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FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLET OF BISOPROLOL FUMARATE

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Keywords:

Orally disintegrating tablets, Bisoprolol fumarate, Croscarmellose sodium, Direct compression, 3^2 Full factorial design

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ABSTRACT: The main objective of this research work was to formulate and evaluate an Orodispersible tablet of Bisoprolol Fumarate for the treatment of hypertension and coronary artery disease. Formulation was designed using systat software version 13.2. 3^2 full factorial design was applied, in which two variables were varied at three levels. The tablets of Bisoprolol Fumarate were developed by direct compression method. The prepared tablets were evaluated for thickness, hardness, friability, weight variation, wetting time, content uniformity, disintegration time and *in-vitro* dissolution. FTIR studies indicated that drug and excipients were compatible. Pre-compression and post-compression parameters were satisfactorily within acceptable limits. The results indicated that concentration of croscarmellose sodium and diluents ratio significantly affected on disintegration and *in-vitro* dissolution study. Formulation SF9 showed shortest disintegration time (7.3 sec.), shortest wetting time (13.4 sec) and better drug release (99.8%) compared to other formulations. Hence it was selected as optimized formulation. The 3D response surface plots indicated that an increase in the concentration of croscarmellose sodium and an increase in the diluent ratio decreased in the *in-vitro* disintegration time and increased the percentage drug release. Kinetic study revealed that drug release from all formulations followed first-order kinetics. It was concluded that oral dispersible tablets of antihypertensive drug can be successfully formulated and used as a novel drug dosage form for pediatrics and geriatrics with improved patient compliance.

INTRODUCTION: For the past decade, there has been an enhanced demand for more patient-friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing annually.

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Since, the development cost of a new drug molecule is very high, pharmaceutical companies are now making efforts to focus on developing new drug dosage forms for existing drugs with improved safety and efficacy together with reduced dosing frequency and the production of more cost-effective dosage forms.

The oral route still represents the preferred way of administration, owing to its several advantages and high patient compliance compared to many other routes [1]. Tablets and hard gelatin capsules constitute a major portion of drug delivery systems

that are currently available. However, many patient groups such as the elderly, children and patients who are mentally disabled, uncooperative, nauseated, or on reduced liquid-intake/diets have difficulties swallowing these dosage forms. Those who are traveling or have little access to water are similarly affected. To fulfill these medical needs, pharmaceutical scientists have developed a novel oral dosage form known as Orally Disintegrating Tablets (ODTs), which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take water. Drug dissolution and absorption as well as the onset of clinical effect and drug bioavailability may be significantly greater than those observed from conventional dosage forms. Recent market studies indicate that more than half of the patient population prefers ODTs to other dosage forms and most consumers would ask their doctors for ODTs (70%), purchase ODTs (70%), or prefer ODTs to regular tablets or liquids (>80%) [2].

The US Food and Drug Administration defined ODT as "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue [1]. Hypertension is a medical condition in which blood pressure is chronically elevated, If not effectively treated, it may lead to stroke, myocardial infarction, and heart failure and is a leading cause of chronic kidney failure [3].

Beta-blockers play a crucial role in the management of patients with essential hypertension [4]. Bisoprolol is one of the cardio selective beta-blockers used to treat hypertension, arrhythmias, coronary heart disease, and angina [5]. Studies have shown that bisoprolol fumarate is more effective in controlling high blood pressure when compared to propranolol, atenolol and metoprolol [6].

Bisoprolol fumarate chemically 1-[4-(2-isopropoxyethoxymethyl) phenoxy] - N-isopropyl – 3 – aminopropan – 2 - ol fumarate [7]. It appears as white crystal, very soluble in water and freely soluble in alcohol, its mp about 100°C [3]. It belongs to BCS class I, and its long half-life of 12 hours make it suitable for designing orally disintegrating tablet. The objective of the present work is to prepare bisoprolol tablets having faster disintegration time, faster dissolution rate, quick on set of action which is beneficial in hypertension and is very convenient for administration without the problem of swallowing and using water.

