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OPTIMIZATION OF CRITICAL PROCESS PARAMETERS FOR NON AQUEOUS FILM COATING OF TABLET - USING 3^2 FULL FACTORIAL DESIGN.

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ABSTRACT

Tablet Coating is perhaps one of the oldest pharmaceutical processes still in origin. During the early years of these development an entirely new form of technology evolved, namely that of Film Coating. Design and development of an immaculate drug product or pharmaceutical process usually involves multiple objectives under its ambit. For decades, this task has been endeavored through trial and error, supplemented by the previous experience, knowledge and wisdom of the formulator. It is very common to see that though one may have decent coating equipment, the final product is still not very satisfactory. One may find various defects in the final products. The basic source of these defects could be 1) Defects arising due to defective core formulation or the tablet shape (like high friability, capping, logo or embossing, cratering, high contact surface area causing twinning. or 2)Non-optimized coating formulation (problems like film cracking and peeling, spray drying, orange peel, poor coating efficiency). Critical coating parameters like atomizing air pressure and inlet air temperature were optimized by using 3^2 full factorial design,Design Expert 8.0.5.2 version soft ware, in that two independent factors were atomizing air pressure (0.5 kg/cm^2,1.25 kg/cm^2 and 2.0 kg/cm^2) and inlet air temperature (40^0c,50^0c,60^0c) three different levels were coded as (-1,0,+1) the prepared tablets were evaluated for Sticking and Picking ,Orange peel and Surface roughness. Optimized process gave tablet coat free from sticking and picking, Orange peel effect.

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Key Words
Film coating, 3^2 Full Factorial design, Inlet air temperature, Atomizing air pressure etc.

1) INTRODUCTION

Advocates of film coating were achieving success by using polymer based coatings dissolved in highly volatile solvents. Film coating has now become an integral part of pharmaceutical industry. During last few decades, many ancillary industries have come up and grown many folds to support the pharma industry for the film coating process.

"Here in this study primary objective was to optimize critical process parameters"

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Coating formula optimization "Basic formula is obtained from past experience or from various sources in the literature. Modifications are required to improve adhesion of the coating to the core, to decrease bridging of installations, to increase coating hardness, etc.

The final product may be satisfactory but sub-optimal, as a better formulation might still exist for the studied conditions. Thus, in the traditional approach the primary aim of the formulator may not be in designing the best formulation, but finding a suitable solution under the given set of restrictions.

2) MATERIALS AND METHODS

MATERIALS

All the materials used in current research work were obtained from Bharat Parenterals Ltd., Savali,Vadodara.Quality was tested by Quality control department.

Methods

2.1) Formulation of Core tablet.

The most common and simplest method available for tablet compression is direct compression in which the drug with other excipients are mixed thoroughly with the help of various mixers followed by the compression of the resulting Powder. Cefixime and Potassium clavulanate tablet was prepared by direct compression method in which Kyron T 314 was added as disintegrant ,Avicel ph102 as diluent, Magnesium stearate as lubricants and Talc as glident.Formula for core tablet preparation showed in Table 1.

Table 1: Formula for core tablet preparation.

Sr.No.	Ingredient	Quantity Per Tablet (mg)
1	Cefeixme	224
2	Potassium Clavulanate with Avicel Ph 102	297.33
3	Avicel Ph 102	138.67
4	Kyron T 314	16
5	Magnesium Stearate	8
6	Talc	16
Total	-	700

2.2) Preparation of Coating Solution

Insta moist shield (Ideal cure) was used as coating material as the drug potassium clavulanate was hygroscopic and it tends to absorb moisture from environment. Required quantity of Moist shield (for 3% weight gain) was taken in 1000 ml beaker which contains Isopropyl alcohol. Mix the solution and add

Dichloromethane till all Moist shield powder get mixed. Filter the solution from 100# sieve. All the operations were done in flam proof area.

2.3) Coating of Tablet

The tablets were coated in auto coater made by Solace Pvt. Ltd. Process parameters were kept as specified in table. As atomizing air pressure and Inlet air temperature need optimization, using Design expert software 3^2 full factorial design different 9 Batches were taken and process parameters were optimized.

Independent variables: Atomizing air pressure and Inlet air temperature

Dependant variables: Sticking and picking, Orange peel effect, Surface roughness .

Three levels : (-1,0,+1)

Coating parameters showed in Table 2 and Trial batches showed in table 3.

