\beta_2}{T^2}\right)$	α_0=6.4942, α_1=-8.1634·10^{-5}, β_0=-6.3544, β_1=-2.4744·10^4, β_2=3.0302·10^6	3.8%

Sparks with six parameters (2008)[25]	$y_2 = \rho^{(\alpha_0+\alpha_1\rho+\alpha_2\rho^2)} exp\left(\beta_0+\frac{\beta_1}{T}+\frac{\beta_2}{T^2}\right)$	α_0=2.6065, α_1=1.654·10^{-3}, α_2=-7.4219·10^{-7}, β_0=7.6313, β_1=-2.0862·10^{4}, β_2=2.3944·10^{6}	3.5%
Garlapati and Madras (2009)[33]	$y_2 = (\rho T)^{\alpha} \exp\left(\beta_0+\frac{\beta_1}{T}\right)$	α=6.0078, β_0=-72.446, β_1=-4.3046·10^{3}	4.1%
Ch and Madras (2010)[40]	$y_2 = \left(\frac{P}{P_{ref}}\right)^{\alpha-1} \exp\left(\beta_0+\frac{\beta_1}{T}+\beta_2\rho\right)$	α=2.6291, β_0=16.716, β_1=-9.7128·10^{3}, β_2=1.4029·10^{-2}	5.0%
Garlapati and Madras (2010)[34]	$y_2 = \rho^{(\alpha_0+\alpha_1\rho)}(\rho T)^{\beta} \exp\left(\gamma_0+\frac{\gamma_1}{T}\right)$	α_0=-47.035, α_1=-8.3531·10^{-5}, β=53.538, γ_0=-3.9829·10^{2}, γ_1=1.1304·10^{4}	3.8%
Jafari Nedjad (2010)[35]	$y_2 = \rho^{\alpha} \exp(\beta_0+\beta_1 P+\beta_2 T^2)$	α=6.2471, β_0=-62.013, β_1=-4.0402·10^{-3}, β_2=9.009·10^{-5}	3.6%
Hezave and Lashkarbolooki (2013)[42]	$y_2 = \frac{P_{ref}}{P} \exp\left[\alpha_0+\frac{\alpha_1}{T}+\alpha_2(\rho-\rho_{ref})\right]+\beta T$	α_0=21.189, α_1=-9.0625·10^{3}, α_2=1.2844·10^{-2}, β=1.9784·10^{-9}	5.8%
Amooey (2014)[45]	$lny_2 = \frac{\alpha_0+\frac{\alpha_1}{\rho}+\frac{\alpha_2}{\rho^2}+\alpha_3 lnT+\alpha_4(lnT)^2}{1+\frac{\alpha_5}{\rho}+\alpha_6 lnT+\alpha_7(lnT)^2+\alpha_8(lnT)^3}$	α_0=4.3248·10^{-2}, α_1=-6.127·10^{-2}, α_2=5.1717, α_3=-1.5148·10^{-2}, α_4=1.3293·10^{-3}, α_5=5.1799·10^{3},	6.3%

		α_6=8.105, α_7=-4.5813·10^{-1}, α_8=-1.9295·10^{-1}	
Hozhabr (2014)[41]	$P^{\alpha} y_2 = \exp\left(\beta_0 + \frac{\beta_1}{T} + \frac{\beta_2 \rho}{T}\right)$	α=3.3643, β_0=28.959, β_1=-1.4784·10^{4}, β_2=5.3355	8.1%
Keshmiri (2014)[26]	$y_2 = \rho^{\left(\alpha_0 + \frac{\alpha_1}{T}\right)} exp\left(\beta_0 + \frac{\beta_1}{T} + \beta_2 P^2\right)$	α_0=5.3051, α_1=2.3951·10^{2}, β_0=-26.835, β_1=-7.9038·10^{3}, β_2=-2.8362·10^{-5}	4.5%
Khansary (2015)[36]	$y_2 = \rho^{(\alpha_0 + \alpha_1 P)} \exp\left(\beta_0 P + \frac{\beta_1}{T} + \beta_2 \frac{P^2}{T}\right)$	α_0=2.7523, α_1=3.4172·10^{-1}, β_0=-9.4283·10^{3}, β_1=-7.4672·10^{-1}, β_2=-2.2363	8.1%
Bian (2016)[37]	$y_2 = \rho^{(\alpha_0 + \alpha_1 \rho)} \exp\left(\beta_0 + \frac{\beta_1}{T} + \frac{\beta_2 \rho}{T}\right)$	α_0=6.6437, α_1=-7.9628·10^{-4}, β_0=-32.176, β_1=-7.4162·10^{3}, β_2=1.6498	4.4%

[a] T(K), P(MPa), ρ (kg·m^{-3})

[b] $AARD\% = \frac{100}{n-z} \sum_{i=1}^{n} \left| \frac{y_{2i}^{exp} - y_{2i}^{cal}}{y_{2i}^{exp}} \right|$