MATERIALS AND METHODS:

Materials: Bisoprolol fumarate was obtained as a gift sample from UniChem laboratories, Goa. Croscarmellose sodium was purchased from Bangalore Fine Chemicals, Bangalore. Prosolv, mannitol, vanilla, sodium saccharin, magnesium stearate, and talc were procured from S.D. FineChem. Ltd. Mumbai.

Methods:

Preformulation Studies:

Determination of Melting Point of Bisoprolol Fumarate by DSC: The melting point of Bisoprolol fumarate was determined by DSC. The DSC is performed to check the drug's thermal behavior and its melting point. DSC scans of the sample were recorded by using DSC Shimadzu-60. The sample was hermetically sealed in aluminum pans and heated at a constant rate of 10°C/min under dry nitrogen flow (10ml/min) between 50 to 200 °C [8].

Drug Excipient Compatibility Studies: The Infrared spectra of pure drug Bisoprolol fumarate physical mixture of drug and excipients were characterized by FTIR. The scanning range was 4000-400cm^{-1}. The IR spectra were obtained by using KBr pellet method [9].

Formulation of Bisoprolol Fumarate or Dispersible Tablet: Trail batch formulation was developed using three different super disintegrating agents, namely Crospovidone, Sodium Starch Glycolate, Croscarmellose Sodium. Based on the results of the trail batch, croscarmellose sodium was selected as super disintegrating agent, and the formulation was designed by using systat software version 13.2 by considering 2 factors and 3 levels. The concentration of Croscarmellose sodium (X1), and diluents ratio (Prosolv: Mannitol) (X2) were selected as independent variables, which were varied at 3 levels (low, medium, high). Friability (Y1), disintegration time (Y2), and *in-vitro* dissolution (Y3) were selected as dependent variables and are shown in **Table 1.** The tablets were prepared by direct compression technique. The composition for each formulation of ODTs of Bisoprololfumarate was shown in **Table 2.**

All the ingredients were sieved through mesh no. 60 separately. Then the ingredients were weighed accurately and mixed by geometrical mixing. Finally, the powder blend was lubricated with magnesium stearate and compressed using 6.5 mm punch using rimek compression.

TABLE 1: CODED VALUES FOR FACTORS AND LEVELS

Coded Value	Factor -1(X_1) Super disintegrant (CCS in mg)	Factor -2(X_2) Diluents Ratio (Prosolv: Mannitol)
Low level (0)	4	1 : 3
Intermediate level (1)	6	2 : 2
High level (2)	8	3 : 1

TABLE 2: FORMULATION DESIGN OF ORODISPERSIBLE TABLET USINGSYSTAT SOFTWARE

Ingredients (mg/tab)	Formulation Code								
	SF1 (mg)	SF2 (mg)	SF3 (mg)	SF4 (mg)	SF5 (mg)	SF6 (mg)	SF7 (mg)	SF8 (mg)	SF9 (mg)
Bisoprolol Fumarate	5	5	5	5	5	5	5	5	5
CCS	4	4	4	6	6	6	8	8	8
Diluents Ratio Prosolv: Mannitol	1:3	2:2	3:1	1:3	2:2	3:1	1:3	2:2	3:1
Vanilla	1	1	1	1	1	1	1	1	1
Sod. saccharine	2	2	2	2	2	2	2	2	2
Mg. stearate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Total weight(mg)	100	100	100	100	100	100	100	100	100

Evaluation Tests:

Precompression Parameters: The powder blend of the formulation was subjected to evaluation for bulk density, tapped density, carr'sindex, hausner's ratio, and angle of repose to determine the characteristics of the powder blend.

Post Compression Parameters:

Thickness: The thickness of the tablet was measured by a vernier caliper, three measurements were taken from each batch. It was recorded in mm [10].

Hardness: Tablets' hardness is a vital parameter that prevents the breakage of the tablet during transportation, handling, and storage. The hardness of tablets was determined using the Monsanto hardness tester, and it was recorded in kg/cm^2 [11].

Weight Variation: In weight variation of tablet studies, twenty tablets from each batch were selected randomly and individually weighed, and the average weight and standard deviation of twenty tablets were calculated [12].

