

# **Supplementary Materials: Co-Delivery of a High Dose of Amphotericin B and Itraconazole by Means of a Dry Powder Inhaler Formulation for the Treatment of Severe Fungal Pulmonary Infections**

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## Results section – Box Behnken model

### 1. Yield

Summary (detailed tables shown below)

Source	Sequential p-value	Lack of Fit p-value	Adjusted R-Squared	Predicted R-Squared	
Linear	0,2474	0,0376	0,0945	-0,4147	
<u>2FI</u>	<u>0,0546</u>	<u>0,0761</u>	<u>0,4321</u>	<u>-0,3021</u>	<u>Suggested</u>
Quadratic	0,2114	0,0872	0,5572	-1,4710	
Cubic	0,0872		0,8259		Aliased

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F
Model	895,06	6	149,18	3,03	0,0590
<i>A-Antibiotics total</i>	253,58	1	253,58	5,15	0,0466
<i>B-Flow rate</i>	81,79	1	81,79	1,66	0,2265
<i>C-Leucina</i>	31,28	1	31,28	0,64	0,4440
<i>AB</i>	175,30	1	175,30	3,56	0,0886
<i>AC</i>	297,91	1	297,91	6,05	0,0337
<i>BC</i>	55,20	1	55,20	1,12	0,3146
Residual	492,49	10	49,25		
<i>Lack of Fit</i>	432,10	6	72,02	4,77	0,0761
<i>Pure Error</i>	60,39	4	15,10		
Cor Total	1387,55	16			

## 2. Particle size

Summary (detailed tables shown below)

	Sequential	Lack of Fit	Adjusted	Predicted	
Source	p-value	p-value	R-Squared	R-Squared	
<u>Linear</u>	<u>0,0199</u>	<u>0,6719</u>	<u>0,4083</u>	<u>0,1741</u>	<u>Suggested</u>
2FI	0,8180	0,5377	0,2961	-0,5098	
Quadratic	0,8076	0,3348	0,1174	-2,5899	
Cubic	0,3348		0,2829		Aliased

