**Table S1-** ANOVA statistics and coefficients for the models obtained for the four responses of the 2^{6-2} fractional factorial design

Factors	YIELD (%W/W)				ASA (%W/W)				FPF (%W/W)				ED (%W/W)			
	Coefficient estimate	Mean Square	F-value	p-value	Coefficient estimate	Mean Square	F-value	p-value	Coefficient estimate	Mean Square	F value	p-value	Coefficient estimate	Mean Square	F-value	p-value
Intercept	70.31	1359.06	46.99	< 0.0001	66.54	10050.03	362.63	< 0.0001	49.40	1419.74	40.09	< 0.0001	79.29	303.02	4.81	0.0142
A	-15.60	3892.20	134.57	< 0.0001	25.06	10050.03	362.63	< 0.0001	-14.51	3368.08	95.10	< 0.0001	-5.08	413.51	6.56	0.0209
B	5.96	568.23	19.65	0.0005	-	-	-	-	-	-	-	-	- 2.69	115.43	1.83	0.1948
D	-4.14	273.65	9.46	0.0077	-	-	-	-	-2.18	75.94	2.14	0.1625	-	-	-	-
AB	-	-	-	-	-	-	-	-	-	-	-	-	4.87	380.13	6.03	0.0259
AD	-	-	-	-	-	-	-	-	7.14	815.19	23.02	0.0002	-	-	-	-
A²	-14.81	702.17	24.28	0.0002	-	-	-	-	-	-	-	-	-	-	-	-
Residual	-	28.92	-	-	-	27.71	-	-	-	35.42	-	-	-	63.04	-	-
Lack of fit	-	20.58	0.3304	0.9288	-	28.34	1.15	0.5201	-	38.60	1.79	0.3493	-	74.56	5.69	0.0890
Pure error	-	62.30	-	-	-	24.57	-	-	-	21.62	-	-	-	13.09	-	-
	S.D.*	5.38	r²*	0.9261	S.D.*	5.26	r²*	0.9527	S.D.*	5.95	r²*	0.8826	S.D.*	7.94	r²*	0.4741