Table 2: Coaing Parameters.

Fixed Parameters	Specification
Solvent	Organic
Solid Content	5%
Batch size	100 tablets(700 gm)
Nozzle diameter	1mm
Number of spray gun	1
Baffles	3
Weight Gain	3.5% to 4%
Preheating	10 TO 15 Min.
Pan speed	5 R.P.M
Atomizing air pressure	0.5-2 Kg./cm^2
Air inlet temperature	40^{o}C to 60^{o}C

Table 3: Trial Batches for optimization

RUN (Batch)	Atomizing air pressure (Kg/cm^2)	Inlet air temperature (^{0}C)
1	2.00	50
2	1.25	50
3	2.00	60
4	0.50	40
5	1.25	40
6	0.50	60
7	1.25	60
8	0.50	50

2.4) Evaluation Parameters

Prepared nine Batches were evaluated for Sticking and picking, Orange peel effect, Surface roughness.Surface roughness, sticking and picking Orange peel effect the dependent factors were represented as relative appearance in grade 0 to 10 (from best to better to worse) for all nine batches and the results were putted in design expert software version 8.0.5.2.Then optimized batch was prepared to check reproducibility.

3) RESULTS AND DISCUSSION

After grading the tablets the data shown in Table 4. and Data obtained from design expert soft ware were showed in Table 5.

Atomizing air pressure

Increasing the spraying air pressure decreases the surface roughness of coated tablets and produces denser and thinner films. If spraying air pressure is excessive, the spray loss is great, the formed droplets are very fine and could spray-dry before reaching the tablet bed, resulting in inadequate

droplet spreading and coalescence . From data atomizing air pressure 1.80 kg/cm^2 gave surface smooth and best appearance.

Table 4 : Results showing coating process optimization and Quadric model suitability

RUN (BATCH)	FACTOR 1(A) Atomizing air pressure(Kg/cm^2)	FACTOR 2(B) Inlet air temperature (^{o}c)	Sticking and picking	Orange peel	Surface roughness
1	2.00	50	0	1	0
2	1.25	50	0	0	1
3	2.00	60	4	9	10
4	0.50	40	10	6	6
5	1.25	40	7	5	4
6	0.50	60	2	8	7
7	1.25	60	3	10	9
8	0.50	50	0	1	0
9	2.00	40	6	2	5

Table 5 : Data Obtained from Design Expert Soft ware.

	Sticking and Picking	Surface roughness	Orange peel
R ^{2}	0.9922	0.9734	0.9762
P Value	0.0023<0.05	0.0144<0.05	0.0122<0.05
Equation in terms of coded factor	Sticking and picking= -0.22 -0.33*A -2.33*B+1.50* A * B +0.33 * A2+5.33 * B2	Surface Roughness = +1.00-0.50 * A +2.33 * B+1.25 * A * B -0.50 *A2+6.00*B2	Orange peel= +0.33+0.33 * A+1.83 * B+1.00 * A *B+0.000*A2+6.50 * B2

Inlet air temperature

The inlet air temperature affects the drying efficiency (i.e. water evaporation) of the coating pan and the uniformity of coatings. High inlet air temperature increases the drying efficiency of the aqueous film coating process and a decrease in the water penetration into the tablet core decreases the core tablet porosity, tensile strength and residual moisture content of coated tablets. From data inlet air temperature 49^{0}c gave best appearance.

Effect of independent variables on individual dependent variales were evaluated with help of experiment design soft ware version 8.0.5.2, which was shown in Figure 1, Figure 2, Figure 3 and Figure 4 in form of contour plot and it's 3-D view.