Table S2. Model equations, regression parameters and *AARD%* of the density-based models used to fit the experimental solubility of tolbutamide[a]

model	equation	parameters	*AARD%*[b]
Chrastil (1982)[28]	$y_2 = \rho^{\alpha} exp\left(\beta_0 + \frac{\beta_1}{T}\right)$	α=5.2507, β_0=-23.359, β_1=-6.7999·10^3	6.6%
Adachi and Lu (1983)[29]	$y_2 = \rho^{(\alpha_0+\alpha_1\rho+\alpha_2\rho^2)} \exp\left(\beta_0 + \frac{\beta_1}{T}\right)$	α_0=2.9901, α_1=1.1518·10^{-3}, α_2=-5.147·10^{-7}, β_0=-11.99, β_1=-6.8665·10^3	6.1%
Del Valle and Aguilera (1988)[30]	$y_2 = \rho^{\alpha} \exp\left(\beta_0 + \frac{\beta_1}{T} + \frac{\beta_2}{T^2}\right)$	α=5.2641, β_0=-28.259, β_1=-3.6013·10^3, β_2=-5.3017·10^5	6.6%
Kumar and Johnston (1988)[38]	$y_2 = \exp\left(\alpha_0 + \frac{\alpha_1}{T} + \alpha_2\rho\right)$	α_0=8.2632, α_1=-8.238·10^3, α_2=9.796·10^{-3}	17.3%
Bartle (1991)[39]	$y_2 = \frac{P_{ref}}{P} \exp\left[\alpha_0 + \frac{\alpha_1}{T} + \alpha_2(\rho - \rho_{ref})\right]$	α_0=24.256, α_1=-9.4994·10^3, α_2=1.1845·10^{-2}	8.9%
Yu (1994)[43]	$y_2 = \alpha_0 + \alpha_1 P + \alpha_2 P^2 + \alpha_3 T + \alpha_4 T^2 + \alpha_5 PT(1 - y_2)$	α_0=-5.8246·10^{-3}, α_1=-1.0284·10^{-4}, α_2=-1.0804·10^{-8}, α_3=3.9912·10^{-5}, α_4=-6.8301·10^{-8}, α_5=3.4182·10^{-7}	10.6%
Gordillo (1999)[44]	$y_2 = \exp(\alpha_0 + \alpha_1 P + \alpha_2 P^2 + \alpha_3 T + \alpha_4 T^2 + \alpha_5 PT)$	α_0=6.7768·10^2, α_1=-7.5584·10^{-1}, α_2=-4.7284·10^{-3},	26.8%

		α_3=-4.1099, α_4=6.0781·10^{-3}, α_5=3.289·10^{-3}	
Méndez-Santiago and Teja (1999)[27]	$T ln(P y_2) = \alpha_0 + \alpha_1 \rho + \alpha_2 T$	α_0=-1.2936·10^{4}, α_1=4.0887, α_2=23.576	11.2%
Sung and Shim (1999)[31]	$y_2 = \rho^{\left(\alpha_0 + \frac{\alpha_1}{T}\right)} \exp\left(\beta_0 + \frac{\beta_1}{T}\right)$	α_0=13.707, α_1=-2.7994·10^{3}, β_0=-79.387, β_1=1.1764·10^{4}	5.1%
Jouyban (2002)[32]	$y_2 = \rho^{\alpha} \exp\left(\beta_0 + \beta_1 P + \beta_2 P^2 + \beta_3 P T + \beta_4 \frac{T}{P}\right)$	α=3.6432, β_0=-39.122, β_1=-2.9768·10^{-1}, β_2=-5.1429·10^{-3}, β_3=1.888·10^{-3}, β_4=7.0368·10^{-2}	12.6%
Sparks with five parameters (2008)[25]	$y_2 = \rho^{(\alpha_0 + \alpha_1 \rho)} exp\left(\beta_0 + \frac{\beta_1}{T} + \frac{\beta_2}{T^2}\right)$	α_0=5.311, α_1=-1.293·10^{-5}, β_0=-29.256, β_1=-3.1323·10^{3}, β_2=-6.0297·10^{5}	6.7%
Sparks with six parameters (2008)[25]	$y_2 = \rho^{(\alpha_0 + \alpha_1 \rho + \alpha_2 \rho^2)} exp\left(\beta_0 + \frac{\beta_1}{T} + \frac{\beta_2}{T^2}\right)$	α_0=2.9901, α_1=1.1518·10^{-3}, α_2=-5.147·10^{-7}, β_0=-11.99, β_1=-6.8665·10^{3}, β_2=1·10^{-7}	6.2%
Garlapati and Madras (2009)[33]	$y_2 = (\rho T)^{\alpha} \exp\left(\beta_0 + \frac{\beta_1}{T}\right)$	α=5.2446, β_0=-59.057, β_1=-5.0451·10^{3}	6.7%
Ch and Madras (2010)[40]	$y_2 = \left(\frac{P}{P_{ref}}\right)^{\alpha - 1} \exp\left(\beta_0 + \frac{\beta_1}{T} + \beta_2 \rho\right)$	α=2.2278, β_0=18.015,	8.7%

