Caffeine is an important naturally occurring compound which can be degraded by bacteria. Previously, Leifsonia sp. strain SIU capable of degrading caffeine was isolated from agricultural soil. Plackett-Burman design was used to screen significant parameters that affect the rate of caffeine degradation. After the design was applied, response surface methodology (RSM) through Central Composite Design (CCD) was used to study significant parameters further, in order to get the most superior degradation conditions. The optimum concentrations of carbon source (sucrose), nitrogen source (NH4Cl), pH and initial caffeine concentration was found to be 5.0 gl(-1), 0.4 gl(-1), 6.0 and 375 ppm respectively. Second order polynomial regression model accurately showed interpretation of experimental data with an R2 value of 0.9989, Adjusted (Adj) R2, Predicted (Pred) R2 and F values of 0.9939, 0.9225 and 88.77 respectively.