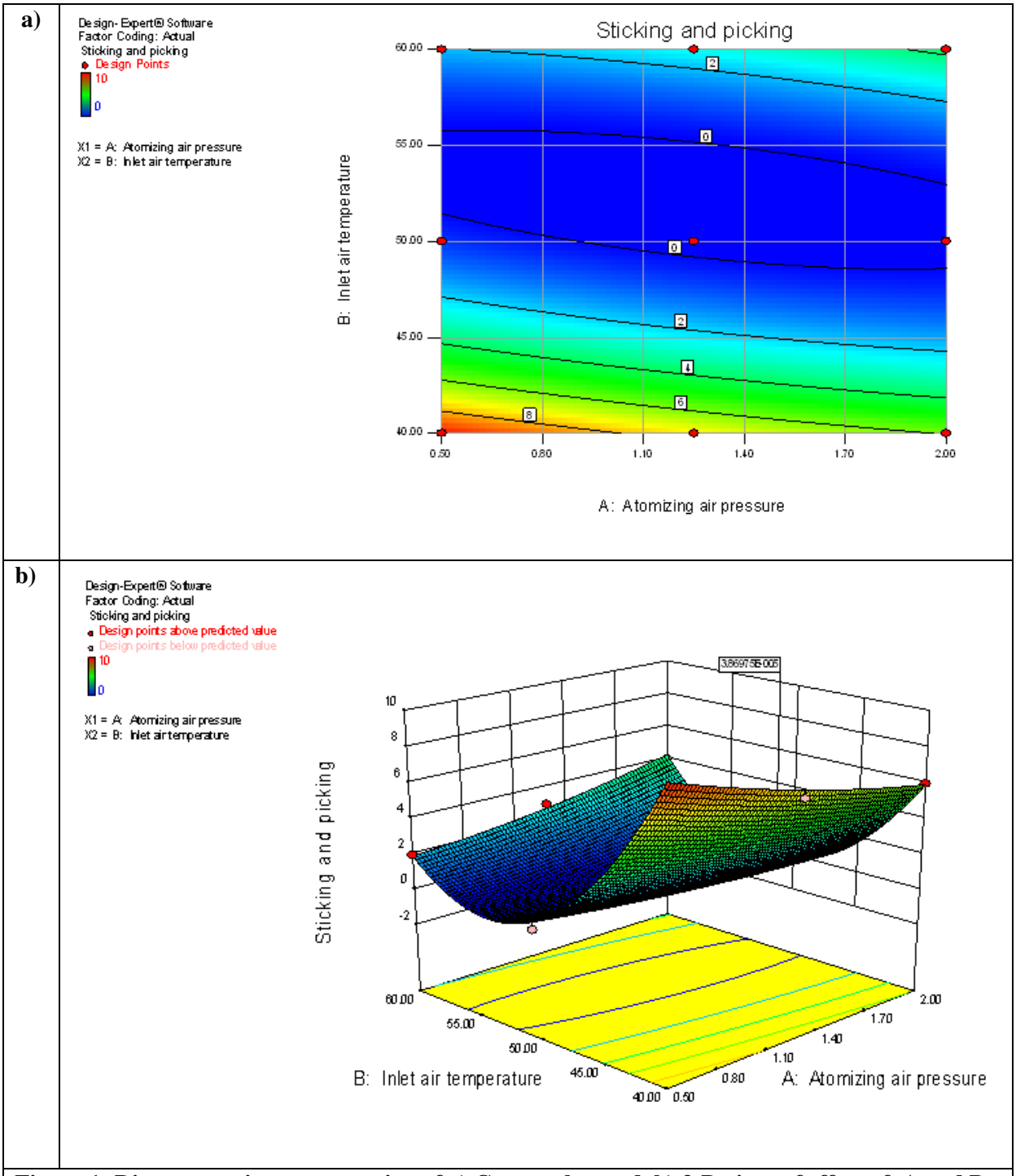


Figure 1: Diagrammatic representation of a) Conter plot and b) 3-D view of effect of A and B on Sticking and picking

