ORIGINAL RESEARCH ARTICLE

Preparation and optimization of sustained release matrix tablets of metoprolol succinate and taro gum using response surface methodology

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In the present study, an effort was made to formulate and evaluate matrix tablets of tarogum utilizing metaprolol succinate as the model drug. 3^2 full optimization procedure was adopted where two factors are studied at three levels. The amount of taro gum (X1) and polyvinylpyrrolidone (PVP) K30 (X2) were selected as independent variables. The time required for 90% of drug release was selected as the dependent variable. Tablets were prepared by direct compression and were evaluated for various post compression parameters such as tablet hardness, friability, weight variation, drug content and *in vitro* dissolution. The results were found to be within the acceptable limits. The release exponent (n) lies between 0.416 and 0.584 indicating drug release from the matrix tablets may be fickian or non-fickian (anomalous) depending upon the concentration of natural polymer. T90 was 10.70, 11.20, 12.05, 12.66 h for B6, B7, B8 and B9 batches respectively showing overriding potential of taro gum, but still the effect of PVP K 30 is noteworthy. PVP K 30 has an indirect effect on all the factors by increasing tensile strength and making the tablet firm and intact.

Key words: *3^2 full factorial design, metoprolol succinate, polyvinylpyrrolidone K30, taro gum*

INTRODUCTION

The use of sustained release formulations has been a breakthrough in the field of novel drug delivery systems. It prevents the use of intricate production techniques like pelletization and coating during the manufacturing. The drug release rate from the dosage form depends on the amount and the type of polymers used. Hydrophilic polymer matrix is widely used in designing a controlled release formulation. A wide variety of statistical experimental designs have been designed to study the process variables.[1] In the present study, a computer based optimization technique with response surface methodology (RSM) utilizing a polynomial equation has been used. Different types of RSM designs include 3-level factorial design, Box-Behnken design, central composite design (CCD) and D-optimal design. RSM is used when only significant factors are used for optimization.[2,3] The technique is cost-effective than the other available conservative techniques and utilizes minimum experimentation and time.

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MATERIALS AND METHODS

Materials

Metoprolol succinate is the model drug obtained as a gift sample from Orchid Chemicals and Pharmaceuticals, Chennai. Polyvinylpyrrolidone K30 and microcrystalline cellulose was obtained from Signet Chemicals, Mumbai. Talc and magnesium stearate were purchased from National Scientific, Vijayawada.

Method of extraction

Fresh taro corms were washed to remove the adherent soil material, later peeled and made in a smooth paste.

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150 g of this taro paste was suspended in 1% NaCl solution and the slurry was passed through a muslin cloth.[4] The filtrate was collected to which equal amount of acetone was added and the mucilage was carefully separated. The mass was then dried in a tray drier at 60°C for 24 h.[5] After complete drying, the powder was sieved using mesh #22 and stored in dessicator for further use.

The aim of the investigation was to develop a sustained release matrix tablet of metoprolol succinate and optimize the formulation using RSM.

Preparation of tablets

Taro gum based sustained release formulations containing metoprolol succinate were prepared using direct compression technique. Metoprolol succinate and the polymers were screened through 80 mesh sieve. Microcrystalline cellulose is used as filler. All the ingredients are weighed accurately and mixed intimately for about 15 min. Then the blend was lubricated with talc and magnesium stearate. Tablets were compressed using 9 mm flat face circular punches which were fixed to the 16 station single rotary tablet compression machine (Cadmach, Ahmedabad, India). Table 1 illustrates the composition of sustained release matrix tablets.

Experimental design

A CCD with $\alpha = 1$ was practiced as per the standard etiquette. The amounts of taro gum (X1) and PVP k30 (X2) were selected as factors and studied at three levels each.[6,7] Table 2 illustrates the nine experimental batches and their translational codes employed during the study. The time required for 90% of drug release (Y) was the dependent response variable.