Friability: Friability was measured to find the strength of the tablet by Roche Friabilator. Ten undusted tablets were weighed and placed in a friability for 100 cycles, undusted, and weighed again. The percentage friability was then calculated using the following equation. A percentage of friability less than 1% is considered acceptable [13].

Percentage friability = Initial weight-Final weight / Initial weight ×100

Wetting Time and Water Absorption Ratio: This evaluation is done by placing a twice folded tissue paper in petridish (with an internal diameter of 5 cm) containing 6ml of water. A tablet was placed on top of this tissue paper in petri dish. Wetting time was noted as the time required for water to reach the tablet's upper surface and thoroughly wet it.

Water absorption ratio 'R' was determined by the following equation.

$$R=100 \times (Wa-Wb)/Wa$$

Where, Wb= Weight of tablets before water absorption. Wa= Weight of tablets after water absorption[14].

Drug Content: Randomly 20 tablets were taken, weighed and powdered. The powder equivalent to 100 mg of drug was weighed accurately and dissolved in 100ml of phosphate buffer 6.8. The solution was shaken thoroughly. The undissolved matter was removed by filtration through Whatman filter paper 41.

The dilutions were made and the absorbance of the diluted solutions was measured at 223nm. The concentration of the drug was computed from the standard curve of the Bisoprolol fumarate [15].

Disintegration Time: The tablet disintegration apparatus was used to determine the disintegration time of all the formulations. One tablet was placed in each of the six tubes having distilled water. The temperature was kept constant at 37± 2°C and the time taken for the entire tablet to disintegrate completely was recorded [16].

***In-vitro* Dissolution Studies:** *In-vitro* drug release performed using USP apparatus-II (paddle) using 900 ml of 6.8 pH phosphate buffer with paddle rotation of 50 rpm at 37± 0.5°C. 1ml of the sample was withdrawn at predetermined time intervals and replaced with the fresh medium of 6.8 pH phosphate buffer. The samples were filtered through Whatman filter paper, suitably diluted, and analyzed at 223 nm [1].

Release Kinetics: The kinetic model of drug release was elucidated by fitting the dissolutions of all ODTs into standard mathematical models of drug release [15].

RESULTS AND DISCUSSION:

Differential Scanning Calorimetry (DSC): The thermal behavior of the pure drug Bisoprolol fumarate was studied by DSC. The DSC curve is shown in **Fig. 1**. The pure drug Bisoprolol fumarate shows a sharp endothermic peak at 104 °C. The peak value matches with literature value; this confirms purity in the drug sample.

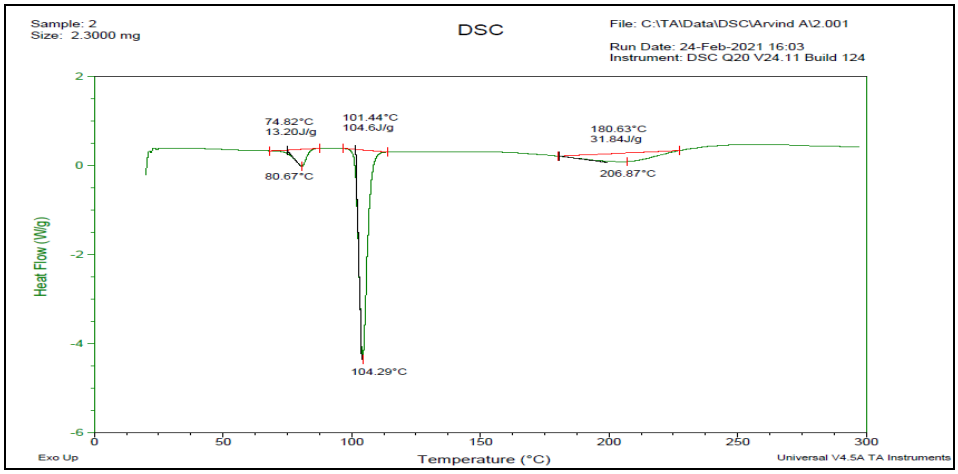

FIG. 1: DSC THERMOGRAM OF PURE DRUG

Compatibility Studies: Physical mixture of drug and excipient characterized by FTIR spectral analysis for physical as well as chemical alteration of drug characteristics. The results concluded that there was no interference in the functional groups, as the principal peaks of the model antihypertensive drug were found to be unaltered in the spectra of the drug excipient mixture**.** IR spectra of drug and mixture are illustrated in **Fig. 2A and 2B.**