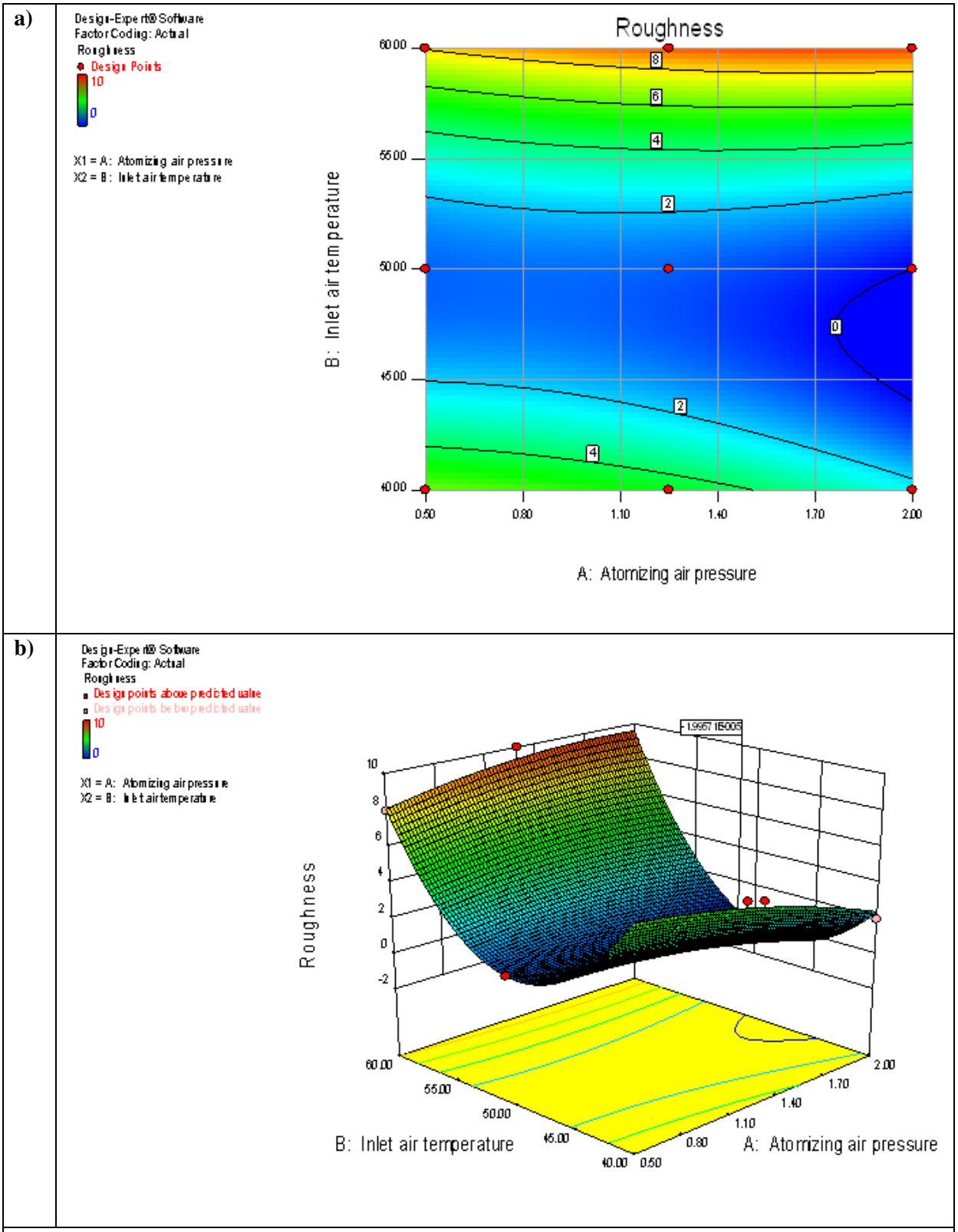


Figure 2: Diagrammatic representation of a) Contour plot and b) 3-D view of effect of A and B on roughness of tablet surface