Evaluation of tablets

Physical parameters

The prepared tablets were characterized for thickness ($n = 20$) using a screw gauge, hardness[8] ($n = 6$) with a Monsanto tester, % friability[9] ($n = 6$, roche friabilator) and weight uniformity ($n = 20$).

Tensile strength

Tensile strength[10] is the force required to break the tablet in a radial direction using Monsanto hardness tester. The following equation can be used:

$$T = 2F/\pi dt$$

Where, F is the crushing load; d is the diameter of the tablet; t is the thickness of the tablet.

Drug content

A total of 20 tablets[11] were finely powdered of which 50 mg of the drug was transferred to a 50 ml volumetric flask and volume was made up using methanol, shaken well for 10 min for complete solubility of the drug. The mixture was centrifuged and 10 ml of the supernatant was quantified spectrophotometrically at 223 nm after sufficient dilution.

Table 1: Composition of formulation batches (B1-B9)

Ingredients (mg)	B1	B2	B3	B4	B5	B6	B7	B8	B9
Metaprolol succinate	100	100	100	100	100	100	100	100	100
Taro gum	25	50	75	25	50	75	25	50	75
PVP k-30	12.5	12.5	12.5	25	25	25	37.5	37.5	37.5
MCC	106.5	81.5	56.5	94	69	44	81.5	56.5	31.5
Talc	3	3	3	3	3	3	3	3	3
Magnesium stearate	3	3	3	3	3	3	3	3	3
Total weight (mg)	250	250	250	250	250	250	250	250	250

PVP: Polyvinylpyrrolidone, MCC: Microcrystalline cellulose

Table 2: Combinations as per the experimental design

Batch codes	Variable levels of coded factors	
	X1 (taro gum)	X2 (PVP k30)
B1	−1 (25)	−1 (12.5)
B2	0 (50)	−1 (12.5)
B3	1 (75)	−1 (12.5)
B4	−1 (25)	0 (25)
B5	0 (50)	0 (25)
B6	1 (75)	0 (25)
B7	−1 (25)	1 (37.5)
B8	0 (50)	1 (37.5)
B9	1 (75)	1 (37.5)

PVP: Polyvinylpyrrolidone

In vitro dissolution studies

The dissolution studies were performed using an eight stage USP dissolution apparatus, type II at a speed of 50 rpm with 6.8 pH phosphate buffer as the dissolution medium of volume 900 ml at 37°C ± 0.5°C. Aliquots of 5 ml each were withdrawn at different time intervals and the metoprolol content was estimated spectrophotometrically at 223 nm. At each time of withdrawal of drug, it was replaced with a fresh buffer of equal amount.[12]

In vitro drug release can be explained through various pharmacokinetic models to describe the drug release kinetics. Five types of models have come into existence for the study.

Zero order model: The models explains that the rate of drug release is independent of the concentration.

$$C = K0t \quad (1)$$

Where, K0 is the zero-order rate constant having the units of concentration/time.

First order model: The model explains the rate of drug release with dependence on concentration.

$$\text{Log } C = \text{Log } Co - K1t / 2.303 \quad (2)$$

where, Co is the initial concentration of the drug.

Higuchi model: The model explains the release of drug based on the fickian diffusion as a square root of time dependent process from the swellable insoluble matrix.[13]

$$Q = KH\,t^{1/2} \quad (3)$$

Where, K_H is the rate constant for Higuchi equation.

Korsmeyer-Peppas model: The model explains the drug release from a polymeric system and the type of release mechanism[14] can be studied.

$$M_t / M^{\infty} = K_{KP}\,t^n \quad (4)$$

Where, M_t/M^{∞} is the fraction of drug released at time 't', K_{KP} is the korsmeyer-Peppas rate constant,[15] n is the release exponent used to characterize the release mechanisms.

Hixon-Crowell cubic root law model: The model explains the release of drug from the systems by erosion or dissolution resulting in a change in surface area of particles.[16]

$$Q_0^{1/3} - Q_t^{1/3} = K_{HC}\,t \quad (5)$$

Where, Q_t is the amount of drug released in 't' time; Q_0 is the initial amount of drug in dosage form; K_{HC} is the Hixson-Crowell rate constant.

