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Electronic Supplementary Information

Crystallization of paracetamol from mixtures of ethanol and water in a planar oscillatory flow crystallizer: effect of the oscillation conditions on the crystal growth kinetics

*Patrícia Cruz, Fernando Rocha and António Ferreira**

LEPABE – Laboratory for Process Engineering, Environment, Biotechnology and Energy, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal

Email: antonio@fe.up.pt

Calibration Curves for the Concentration of Paracetamol in a 40% (v/v) Mixture of Ethanol and Water

The linear regression equation, variables and parameters for each calibration curve are presented in **Table S.1**. Five validation parameters were used to validate each calibration curve: linearity, precision, accuracy, limit of detection and limit of quantitation. The methodology used to assess each validation parameter is presented in **Table S.2** and the result for each validation parameter is presented in **Table S.3**.

Table S.1 – Linear regression: equation, variables and parameters.

Linear regression equation: $y = (a \pm ts_a)x + (b + ts_b)$							
Variable	**Definition**						
y	Dependent variable: absorbance (Abs)						
x	Independent variable: concentration of paracetamol (C) in g kg^{-1}						
Parameter	**Definition**	**Value**					
		T**=10 °C**	T**=15 °C**	T**=20 °C**	T**=25 °C**	T**=30 °C**	T**=35 °C**
n	Number of calibration points	6	6	6	6	6	6
a	Slope (kg g^{-1})	0.00236	0.00250	0.00232	0.00249	0.00241	0.00231
b	Intercept	-0.001	0.003	-0.001	0.001	0.002	0.01
t	t-statistic for $n-2$ degrees of freedom	2.7764 with a significance level $\alpha = 0.05$					
s_a	Standard deviation of the slope (kg g^{-1})	0.00003	0.00003	0.00003	0.00004	0.00002	0.00005
s_b	Standard deviation of the intercept	0.002	0.002	0.002	0.004	0.003	0.01
ts_a	Confidence interval of a (kg g^{-1})	0.00009	0.00008	0.00007	0.00012	0.00007	0.00013
ts_b	Confidence interval of b	0.005	0.005	0.007	0.011	0.008	0.02

Table S.2 – Methodology used to assess each validation parameter

Parameter	**Methodology**
Linearity	Linearity was assessed based on the coefficient of determination (R^2) and the statistical significance of a and b. $R^2 > 0.995$ is generally considered as evidence of acceptable linearity. In addition, a should differ statistically and significantly from 0, whilst b should not differ statistically and significantly from 0. Therefore, the t-statistics of a (t_a) should be higher than the critical value ($t_{crit} = 2.7764$) and the t-statistics of b (t_b) should be lower than t_{crit}.
Precision	Precision was assessed based on repeatability. The concentrations of 3 replicates of 3 standard solutions of paracetamol were calculated from the calibration curve. The average coefficient of variation of the three series (CV_{rep}) was calculated to express precision.
Accuracy	Accuracy was assessed based on percent recovery (RE), calculated as the ratio between the concentration obtained from the calibration curve and the actual concentration of a standard solution of paracetamol. The concentrations of 3 replicates of 3 standard solutions of paracetamol were calculated from the calibration curve. The average RE of the three series was calculated to express accuracy.
Limit of detection	LOD was calculated based on s_b and a as $LOD = 3.3s_b/a$.
Limit of quantitation	LOQ was calculated based on s_b and a as $LOQ = 10s_b/a$.

Table S.3 – Result for each validation parameter.

	Result					
Parameter	**T=10 °C**	**T=15 °C**	**T=20 °C**	**T=25 °C**	**T=30 °C**	**T=35 °C**
Linearity	$R^2 = 0.999$ $t_a = 75.321$ $t_b = -0.93$	$R^2 = 0.999$ $t_a = 84.318$ $t_b = 1.468$	$R^2 = 0.999$ $t_a = 87.603$ $t_b = -0.247$	$R^2 = 0.999$ $t_a = 57.678$ $t_b = 0.364$	$R^2 = 1.000$ $t_a = 101.011$ $t_b = 0.555$	$R^2 = 0.998$ $t_a = 47.719$ $t_b = 1.048$
Precision	$CV_{rep} = 4\%$	$CV_{rep} = 6\%$	$CV_{rep} = 1\%$	$CV_{rep} = 1\%$	$CV_{rep} = 1\%$	$CV_{rep} = 1\%$
Accuracy	$RE = 100\%$	$RE = 101\%$	$RE = 100\%$	$RE = 100\%$	$RE = 101\%$	$RE = 100\%$
Limit of detection	$LOD = 3$ g kg^{-1}	$LOD = 2$ g kg^{-1}	$LOD = 3$ g kg^{-1}	$LOD = 5$ g kg^{-1}	$LOD = 4$ g kg^{-1}	$LOD = 8$ g kg^{-1}
Limit of quantitation	$LOQ = 8$ g kg^{-1}	$LOQ = 7$ g kg^{-1}	$LOQ = 11$ g kg^{-1}	$LOQ = 16$ g kg^{-1}	$LOQ = 12$ g kg^{-1}	$LOQ = 25$ g kg^{-1}