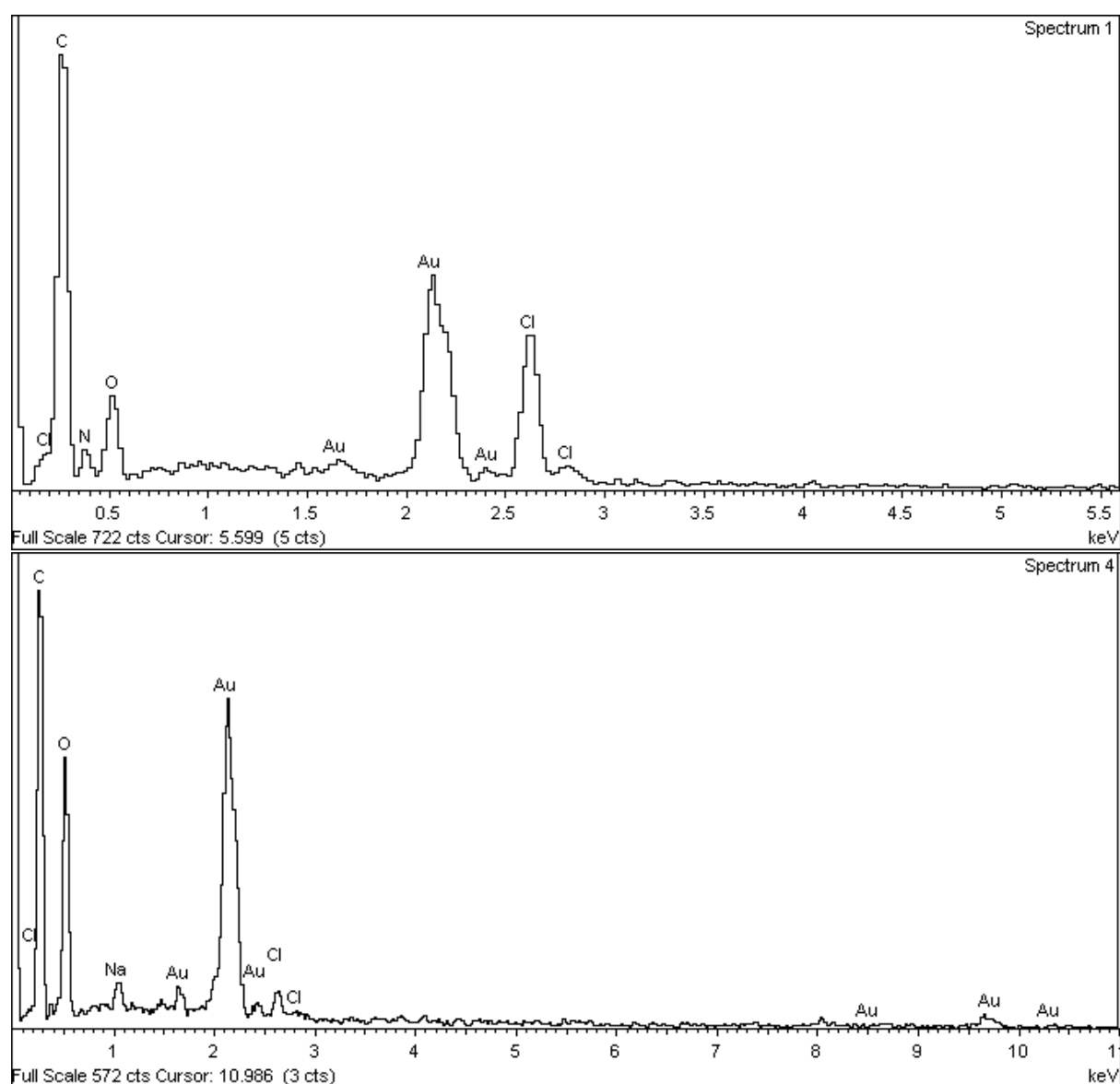
Source	Sum of Squares	df	Mean Square	F Value	p-value	
Model	3,05	3	1,02	4,68	0,0199	significant
<i>A-Antibiotics total</i>	<i>0,48</i>	<i>1</i>	<i>0,48</i>	<i>2,21</i>	<i>0,1612</i>	
<i>B-Flow rate</i>	<i>2,48</i>	<i>1</i>	<i>2,48</i>	<i>11,38</i>	<i>0,0050</i>	
<i>C-Leucina</i>	<i>0,099</i>	<i>1</i>	<i>0,099</i>	<i>0,46</i>	<i>0,5118</i>	
Residual	2,83	13	0,22			
<i>Lack of Fit</i>	<i>1,77</i>	<i>9</i>	<i>0,20</i>	<i>0,75</i>	<i>0,6719</i>	<i>not significant</i>
<i>Pure Error</i>	<i>1,05</i>	<i>4</i>	<i>0,26</i>			
Cor Total	5,88	16				

### 3. Aggregation state

Summary (detailed tables shown below)

Source	Sequential Lack of Fit p-value	Adjusted R-Squared	Predicted R-Squared	
Linear	0,0466	0,2288	0,3192	0,0130 Suggested
2FI	0,9958	0,1329	0,1203	-1,1143
Quadratic	0,3704	0,1110	0,1754	-3,4440
Cubic	0,1110		0,6320	Aliased

Source	Sum of Squares	df	Mean Square	F Value	p-value	
Model	0,093	3	0,031	3,50	0,0466	significant
A-Antibiotics total	0,092	1	0,092	10,45	0,0066	
B-Flow rate	2,645E-004	1	2,645E-004	0,030	0,8653	
C-Leucina	2,311E-004	1	2,311E-004	0,026	0,8740	
Residual	0,11	13	8,830E-003			
Lack of Fit	0,096	9	0,011	2,23	0,2288	not significant
Pure Error	0,019	4	4,773E-003			
Cor Total	0,21	16				