RSM optimization: Mathematical modeling

A 3^2 randomized full factorial design was used in this study. Two factors were evaluated, each at three levels, and experimental trials were performed at all nine possible combinations [Table 2]. The amount of Taro gum (X1) and the amount of PVP K30 (X2) were selected as independent variables. The time required for 90% *in vitro* drug dissolution, was selected as dependent variable. A statistical model incorporating interactive and polynomial terms was used to evaluate the responses.

$$Y = B_0 + B_1X_1 + B_2X_2 + B_3X_1X_2 + B_4X_1^2 + B_5X_2^2 + B_6X_1X_2^2 + B_7X_1^2X_2 + B_8X_1^2X_2^2$$

Where Y is the dependent variable, B_0 is the arithmetic mean response of the nine runs, and B_1 and B_2 are the estimated coefficient for the factor X_1 and X_2. The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high value. The interaction terms (X_1X_2) show how the response changes when two factors are simultaneously changed. The polynomial terms (X_1^2 and X_2^2) are included to investigate nonlinearity. The statistical analysis of the factorial design batches was performed by multiple linear regression analysis using Microsoft Excel. The results depicted in Table 3 clearly indicate that the dependent variable is strongly dependent on the selected independent variables, as shown by the wide variation among the nine batches (B1-B9). The polynomial equations can be used to draw conclusions after considering the magnitude of the coefficient and the mathematical sign it carries (i.e., positive or negative).

RESULTS AND DISCUSSION

The prepared tablets are subjected to assess different post-compression parameters. The thickness of all nine batches was in the range of 2.38 ± 0.08-2.56 ± 0.05, tablet hardness ranged from 5.3 ± 0.07 to 6.18 ± 0.1, friability ranged from 0.54 ± 0.03 to 0.79 ± 0.09, and the weight uniformity was within limits. The thickness may vary with no change in weight due to the difference in the granulation and pressure applied to the tablets, wear and tear on the length of punches as well as on the speed of tablet compression. It may be especially important to carefully monitor tablet hardness for drug products that possess real or potential bioavailability problems or are sensitive to altered dissolution-release profiles as a function of the compressive force employed. The % drug content ranged from 99.23 ± 0.02 to 99.76 ± 0.04 and the tablet tensile strength was within 0.54-1.68. All the post compression parameter results revealed that the formulated tablets are within the permissible limits of USP. Tables 4 and 5 listed out the various parameters.

Tables 6 and 7 explain the time for 90% drug release and kinetic data for all formulation batches respectively. The plot of cumulative % drug release versus time was depicted in Figure 1 for all nine batches. The drug release was diffusion controlled as the plot of Higuchi's model was found to be linear ($r > 0.9683$) for all formulations. The formulations B1 to B4 showed higher R values for first order plot indicating that the drug release from these formulations was concentration dependent and followed first order kinetics. While the formulations B5 to B9 showed higher R values for zero order plot indicating that drug release followed zero order kinetics and drug release from these tablets were by both diffusion and erosion.