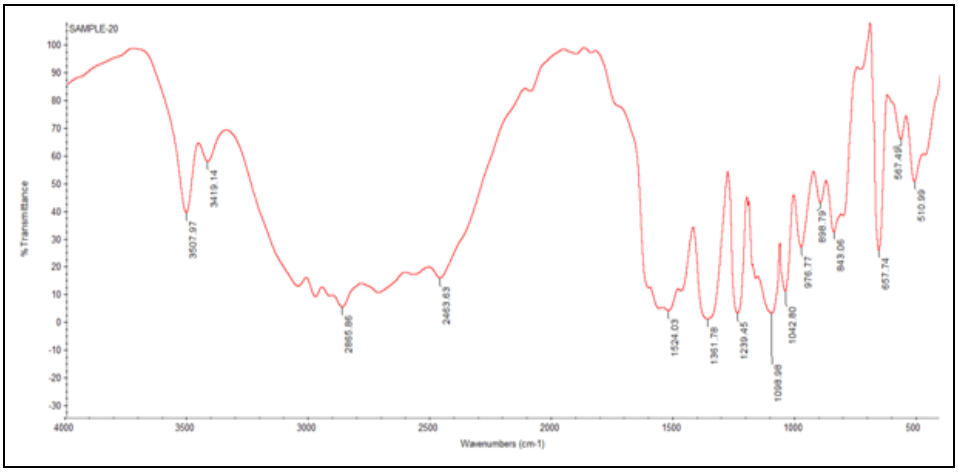

FIG. 2A: FTIR SPECTRA OF PURE DRUG

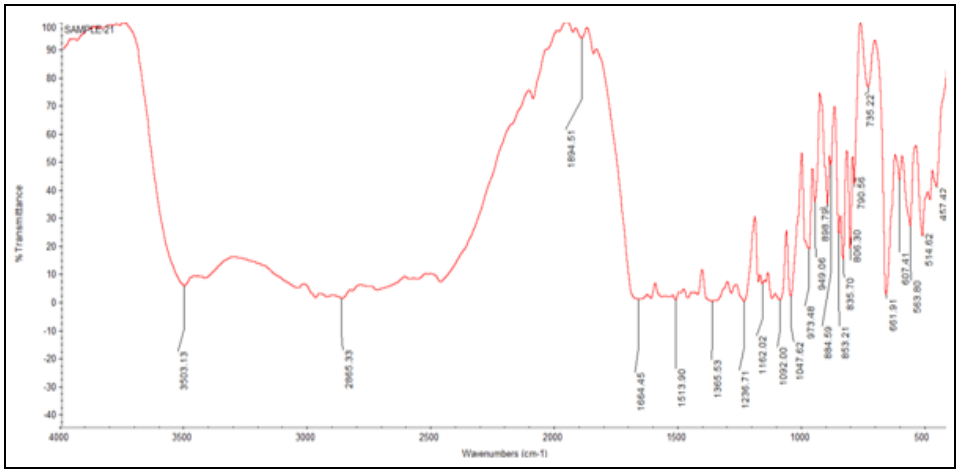

FIG. 2B: FTIR SPECTRA OF DRUG + EXCIPIENTS

Pre Compression Parameters: The angle of repose values was found to be 26.13° to 30.28° which indicates that all formulations exhibited passable to good flow properties. The bulk density of all the formulations varied from 0.18 to 0.19 gm/cc. Tapped density of the entire formulation blend varied from 0.230 to 0.239gm/cc. The results of carr's index of all the formulations were found to be varied from 17.4 to 20.5%, which indicates a good flow property. Hausner's ratio was found to be in the range of 1.20 to 1.26. The results of the pre-compression of the powder blend are represented in **Table 3.**

