|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Std** | **No.** | **Factor 1(A)** | **Factor 2(B)** | **Factor 3 (C)** | **Experimental Results** |
| Scaling | Infill  Density | Wall Thickness | Average mass of the  tablet obtained |
|  |  | % | % | mm | mg |
| 4 | 1 | 125.00 | 100.00 | 1.00 | 2200 |
| 8 | 2 | 125.00 | 55.00 | 1.60 | 1800 |
| 11 | 3 | 100.00 | 10.00 | 1.60 | 866 |
| 7 | 4 | 75.00 | 55.00 | 1.60 | 466 |
| 2 | 5 | 125.00 | 10.00 | 1.00 | 1066 |
| 13 | 6 | 100.00 | 55.00 | 1.00 | 866 |
| 12 | 7 | 100.00 | 100.00 | 1.60 | 1133 |
| 10 | 8 | 100.00 | 100.00 | 0.40 | 1133 |
| 9 | 9 | 100.00 | 10.00 | 0.40 | 330 |
| 6 | 10 | 125.00 | 55.00 | 0.40 | 1400 |
| 3 | 11 | 75.00 | 100.00 | 1.00 | 466 |
| 1 | 12 | 75.00 | 10.00 | 1.00 | 333 |
| 5 | 13 | 75.00 | 55.00 | 0.40 | 333 |

**Table S1.** Experimental values ​​proposed by the Design-Expert software at different levels of each factor, along with the experimentally obtained response.

**Tabel S2.** Design features

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study**  **type** | | **Design**  **Type** | | | **Design**  **Model** | | | | **Experiments**  **number** | | | | **Blocks** | |
| Response  surface | | Box-  Behnken | | | Quadratic | | | | 13 | | | | 1 | |
| **Factor** | **Subtype** | | | **Minimum** | **Maximum** | | | **Code Values** | | | | | **Media** | **Std. Dev.** |
| A | Continuous | | | 75.00 | 125.00 | | | -1.000=75.00 | | | 1.000=125.00 | | 100.00 | 20.41 |
| B | Continuous | | | 10.00 | 100.00 | | | -1.000=10.00 | | | 1.000=100.00 | | 55.00 | 36.74 |
| C | Continuous | | | 0.40 | 1.60 | | | -1.000=0.40 | | | 1.000=1.60 | | 1.00 | 0.49 |
| **Response**  **R1** | | **Obs** | **Analysis** | | | **Minim** | **Maxim** | | | **Media** | | **Std. Dev.** | **Ratio** | **Trans** |
| Weight (mg)  Weight (mg) | | 13 | Polynomial | | | 330 | 2200 | | | 953.231 | | 591.34  Quadratic | 6.66667 | None |

**Table S3.** The 3D-printed tablet model analysis

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | | **Response** | **1** | **Tablet Mass** | | **Transform:** | | **None** | **The Cubic Model and higher are Aliased** | | **Summary (detailed tables shown below)** | | | | | | | | | **Source** | **Sequential**  **p-value** | **Lack of Fit**  ***p*-value** | **Adjusted**  **R2** | | **Predicted**  **R2** | |  | | Linear | < 0.0001 |  | 0.8702 | | 0.7870 | |  | | 2FI | 0.0096 |  | 0.9674 | | 0.9170 | | Suggested | | Quadratic | 0.0368 |  | 0.9949 | |  | | Suggested | | Cubic |  |  |  | |  | | Aliased | |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Sequential Model Sum of Squares [Type I]** | | | | | | | | **Source** | **Sum of**  **Sqares** |  | **Mean**  **Square** | **F**  **Value** | **P value**  **Prob > F** |  | | **df** |  | | Mean vs Total | 1.181E+007 | 1 | 1.181E+007 |  |  |  | | Linear vs Mean | 3.788E+006 | 3 | 1.263E+006 | 27.82 | < 0.0001 |  | | 2FI vs Linear | 3.401E+005 | 3 | 1.134E+005 | 9.96 | 0.0096 | 2FI is suggested | | Quadratic vs 2FI | 62937.81 | 3 | 20979.27 | 11.66 | 0.0368 | Quadratic is suggested | | Cubic vs Quadratic | 5396.75 | 3 | 1798.92 |  |  | Undifferentiated | | Residual | 0.000 | 0 |  |  |  | In this case, the polynomial model with the highest order will be selected where the additional terms are significant, and the model is not replicated. | | Total | 1.601E+007 | 13 | 1.231E+006 |  |  |  | |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Model Summary Statistics** | | | | | | | | **Source** | **Std.**  **Dev.** | **R2** | **Adjusted**  **R2** | **Predicted**  **R2** | **PRESS** | **Observation** | | Linear | 213.04 | 0.9027 | 0.8702 | 0.7870 | 8.938E+005 |  | | 2FI | 106.72 | 0.9837 | 0.9674 | 0.9170 | 3.482E+005 | Suggested | | Quadratic | 42.41 | 0.9987 | 0.9949 |  | + | Suggested | | Cubic |  |  |  |  | + | Aliased | |