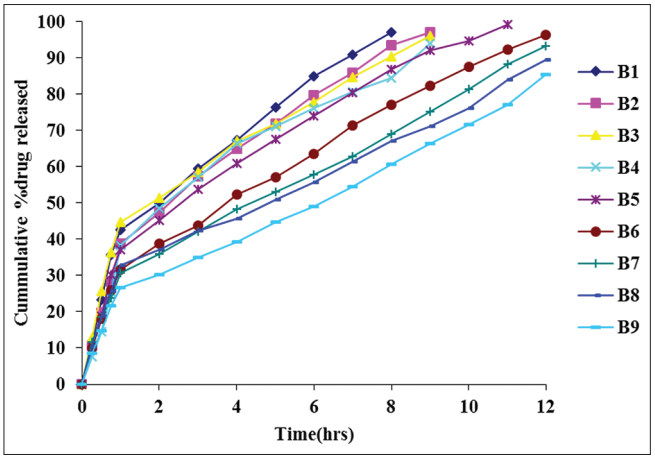

Figure 1: Comparative *in vitro* release profile of formulations B1-B9

Table 3: Yates algorithm

Formulation code	Level of factor in an experiment		Interaction						Response
	X_1	X_2	X_1X_2	X_1^2	X_2^2	$X_1X_2^2$	$X_1^2X_2$	$X_1^2X_2^2$	Y ($t_{90\%}$)
B1	−1	−1	+1	+1	+1	−1	−1	+1	6.93
B2	−1	0	0	+1	0	0	0	0	7.70
B3	−1	+1	−1	+1	+1	−1	+1	+1	7.96
B4	0	−1	0	0	+1	0	0	0	8.62
B5	0	0	0	0	0	0	0	0	8.81
B6	0	+1	0	0	+1	0	0	0	10.70
B7	+1	−1	−1	+1	+1	+1	−1	+1	11.20
B8	+1	0	0	+1	0	0	0	0	12.05
B9	+1	+1	+1	+1	+1	+1	+1	+1	12.66

Calculation of coefficient

$B_0 = ((1) * (Y1) + (1) * (Y2) + (1) * (Y3) + (1) * (Y4) + (1) * (Y5) + (1) * (Y6) + (1) * (Y7) + (1) * (Y8) + (1) * (Y9))/9$
$= ((1 * 6.93) + (1 * 7.70) + (1 * 7.96) + (1 * 8.62) + (1 * 8.81) + (1 * 10.70) + (1 * 11.20) + (1 * 12.05) + (1 * 12.66))/9$
$= 9.6255$

$B_1 = ((-1) * (Y1) + (-1) * (Y2) + (-1) * (Y3) + (0) * (Y4) + (0) * (Y5) + (0) * (Y6) + (1) * (Y7) + (1) * (Y8) + (1) * (Y9))/9$
$= ((-1) * (6.93) + (-1) * (7.70) + (-1) * (7.96) + (0) * (8.62) + (0) * (8.81) + (0) * (10.70) + (1) * (11.20) + (1) * (12.05) + (1) * (12.66))/9$
$= 1.48$

$B_2 = ((-1) * (Y1) + (0) * (Y2) + (1) * (Y3) + (-1) * (Y4) + (0) * (Y5) + (1) * (Y6) + (-1) * (Y7) + (0) * (Y8) + (1) * (Y9))/9$
$= ((-1) * (6.93) + (0) * (7.70) + (1) * (7.96) + (-1) * (8.62) + (0) * (8.81) + (1) * (10.70) + (-1) * (11.20) + (0) * (12.05) + (1) * (12.66))/9$
$= 0.5077$

$B_3 = ((1) * (Y1) + (0) * (Y2) + (-1) * (Y3) + (0) * (Y4) + (0) * (Y5) + (0) * (Y6) + (-1) * (Y7) + (0) * (Y8) + (1) * (Y9))/9$
$= ((1) * (6.93) + (0) * (7.70) + (-1) * (7.96) + (0) * (8.62) + (0) * (8.81) + (0) * (10.70) + (-1) * (11.20) + (0) * (12.05) + (1) * (12.66))/9$
$= 0.0477$

$B_4 = ((1) * (Y1) + (1) * (Y2) + (1) * (Y3) + (0) * (Y4) + (0) * (Y5) + (0) * (Y6) + (1) * (Y7) + (1) * (Y8) + (1) * (Y9))/9$
$= ((1) * (6.93) + (1) * (7.70) + (1) * (7.96) + (0) * (8.62) + (0) * (8.81) + (0) * (10.70) + (1) * (11.20) + (1) * (12.05) + (1) * (12.66))/9s$
$= 6.5$