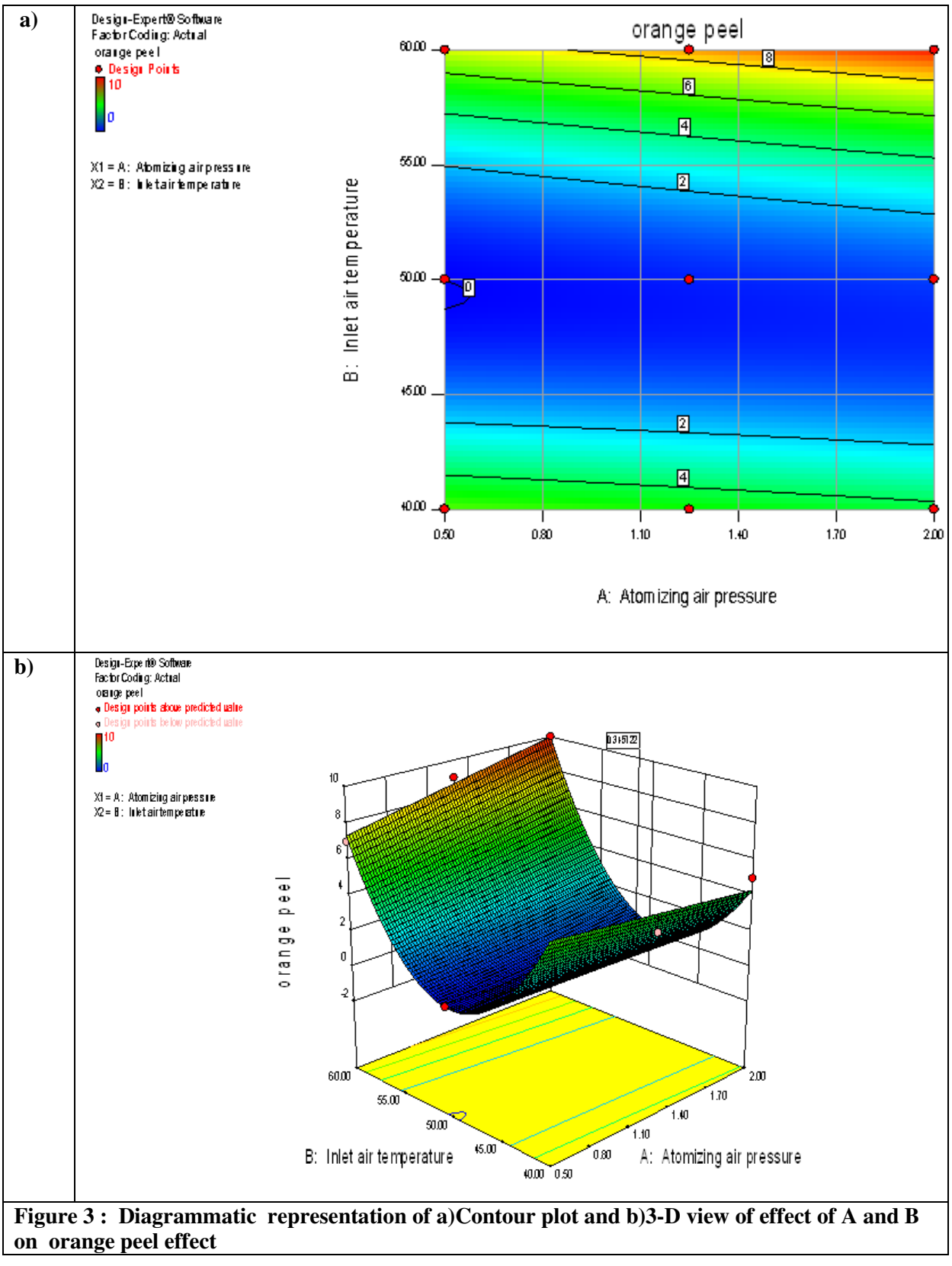
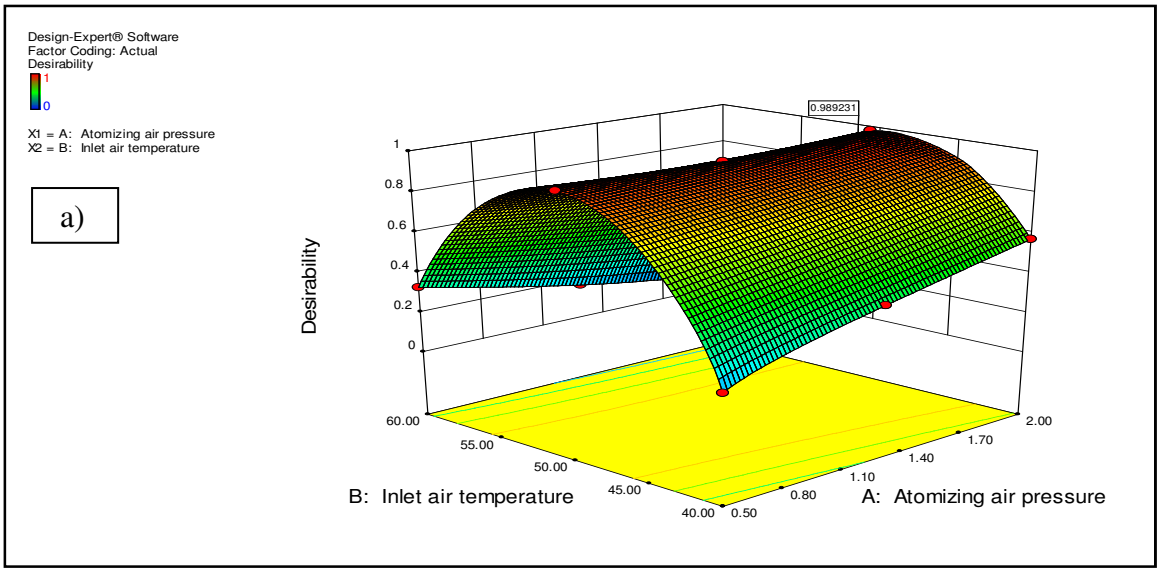