**Table S4.** Quadratic model - Analysis of variances

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Source** | **Sum of**  **Squares** | **df** | **Mean**  **Square** | **F**  **Value** | **p-value**  **Prob > F** |  | | Model | 4.191E+006 | 9 | 4.656E+005 | 258.85 | 0.0004 | significant | | A-Scaling | 2.962E+006 | 1 | 2.962E+006 | 1646.65 | < 0.0001 |  | | B-Infill density | 6.827E+005 | 1 | 6.827E+005 | 379.50 | 0.0003 |  | | C-Wall thickness | 1.428E+005 | 1 | 1.428E+005 | 79.41 | 0.0030 |  | | AB | 2.505E+005 | 1 | 2.505E+005 | 139.25 | 0.0013 |  | | AC | 17822.25 | 1 | 17822.25 | 9.91 | 0.0514 |  | | BC | 71824.00 | 1 | 71824.00 | 39.93 | 0.0080 |  | | A2 | 46251.57 | 1 | 46251.57 | 25.71 | 0.0148 |  | | B2 | 146.29 | 1 | 146.29 | 0.081 | 0.7941 |  | | C2 | 165.14 | 1 | 165.14 | 0.092 | 0.7817 |  | | Residual | 5396.75 | 3 | 1798.92 |  |  |  | | Cor Total | 4.196E+006 | 12 |  |  |  |  | | |
| |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | | **Final data** | | | | | | | | | **Std. Dev.** | 42.41 | | | **R2** | 0.9987 | | | | **Mean** | 953.23 | | | **Adjusted R2** | 0.9949 | | | | **C.V. %** | 4.45 | | | **Predicted R2** | N/A | | | | **PRESS** | N/A | | | **Adeq Precision** | 50.038 | | | | **-2 Log Likelihood** | 115.26 | | | **BIC** | 140.91 | | | |  |  | | | **AICc** | 245.26  Case(s) with leverage of 1.0000: Pred R-Squared and PRESS statistic not defined | | | | **Factor** | **Coefficient**  **Estimate** | **df** | **Standard**  **Error** | | **95% CI** | **95% CI** | **VIF** | | | **Low** | **High** | | Intercept | 866.00 | 1 | 42.41 | | 731.02 | 1000.98 |  | | | A-Scaling | 608.50 | 1 | 15.00 | | 560.78 | 656.22 | 1.00 | | | B-Infill density | 292.13 | 1 | 15.00 | | 244.40 | 339.85 | 1.00 | | | C-Wall thickness | 133.63 | 1 | 15.00 | | 85.90 | 181.35 | 1.00 | | | AB | 250.25 | 1 | 21.21 | | 182.76 | 317.74 | 1.00 | | | AC | 66.75 | 1 | 21.21 | | -0.74 | 134.24 | 1.00 | | | BC | -134.00 | 1 | 21.21 | | -201.49 | -66.51 | 1.00 | | | A2 | 142.25 | 1 | 28.05 | | 52.97 | 231.53 | 1.35 | | | B2 | 8.00 | 1 | 28.05 | | -81.28 | 97.28 | 1.35 | | | C2 | -8.50 | 1 | 28.05 | | -97.78 | 80.78 | 1.35 | | | |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Factor** | **Coefficient**  **Estimate** | **df** | **Standard**  **Error** | **95% CI** | **95% CI** | **VIF** | | **Low** | **High** | | Intercept | 866.00 | 1 | 42.41 | 731.02 | 1000.98 |  | | A-Scaling | 608.50 | 1 | 15.00 | 560.78 | 656.22 | 1.00 | | B-Infill density | 292.13 | 1 | 15.00 | 244.40 | 339.85 | 1.00 | | C-Wall thickness | 133.63 | 1 | 15.00 | 85.90 | 181.35 | 1.00 | | AB | 250.25 | 1 | 21.21 | 182.76 | 317.74 | 1.00 | | AC | 66.75 | 1 | 21.21 | -0.74 | 134.24 | 1.00 | | BC | -134.00 | 1 | 21.21 | -201.49 | -66.51 | 1.00 | | A2 | 142.25 | 1 | 28.05 | 52.97 | 231.53 | 1.35 | | B2 | 8.00 | 1 | 28.05 | -81.28 | 97.28 | 1.35 | | C2 | -8.50 | 1 | 28.05 | -97.78 | 80.78 | 1.35 | | |
| |  |  | | --- | --- | | **Final Equation in Terms of Coded Factors:** | | | Weight | = | | +866.00 |  | | +608.50 | \* A | | +292.13 | \* B | | +133.63 | \* C | | +250.25 | \* AB | | +66.75 | \* AC | | -134.00 | \* BC | | +142.25 | \* A2 | | +8.00 | \* B2 | | -8.50 | \* C2 | | |  |  | | --- | --- | | **Final Equation in Terms of Actual Factors:** | | | Weight | = | | +1512.07099 |  | | -37.86444 | \* Scaling | | -11.22438 | \* Infill density | | +97.89352 | \* Wall thickness | | +0.22244 | \* Scaling \* Infill density | | +4.45000 | \* Scaling \* Wall thickness | | -4.96296 | \* Infill density \* Wall thickness | | +0.22760 | \* Scaling2 | | +3.95062E-003 | \* Infill density2 | | -23.61111 | \* Wall thickness2 | |