$B_5 = ((1) * (Y1) + (0) * (Y2) + (1) * (Y3) + (1) * (Y4) + (0) * (Y5) + (1) * (Y6) + (1) * (Y7) + (0) * (Y8) + (1) * (Y9))/9$
$= ((1) * (6.93) + (0) * (7.70) + (1) * (7.96) + (1) * (8.62) + (0) * (8.81) + (1) * (10.70) + (1) * (11.20) + (0) * (12.05) + (1) * (12.66))/9$
$= 6.45$

Table 4: Post compression parameters

Formulation code	Mean±SD			
	n=5		*n*=3 (%)	
	Thickness (mm)	Hardness (kg/cm²)	Friability	Weight uniformity
B1	2.5±0.07	5.52±0.08	0.54±0.03	251.29±0.05
B2	2.5±0.15	5.8±0.07	0.64±0.05	250.46±0.1
B3	2.44±0.09	5.5±0.07	0.59±0.13	248.9±0.04
B4	2.38±0.08	5.78±0.08	0.56±0.1	252.5±0.02
B5	2.56±0.05	5.3±0.07	0.79±0.06	250±0.05
B6	2.5±0.11	6.18±0.1	0.54±0.19	251.5±0.04
B7	2.4±0.1	5.7±0.07	0.77±0.05	247.9±0.04
B8	2.52±0.04	5.4±0.07	0.79±0.09	245.6±0.05
B9	2.48±0.08	6.02±0.08	0.69±0.08	256±0.04

SD: Standard deviation

Table 5: Post compression parameters

Formulation code	Drug content uniformity (%) mean±SD, *n*=3	Tensile strength (MN/cm²)
B1	99.29±0.05	0.54
B2	99.46±0.1	0.62
B3	99.66±0.04	0.79
B4	99.23±0.02	1.02
B5	99.49±0.05	1.15
B6	99.72±0.04	1.26
B7	99.76±0.04	1.28
B8	99.52±0.05	1.56
B9	99.52±0.04	1.68

SD: Standard deviation

Table 6: Time taken to release 90% of drug for all formulations ($t_{90\%}$)

Formulation code	$t_{90\%}$ (h)
B1	6.93
B2	7.70
B3	7.96
B4	8.62
B5	8.81
B6	10.70
B7	11.20
B8	12.05
B9	12.16

Table 7: Kinetic values from different plots of formulation batches (B1-B9)

Formulation code	Zero order plot		First order plot			Higuchi plot	Korsmeyer peppas plot		Possible mechanism of drug release
	R^2	Zero order rate constant K_0 (mg/h)	R^2	*n*	First order rate constant K_1 (h^{-1})	R^2	R^2	*n*	
B1	0.911	10.699	0.9325	−0.1547	0.3563	0.9827	0.9966	0.4364	First order fickian diffusion
B2	0.9254	9.8095	0.9364	−0.1401	0.3226	0.9914	0.998	0.4433	First order fickian diffusion
B3	0.8866	8.9977	0.9381	−0.1255	0.2890	0.9766	0.9925	0.417	First order fickian diffusion
B4	0.8943	9.397	0.9507	−0.1147	0.2642	0.9742	0.992	0.4163	First order fickian difussion
B5	0.9213	8.0802	0.8698	−0.1321	0.3042	0.9909	0.9978	0.4715	Zero order non fickian difussion
B6	0.9514	7.186	0.929	−0.0967	0.2227	0.9919	0.9906	0.5362	Zero order non fickian difussion
B7	0.9574	6.6453	0.9217	−0.0776	0.1787	0.9838	0.9817	0.5355	Zero order non fickian difussion
B8	0.9414	6.1798	0.9333	−0.0682	0.1571	0.9769	0.9683	0.4973	Zero order non fickian difussion
B9	0.9646	6.0189	0.9412	−0.0576	0.1327	0.9711	0.9742	0.5844	Zero order non fickian difussion

Table 8: Calculation for converting the transformed values in to actual polymer concentrations

Factor	Low level	Median level	High level	Average of two levels	1/2 of difference of two levels
Taro gum	25	50	75	50	25
PVP K30	12.5	25	37.5	25	12.5

PVP: Polyvinylpyrrolidone

Table 9: Formulation of extra design checkpoint batch (F_{ED})

Ingredients	Quantity of drug (mg)
Metaprolol succinate	100
Taro gum	56.25
PVP k-30	28.125
MCC	59.625
Talc	3
Magnesium stearate	3

PVP: Polyvinylpyrrolidone, MCC: Microcrystalline cellulose, F_{ED}: ???