		β_1=-9.9537·10^3, β_2=1.2574·10^{-2}	
Garlapati and Madras (2010)[34]	$y_2 = \rho^{(\alpha_0+\alpha_1\rho)}(\rho T)^{\beta}\exp\left(\gamma_0 + \frac{\gamma_1}{T}\right)$	α_0=15.121, α_1=-3.1421·10^{-5}, β=-9.7429, γ_0=42.11, γ_1=-9.981·10^3	6.7%
Jafari Nedjad (2010)[35]	$y_2 = \rho^{\alpha}\exp(\beta_0 + \beta_1 P + \beta_2 T^2)$	α=5.0772, β_0=-52.913, β_1=4.3556·10^{-3}, β_2=9.0851·10^{-5}	8.4%
Hezave and Lashkarbolooki (2013)[42]	$y_2 = \frac{P_{ref}}{P}\exp\left[\alpha_0 + \frac{\alpha_1}{T} + \alpha_2(\rho - \rho_{ref})\right] + \beta T$	α_0=23.519, α_1=-9.2402·10^3, α_2=1.1393·10^{-2}, β=-1.6437·10^{-9}	7.8%
Amooey (2014)[45]	$\ln y_2 = \frac{\alpha_0 + \frac{\alpha_1}{\rho} + \frac{\alpha_2}{\rho^2} + \alpha_3 \ln T + \alpha_4(\ln T)^2}{1 + \frac{\alpha_5}{\rho} + \alpha_6 \ln T + \alpha_7(\ln T)^2 + \alpha_8(\ln T)^3}$	α_0=-1.9923·10^{-2}, α_1=-4.1678·10^{-2}, α_2=6.6627, α_3=6.768·10^{-3}, α_4=-5.7275·10^{-4}, α_5=4.2727·10^2, α_6=7.8361·10^{-1}, α_7=-2.4225·10^{-2}, α_8=-2.6113·10^{-2}	8.9%
Hozhabr (2014)[41]	$P^{\alpha} y_2 = \exp\left(\beta_0 + \frac{\beta_1}{T} + \frac{\beta_2 \rho}{T}\right)$	α=2.377, β_0=26.036, β_1=-1.3536·10^4, β_2=4.3265	9.9%
Keshmiri (2014)[26]	$y_2 = \rho^{\left(\alpha_0 + \frac{\alpha_1}{T}\right)} exp\left(\beta_0 + \frac{\beta_1}{T} + \beta_2 P^2\right)$	α_0=12.692, α_1=-2.5352·10^3, β_0=-73.187, β_1=1.0149·10^4, β_2=1.7158·10^{-4}	4.8%

Khansary (2015)[36]	$y_2 = \rho^{(\alpha_0+\alpha_1 P)}\exp\left(\beta_0 P + \frac{\beta_1}{T} + \beta_2 \frac{P^2}{T}\right)$	α_0=3.6592, α_1=2.6533·10^{-1}, β_0=-1.8483, β_1=-1.0442·10^{4}, β_2=1.2215·10^{-1}	5.1%
Bian (2016)[37]	$y_2 = \rho^{(\alpha_0+\alpha_1 \rho)}\exp\left(\beta_0 + \frac{\beta_1}{T} + \frac{\beta_2 \rho}{T}\right)$	α_0=6.2905, α_1=-1.6305·10^{-3}, β_0=-38.534, β_1=-3.2698·10^{3}, β_2=-4.5919	5.0%

[a] T(K), P(MPa), ρ (kg·m^{-3})

[b] $AARD\% = \frac{100}{n-z}\sum_{i=1}^{n}\left|\frac{y_{2i}^{exp}-y_{2i}^{cal}}{y_{2i}^{exp}}\right|$

Table S3. Total (ΔH_{tot}), solvation (ΔH_{solv}) and sublimation (ΔH_{sub}) enthalpies for the drugs

	Chlorpropamide	Tolbutamide
Chrastil[28]		
$\Delta H_{tot}=\Delta H_{sub}+\Delta H_{solv}=-\beta_1 R^a$ (kJ·mol^{-1})	52.36	56.54
$\Delta H_{solv}= \Delta H_{tot}-\Delta H_{sub}{}^b$ (kJ·mol^{-1})	-18.19	-22.44
Kumar-Johnston[38]		
$\Delta H_{tot}=\Delta H_{sub}+\Delta H_{solv}=-\alpha_1 R^a$ (kJ·mol^{-1})	50.77	68.49
$\Delta H_{solv}= \Delta H_{tot}-\Delta H_{sub}{}^b$ (kJ·mol^{-1})	-19.78	-10.49
Bartle[39]		
$\Delta H_{sub} =- \alpha_1 R^a$ (kJ·mol^{-1})	70.55	78.98

[a]ideal gas constant (8.314472 J·mol^{-1}·K^{-1})

[b]obtained from Bartle model