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Supplementary material to

Investigation of magnesium aluminometasilicate (Neusilin US2) based surface solid dispersion of sorafenib tosylate using QbD approach: *In vitro* and *in vivo* pharmacokinetic study

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Data for optimization of formulation by DOE

ANOVA for Linear model

Response 1: Solubility

Source	Sum of squares	df	Mean Square	*F*-value	*p*-value	
Model	0.0811	2	0.0406	11.86	0.0082	significant
A-SDS	0.0359	1	0.0359	10.49	0.0177	
B-NU2	0.0452	1	0.0452	13.23	0.0109	
Residual	0.0205	6	0.0034			
Cor Total	0.1016	8				

Factor coding is **Coded**

Sum of squares is **Type III - Partial**

The Model F-value of 11.86 implies the model is significant. There is only a 0.82 % chance that an *F*-value this large could occur due to noise.

P-values less than 0.0500 indicate model terms are significant. In this case A, B are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

Fit statistics

Std. Dev.	0.0585	R^2	0.7982
Mean	0.5982	Adjusted R^2	0.7309
C.V., %	9.77	Predicted R^2	0.5846
		Adeq Precision	9.7256

The predicted R^2 of 0.5846 is in reasonable agreement with the adjusted R^2 of 0.7309; *i.e.* the difference is less than 0.2.

Adeq Precision measures the signal to noise ratio. A ratio greater than 4 is desirable. Your ratio of 9.726 indicates an adequate signal. This model can be used to navigate the design space.

Model comparison statistics

PRESS	0.0422
-2 log likelihood	-29.21
BIC	-22.62
AICc	-18.41

Coefficients in terms of coded factors

Factor	Coefficient estimate	df	Standard error	95 % CI Low	95 % CI High	VIF
Intercept	0.5982	1	0.0195	0.5505	0.6459	
A-SDS	0.0773	1	0.0239	0.0189	0.1357	1.0000
B-NU2	0.0868	1	0.0239	0.0284	0.1452	1.0000

The coefficient estimate represents the expected change in response per unit change in factor value when all remaining factors are held constant. The intercept in an orthogonal design is the overall average response of all the runs. The coefficients are adjustments around that average based on the factor settings. When the factors are orthogonal the VIFs are 1; VIFs greater than 1 indicate multi-colinearity, the higher the VIF the more severe the correlation of factors. As a rough rule, VIFs less than 10 are tolerable.

Final equation in terms of coded factors

Solubility	=
+0.5982	
+0.0773	A
+0.0868	B

The equation in terms of coded factors can be used to make predictions about the response for given levels of each factor. By default, the high levels of the factors are coded as +1 and the low levels are coded as -1. The coded equation is useful for identifying the relative impact of the factors by comparing the factor coefficients.

Final equation in terms of actual factors

Solubility	=
+0.144389	
+0.007733	SDS
+0.001737	NU2

The equation in terms of actual factors can be used to make predictions about the response for given levels of each factor. Here, the levels should be specified in the original units for each factor. This equation should not be used to determine the relative impact of each factor because the coefficients are scaled to accommodate the units of each factor and the intercept is not at the center of the design space.