$B_6 = ((-1) * (Y1) + (0) * (Y2) + (-1) * (Y3) + (0) * (Y4) + (0) * (Y5) + (0) * (Y6) + (1) * (Y7) + (0) * (Y8) + (1) * (Y9))/9$
$= ((-1) * (6.93) + (0) * (7.70) + (-1) * (7.96) + (0) * (8.62) + (0) * (8.81) + (0) * (10.70) + (1) * (11.20) + (0) * (12.05) + (1) * (12.66))/9$
$= 0.9966$

$B_7 = ((-1) * (Y1) + (0) * (Y2) + (1) * (Y3) + (0) * (Y4) + (0) * (Y5) + (0) * (Y6) + (-1) * (Y7) + (0) * (Y8) + (1) * (Y9))/9$
$= ((-1) * (6.93) + (0) * (7.70) + (1) * (7.96) + (0) * (8.62) + (0) * (8.81) + (0) * (10.70) + (-1) * (11.20) + (0) * (12.05) + (1) * (12.66))/9$
$= 0.2766$

$B_8 = ((1) * (Y1) + (0) * (Y2) + (1) * (Y3) + (0) * (Y4) + (0) * (Y5) + (0) * (Y6) + (1) * (Y7) + (0) * (Y8) + (1) * (Y9))/9$
$= ((1) * (6.93) + (0) * (7.70) + (1) * (7.96) + (0) * (8.62) + (0) * (8.81) + (0) * (10.70) + (1) * (11.20) + (0) * (12.05) + (1) * (12.66))/9$
$= 4.3055.$

Table 10: *In vitro* drug release data for extra design check point formulation (F_{ED})

Time (h)	Cumulative percent of drug released (mean±SD)		
	Trial I	Trial II	Trial III
0	0	0	0
0.25	9.662±0.1448	9.843±0.1448	10.34±0.1448
0.5	17.63±0.1451	17.78±0.1451	16.77±0.1451
0.75	23.26±0.1455	24.99±0.1455	23.78±0.1455
1	30.52±0.1458	31.19±0.1458	31.51±0.1458
2	37.22±0.1461	37.73±0.1461	37.48±0.1461
3	42.10±0.1464	42.35±0.1464	43.03±0.1464
4	49.83±0.1467	50.22±0.1467	50.52±0.1467
5	55.40±0.1471	55.71±0.1474	56.01±0.1476
6	62.70±0.1474	62.23±0.1474	62.95±0.1474
7	69.18±0.1477	69.51±0.1477	68.65±0.1477
8	75.02±0.1480	75.35±0.1480	74.91±0.1480
9	79.93±0.1484	79.70±0.1484	81.64±0.1484
10	85.85±0.1487	86.08±0.1487	86.88±0.1487
11	91.42±0.1490	91.07±0.1490	91.15±0.1490
12	95.96±0.1493	95.65±0.1493	96.27±0.1493

SD: Standard deviation, F_{ED}: ???

Applying the above values of coefficients in the polynomial equation,

$Y = 9.6255 + 1.48 (X_1) + 0.5077 (X_2) + 0.0477 (X_1 X_2) + 6.5 (X_1^2) + 6.45 (X_2^2) + 0.9966 (X_1 X_2^2) + 0.2766 (X_1^2 X_2) + 4.3055 (X_1^2 X_2^2).$

$Y = 9.6255 + 1.48 (0.25) + 0.5077 (0.25) + 0.0477 ((0.25) (0.25)) + 6.5 ((0.25) (0.25)) + 6.45 ((0.25) (0.25)) + 0.9966 ((0.25) (0.25) (0.25)) + 0.2766 ((0.25) (0.25) (0.25)) + 4.3055 ((0.25) (0.25) (0.25) (0.25))$

$Y = 9.6255 + 0.37 + 0.1269 + 0.003 + 0.4063 + 0.4063 + 0.016 + 0.0043 + 0.01681$

Predicted response Y = 10.9751.

