

Table S1: Two level Plackett-Burman design table for the screening of carbon sources. +1 is for higher concentration and -1 for lower concentration.

<i>Variable codes</i>	A	B	C	D	E	F	G
<i>Carbon sources</i>	Dextrose	Sucrose	Fructose	Maltose	Galactose	Lactose	Glycerol
1	+1	+1	-1	+1	-1	-1	-1
2	-1	+1	-1	-1	+1	-1	+1
3	-1	-1	+1	+1	-1	-1	+1
4	-1	+1	+1	-1	-1	+1	-1
5	+1	+1	+1	+1	+1	+1	+1
6	+1	-1	+1	-1	+1	-1	-1
7	+1	-1	-1	-1	-1	+1	+1
8	-1	-1	-1	+1	+1	+1	-1

Table S2: Two level Plackett-Burman design table for the screening of organic nitrogen sources. +1 is for higher concentration and -1 for lower concentration.

<i>Variable codes</i>	A	B	C	D	E	F	G
<i>Organic Nitrogen sources</i>	Peptone	Yeast extract	Tryptone	Casamino acids	Beef extract	Corn steep liquor	Polypeptone
1	+1	+1	-1	+1	-1	-1	-1
2	-1	+1	-1	-1	+1	-1	+1
3	-1	-1	+1	+1	-1	-1	+1

4	-1	+1	+1	-1	-1	+1	-1
5	+1	+1	+1	+1	+1	+1	+1
6	+1	-1	+1	-1	+1	-1	-1
7	+1	-1	-1	-1	-1	+1	+1
8	-1	-1	-1	+1	+1	+1	-1

Table S3: Range and Levels of the Variables in Coded Units for RSM Studies

Variables	-2	-1	0	1	2	ΔX
Yeast Extract, x1, % (w/v)	1.6	2.1	2.6	3.1	3.6	0.5
Dextrose, x3, % (w/v)	1.7	2.2	2.7	3.2	3.7	0.5
pH, x4	6.1	6.5	7.1	7.5	7.9	0.4
Temperature, °C	26	28	30	32	34	2

* ΔX step increment in the input variable values

Table S4: Design of Experiments by Central Composite Design (CCD) for RSM Studies

Run number	x1	x2	x3	x4	Coefficients assessed by	SK production	SK production
						Measured (IU/ml)	Predicted (IU/ml)
1	-1	-1	-1	-1	Fractional factorial 2^4 design (16 expts)	1750	2249.79
2	1	-1	-1	-1		2100	2071.25
3	-1	1	-1	-1		1775	2068.33
4	1	1	-1	-1		1850	2166.04

5	-1	-1	1	-1		1320	1799.58
6	1	-1	1	-1		1950	1872.29
7	-1	1	1	-1		1850	1881.87
8	1	1	1	-1		2000	2230.83
9	-1	-1	-1	1		1450	1838.33
10	1	-1	-1	1		1500	1848.54
11	-1	1	-1	1		1750	1830.62
12	1	1	-1	1		1600	2117.08
13	-1	-1	1	1		1750	1989.37
14	1	-1	1	1		2100	2250.83
15	-1	1	1	1		2150	2245.41
16	1	1	1	1		2350	2783.12
17	-2	0	0	0		1750	1804.37
18	2	0	0	0		2000	2163.54
19	0	-2	0	0		1550	1958.54
20	0	2	0	0		1900	2309.37
21	0	0	-2	0		1950	1901.04
22	0	0	2	0		1750	2116.87
23	0	0	0	-2		1900	2113.54
24	0	0	0	2	8 star points	1450	2254.37
25	0	0	0	0		1950	1945.00
26	0	0	0	0		1850	1945.00
27	0	0	0	0		2020	1945.00
28	0	0	0	0	6 central points	1950	1945.00

29	0	0	0	0	1900	1945.00
30	0	0	0	0	2000	1945.00

Table S5: Model Summary and Analysis of Variance (ANOVA) for the Quadratic Model

Model estimates	Sum of Squares	Degrees of freedom	Mean Square	F value	Sig.
Regression	1254548.750	14	89610.625	4.764	0.002
Residual	282135.417	15	18809.028		
Total	1536684.167	29			

R, 0.904; R², 0.816; Adjusted R², 0.645; Std. Error of the Estimate, 137.146; CV, 11.13%

Table S6: Model Coefficients Estimated By Multiple Linear Regressions (Significance of Regression Coefficients)

Variables	Beta	Standard Error	t	p-value (Sig. at <0.05)
(Constant)	1945.000	55.990	34.739	0.0002
x1	89.792	27.995	3.207	0.006
x2	87.708	27.995	3.133	0.007
x3	53.958	27.995	1.927	0.073
x4	-35.208	27.995	-1.258	0.228
x1x1	-9.740	26.187	-0.372	0.715
x1x2	-69.063	34.287	-2.014	0.062
x1x3	62.813	34.287	1.832	0.087

x1x4	-47.188	34.287	-1.376	0.189
x2x2	-47.240	26.187	-1.804	0.091
x2x3	65.938	34.287	1.923	0.074
x2x4	43.438	34.287	1.267	0.225
x3x3	-15.990	26.187	-0.611	0.551
x3x4	150.313	34.287	4.384	0.001
x4x4	-59.740	26.187	-2.281	0.038