	Mean	58.46	Adj r²*	0.9064	Mean	66.54	Adj r²*	0.9501	Mean	49.40	Adj r²*	0.8606	Mean	79.29	Adj r²*	0.3754
	C.V. %*	9.20	Pred r²*	0.8686	C.V. %*	7.91	Pred r²*	0.9412	C.V. %*	12.05	Pred r²*	0.8107	C.V. %*	10.01	Pred r²*	0.1407
	PRESS*	771.29	Adeq Precision*	19.1086	PRESS*	620.50	Adeq Precision*	30.109	PRESS*	913.35	Adeq Precision*	16.2665	PRESS*	1647.75	Adeq Precision*	5.6091

*S.D., standard deviation associated with the experimental error; Mean, dependent mean (average of all the values of the response); C.V.%, coefficient of variance of the model; PRESS, Predicted Residual Sum of Squares for the model; r^2, multiple correlation coefficient; Adj r^2, r^2 adjusted for the number of parameters in the model; Pred r^2, predicted r^2 is a measure of how the model predicts a response value; Adeq Precision, adequate precision a measure of the range in predicted response relative to its associated error.
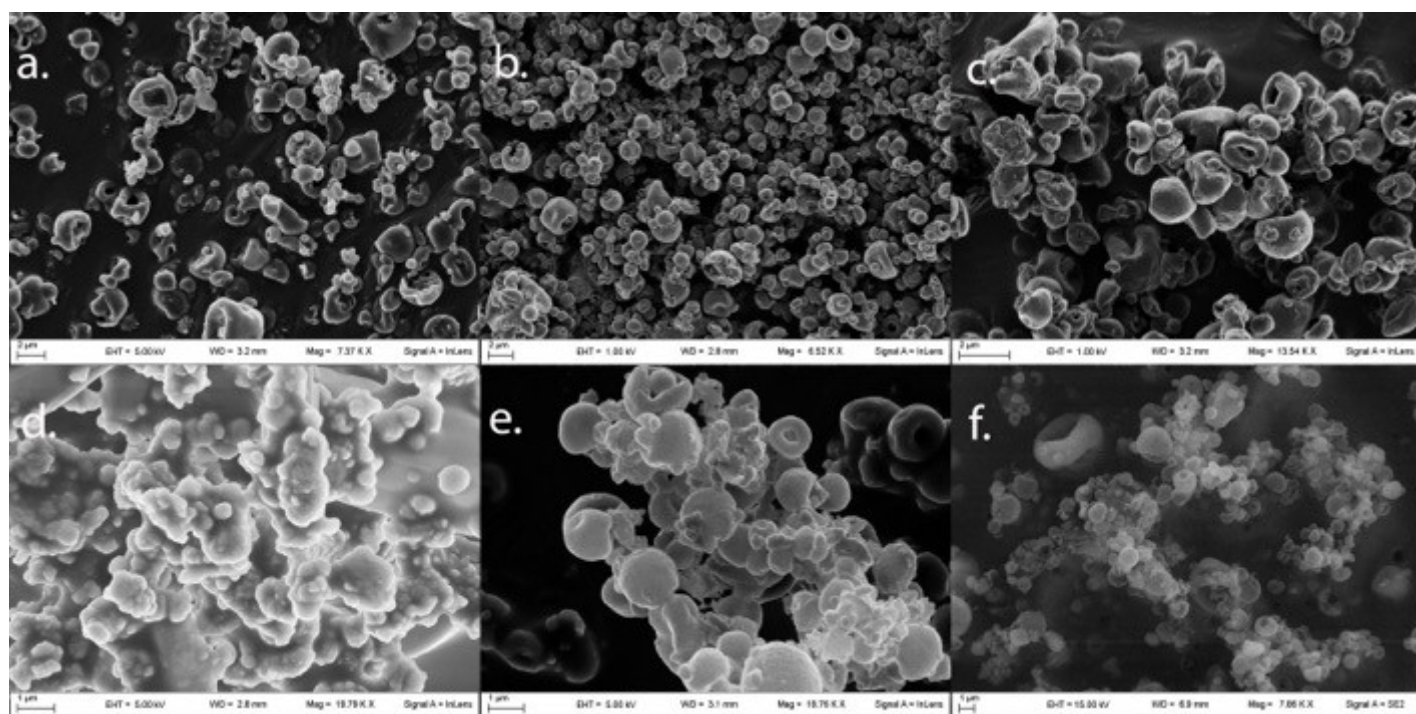
Figure S1. Morphology of representative preparations of the 20 runs of the experimental design in Table 2. In detail: a. run# 1, b. run#2, c. run#3, d. run#4, e. run#8, f. run# 10.
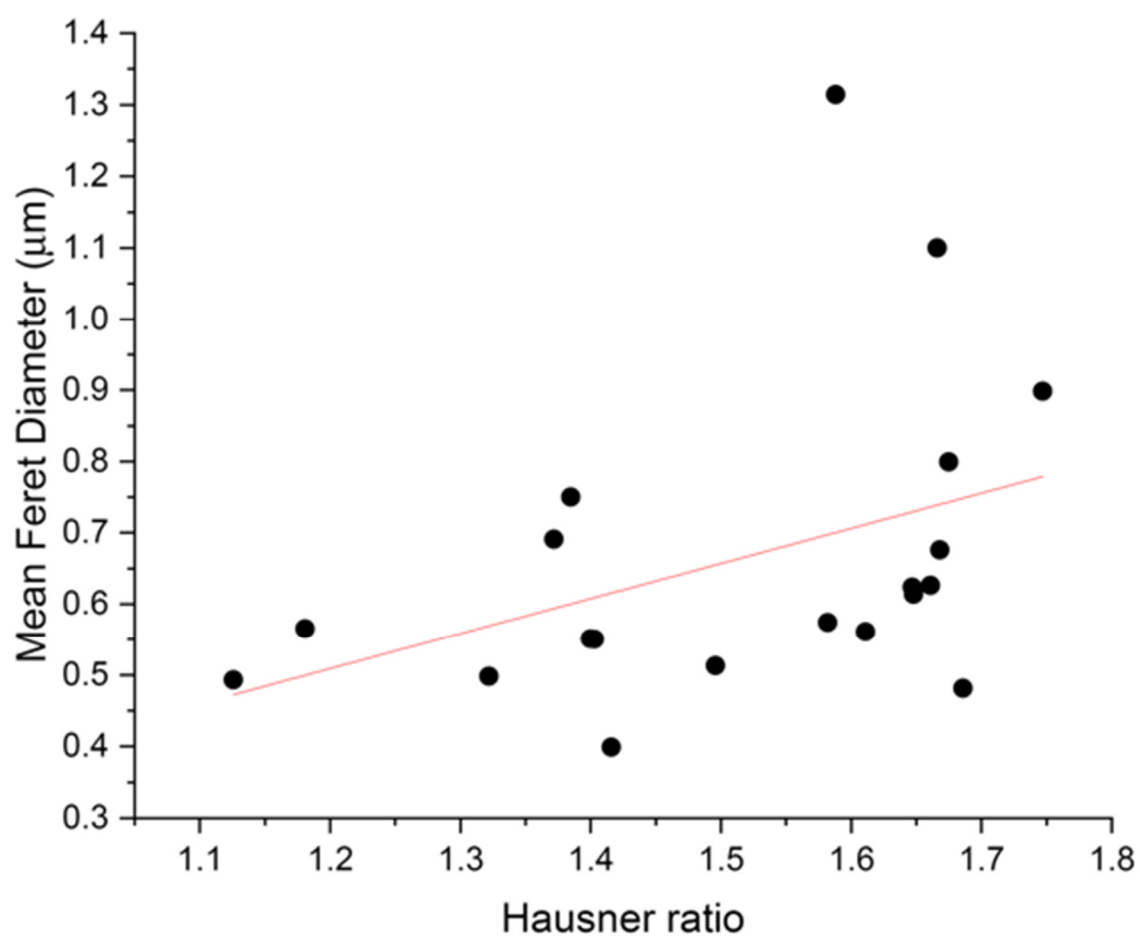
Figure S2. Correlation between theoretical flowability and particle size of the 20 runs of the experimental design in Table 2.