**Figure S1. EDX spectra for F1.**

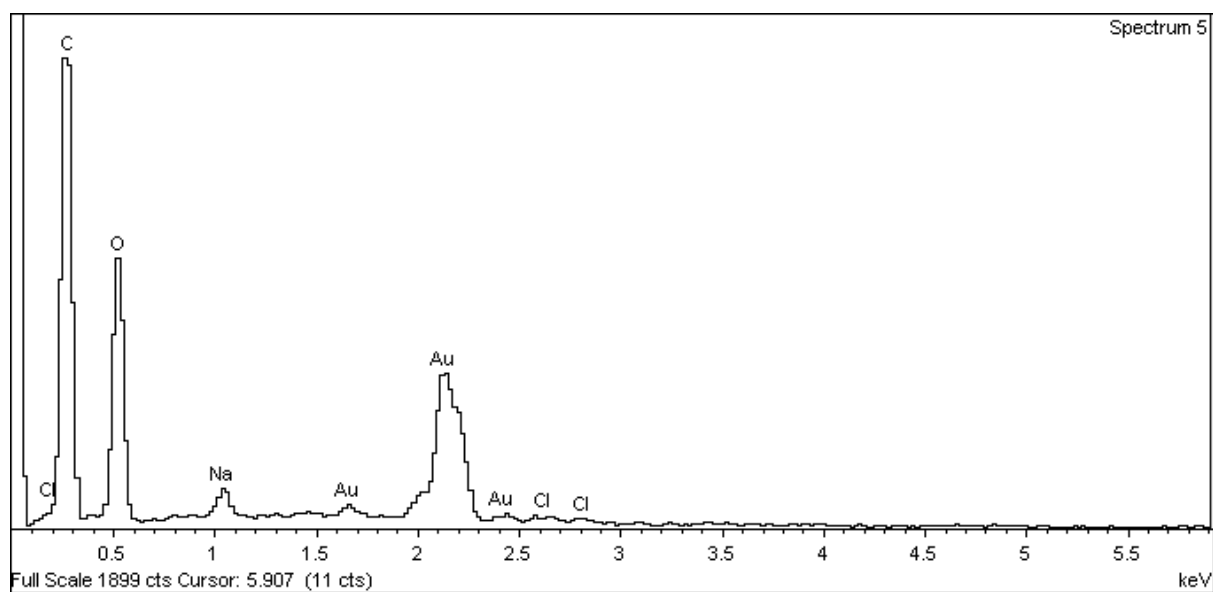


Figure S2. EDX spectra for F2.

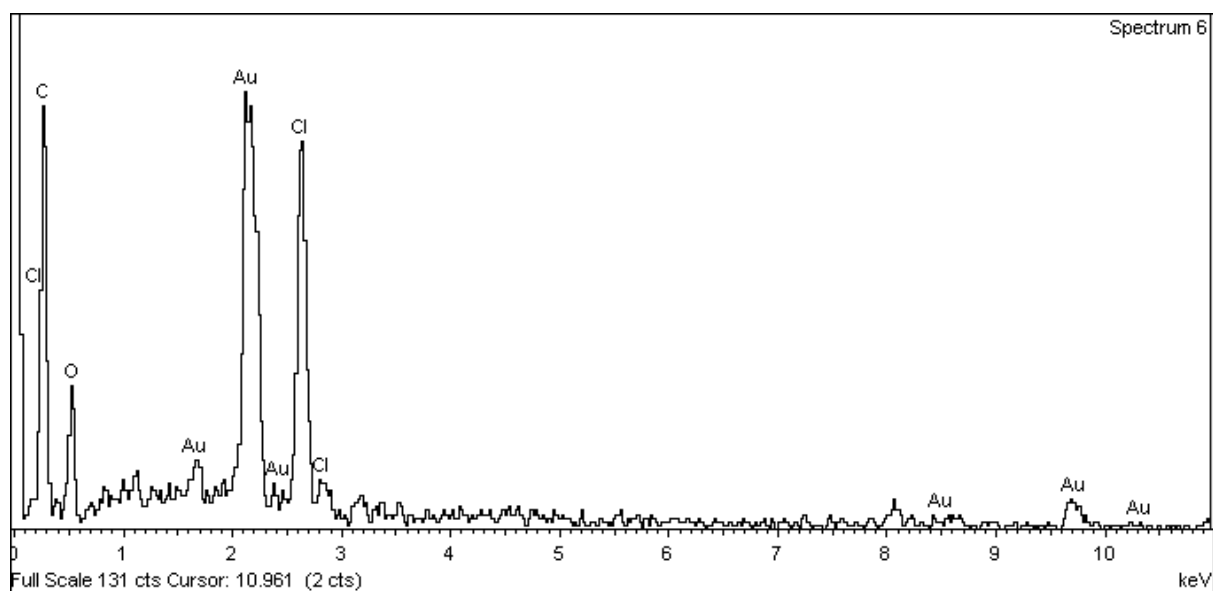


Figure S3. EDX spectra for F3