Transformation

$$\text{Arbitrary value}: \frac{X - \text{Average of two levels}}{\frac{1}{2}\text{ the difference of two levels}}$$

X_1 = Concentration of taro gum; X_2 = Concentration of PVP K30

For taro gum

$0.25 = X_1 - 50/25$

$X_1 = 25 * 0.25 + 50$

$X_1 = 56.25$

For PVP K30

$0.25 = X_2 - 25/12.5$

$X_2 = 12.5 * 0.25 + 25$

$X_2 = 28.125$

Variables in extra design check point

Taro gum (X_1) = 56.25 mg

PVP K30 (X_2) = 28.125 mg

Validation of extra design check point formulation by Student's *t*-test

Having designed using appropriate statistical calculations, the polynomial equation was used to predict the response that would fulfill the aim of the present study. By calculating actual polymer concentration from transformed proportions of each variable, the extra design checkpoint formulation was designed. Predicted to exhibit t_{90} value of 10.97, the extra design checkpoint batch was observed to have t_{90} value of the 10.82, 10.87, and 10.86 h in the three trials respectively [Table 11]. The statistical insignificance of the observed t_{90} was evaluated with the predicted value using Student's *t*-test in Microsoft Excel [Table 12].

The Student *t*-test *P* value should be <0.05; in our study it was found to be 0.0079 with 95% confidence. This statistical insignificance of the difference between the predicted and observed responses not only validate the design adopted for optimization, but also confirmed the usefulness of a polynomial equation in predicting the *in vitro* kinetic parameters.

Application of *f*2 similarity factor

For the purpose of selecting the optimized formulation *f*2 similarity factor was used. The batch having maximum *f*2 value when compared with the *in vitro* drug release data of the extra design check point batch can be considered as the optimized batch. The cumulative percent drug release of all 9 formulations were compared with the mean value of cumulative percent drug release of three trial of the extra design check point formulation at four different time points, namely drug release at the end of 1 h, 2 h, 4 h and 8 h and the *f*2 similarity factor was calculated using the following formula:

Table 11: Time taken to release 90% of drug for check point formulations ($T_{90\%}$)

Formulation code	$T_{90\%}$ (h)
CP1	10.82
CP2	10.87
CP3	10.86

CP: ???

Table 12: Student *t* test

Formulation	Predicted	Experimental
Trial 1	10.97	10.82
Trial 2	10.97	10.87
Trial 3	10.97	10.86
t test; *P* value		0.0079101

Table 13: *F*2 similarity factor for all formulation batches

Formulation	*f*2 value
B1	39.39
B2	43.74
B3	41.18
B4	46.94
B5	51.25
B6	86.33
B7	72.99
B8	65.67
B9	49.93

$$f2 = 50 \times \log\left\{\left[1 + (1/n)\, S_{t=1}^{n} (R_t - T_t)^2\right]^{-0.5} \times 100\right\}$$

The *f*2 similarity factor for all the formulations is shown in Table 13. It is clear from the table that formulation B1, B2, B3, B4 and B9 are having $f2 < 50$ indicating dissimilar drug release pattern compared to the extra design check point batch. While the formulations B5, B6, B7 and B8 are having $f2 > 50$, indicating similarity between two dissolution profiles.

CONCLUSION

Out of all of them formulation F6 was having maximum $f2 = 86.33$. Furthermore, formulation B6 was having t_{90} of 10.70, which is the closest among all the formulations to the t_{90} of the extra design checkpoint batch. Based on these results we can say that formulation B6 was found to be the optimized formulation.

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