The model F value of 258.85 implies that the model is significant. It's just a 0.04% chance that such a large F-value could occur due to noise. "Prob>F" values ​​less than 0.0500 indicate that the model terms are significant. A, B, C, AB, BC, A^2 are significant pattern terms in this case. Values ​​greater than 0.1000 indicate that the model terms are not important. If there are many insignificant model terms (not including those needed to support the hierarchy), the model reduction can improve it.

"Adeq Precision" measures the signal-to-noise ratio. A ratio greater than 4 is desirable. The ratio of 50.038 indicates an adequate signal. This model can be used to navigate the design space.

The coded factors equation can be used to predict 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 helps identify the relative impact of the elements by comparing the factor coefficients.

The equation in terms of fundamental factors can be used to predict the response for given levels of each element. 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. The following aspects were taken into account:

* A normal probability plot of the studentized residuals is needed to check for the normality of residuals.
* Studentized residuals vs. predicted values to check for constant error.
* Externally Studentized Residuals, to look for outliers, i.e., significant values.
* Box-Cox plot for power transformations.

**Table S5**. Data analysis. The software's suggested values for obtaining the desired tablet mass.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Factor** | **Name** | **Level** | **Low Level** | **High Level** | **Std. Dev.** | **Coding** | | A | Scaling | 107.02 | 75.00 | 125.00 | 0.000 | Actual | | B | Infill density | 27.88 | 10.00 | 100.00 | 0.000 | Actual | | C | Wall thickness | 1.44 | 0.40 | 1.60 | 0.000 | Actual | |
| |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | |  | **Predicted** | |  |  |  | **CI for** | **Mean** | **99% of** | **Population** | | **Response** | **Mean** | **Median1** | **Observed** | **Std Dev** | **SE Mean** | **95% CI low** | **95% CI high** | **95% TI low** | **95% TI high** | | Tablet mass | 1000 | 1000 | - | 42.4136 | 29.8469 | 905.015 | 1094.99 | 610.749 | 1389.25 | |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Confirmation Report** | | | | | | | | **Two-sided** | **Confidence =** | **95%** | **n =** | **1** |  |  | | **Factor** | **Name** | **Level** | **Low Level** | **High Level** | **Std. Dev.** | **Coding** | | A | Scaling | 107.02 | 75.00 | 125.00 | 0.000 | Actual | | B | Infill density | 27.88 | 10.00 | 100.00 | 0.000 | Actual | | C | Wall thickness | 1.44 | 0.40 | 1.60 | 0.000 | Actual | |
| |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **Response** | **Predicted**  **Mean** | **Predicted**  **Median1** | **Observed** | **Std**  **Dev** | **n** | **SE**  **Pred** | **95%PI**  **low** | **Data**  **Mean** | **95% PI**  **high** | | Tablet mass | 1000 | 1000 | - | 42.4136 | 1 | 51.86 | 834.95 |  | 1165.05 | |