Figure 3 : Diagrammatic representation of a)Contour plot and b)3-D view of effect of A and B on orange peel effect



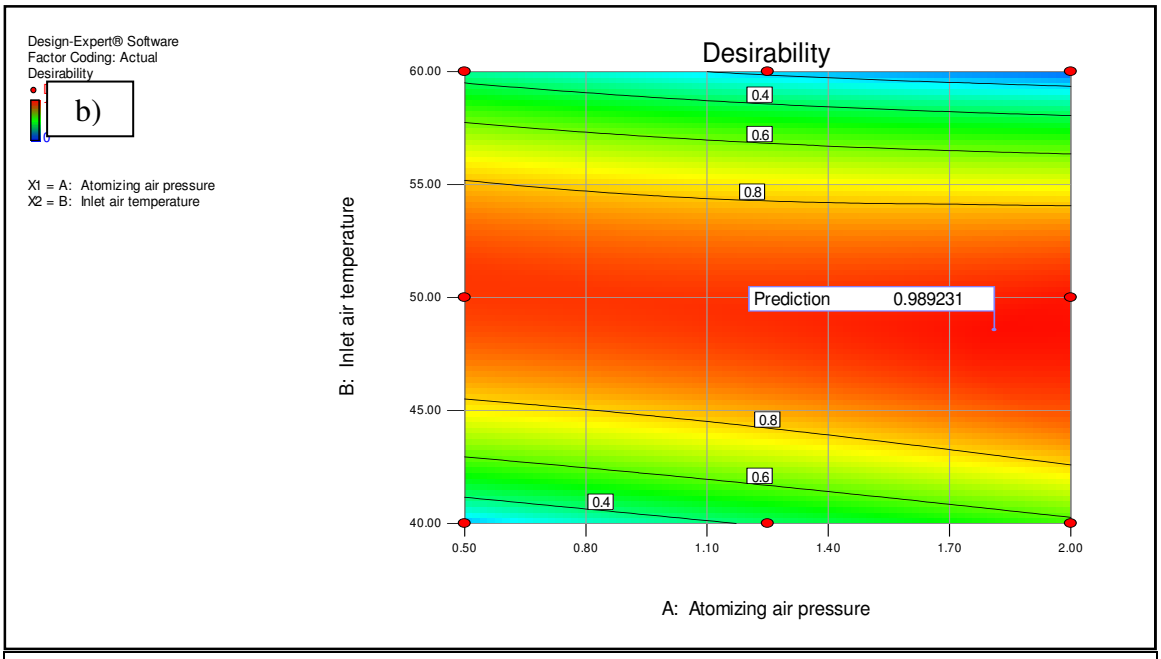


Figure 4 : Diagrammatic representation of a) 3-D view and b) contour plot , showing effect of all independent factors on all dependent factors.

Sticking and Picking: From figure 1, as temperature increases above 49 ^{0}C sticking and picking problem disappears. Below 49^{0}C much more sticking and picking were observed.

Surface roughness: From figure 2, as Atomizing air pressure increases above 1.80 Kg/cm^2 surface roughness problem disappears. Below 1.80 Kg/cm^2 much more surface roughness were observed.As

degree of atomizing increases droplet size going to decrease and surface becomes more smooth.

Orange peel effect: From figure 3, as inlet air temperature increases above 55^0C Orange peel effect problem seen and, as inlet air temperature below 42^0C much more Orange peel effect problem were observed.

4) Conclusion

From the data shown in figure 1,figure 2, figure 3, figure 4 and table 5, it was concluded that quadric model best suits for this 3^2factorial design and give point prediction with desirability 0.9892 nearer to 1.When coating batch taken at atomizing air pressure 1.80 kg/cm^2 and inlet air temperature 49 ^{0}C batch shown less then 1% error between predicted value and observed value.Optimization of critical coating parameters were done by design Expert soft ware.

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