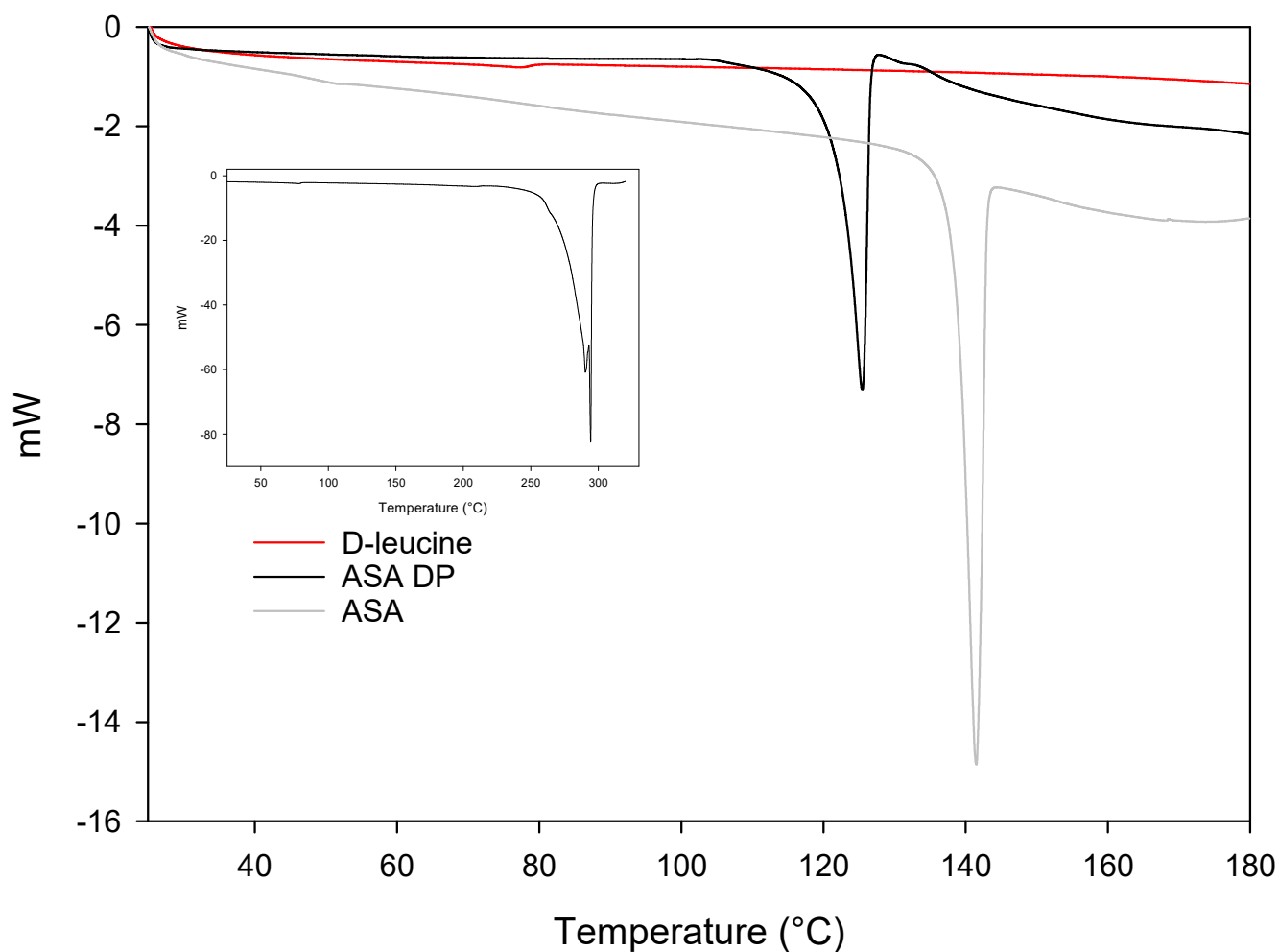
Figure S3. DSC analysis of the obtained ASA dry powder corresponding to the run# 7 of the experimental design (Table 2) (Endo down). Insert) Complete DSC profile of D-leucine showing melting and decomposition at 280-290 °C. ASA is present as a crystalline phase, note the significant downshift of the melting temperature, from 141 °C to 125 °C. This effect can be ascribed to phase mixing between ASA and D-leucine.