TABLE 3: RESULTS OF PRE-COMPRESSION PARAMETERS

Formulation Code	Angle of Repose (θ)	Bulk Density (g/cc)	Tap Density(g/cc)	Carr's Index (%)	Hausner's Ratio
SF1	30.28 ˚± 0.02	0.19 ± 0.01	0.239± 0.02	20.5	1.26
SF2	28.28 ˚± 0.04	0.19 ± 0.03	0.236± 0.03	19.4	1.243
SF3	26.56 ˚± 0.02	0.19 ± 0.01	0.234±0.012	18.8	1.234
SF4	29.92 ˚± 0.09	0.19 ± 0.02	0.239± 0.04	20.5	1.258
SF5	28.82 ˚± 0.05	0.19 ± 0.01	0.237± 0.02	19.8	1.25
SF6	26.13 ˚± 0.03	0.188 ± 0.05	0.231± 0.04	18.01	1.22
SF7	29.72 ˚± 0.02	0.19 ± 0.02	0.238±0.023	20.16	1.256
SF8	27.93 ˚± 0.08	0.19 ± 0.01	0.239±0.031	20.5	1.26
SF9	26.38 ˚± 0.1	0.19 ± 0.02	0.230±0.022	17.4	1.20

Values are expressed in mean ± S.D (n=3)

Post Compression Parameters:

Thickness: The thickness of all formulations was found to be 2.5± 0.2 mm.

Hardness: The hardness of all formulations was found to be 3.5± 0.1 kg/cm^2. The hardness of all batches was uniform and possessed good mechanical strength.

Weight Variation: All the tablets passed the weight variation test as the percentage weight variation was within the standard limit of ±5%. From the results was evident that all the tablets were found to be uniform. This is due to all the formulations' good flow properties and compressibility.

Friability: The Friability test for all the formulations was performed using Roche Friabilator. The percentage of friability of all formulations was found to be less than 1%. Therefore it indicates that all the tablets possess good mechanical strength. The results of post-compression parameters of all formulations are represented in **Table 4.**

TABLE 4: RESULTS OF POST COMPRESSION PARAMETERS

Formulation Code	Thickness(mm)	Hardness (kg/cm²)	Weight Variation (mg)	Friability (%)
SF1	2.5 ± 0.2	3.5 ± 0.15	100.4 ± 3.53	0.76
SF2	2.5 ± 0.21	3.5 ± 0.1	100.4 ± 2.53	0.77

SF3	2.5 ± 0.1	3.5 ± 0.1	100.5 ± 2.43	0.84
SF4	2.5 ± 0.11	3.5 ± 0.1	100.5 ± 2.43	0.76
SF5	2.5 ± 0.1	3.5 ± 0.1	100.6 ± 2.48	0.79
SF6	2.5 ± 0.21	3.5 ± 0.15	100.1 ± 2.33	0.85
SF7	2.5 ± 0.2	3.5 ± 0.1	100.5 ± 3.84	0.79
SF8	2.5 ± 0.1	3.5 ± 0.1	100.6 ± 2.48	0.8
SF9	2.5 ± 0.11	3.5 ± 0.15	100.1 ± 3.89	0.865

Values are expressed in mean ± S.D (n=3)

Wetting Time: This test mimics the action of saliva in contact with a tablet to illustrate the water uptake. The wetting time of all formulations was found to be in the range of 13.4 to 30 sec. The formulation SF9 (containing the highest quantity of CCS) showed the shortest wetting time of 13.4 sec, which may be attributed to the strong wicking action of CCS. Since, CCS has more sites for moisture uptake thus enhances the wicking ability of CCS.

Water Absorption Ratio: The water absorption ratio helps to understand the capacity of a disintegrant to swell in the presence of a little amount of water. The values of all formulations are ranged from 60 to 72.06%. Formulations SF9 showed the highest value of water absorption ratio 72.06%. It indicates that formulation SF9 has high water absorbing capacity. The wetting time and water absorption ratio of all formulations are represented in **Table 5.**

Drug Content: All the formulations were evaluated for drug content according to the procedure described in the methodology section, and the results are shown in **Table 5.** The assay values for all the formulations were found to be in the range of 98.8 to 100.2 %, indicating the uniformity in drug content. According to IP standards, the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the ODT formulations comply with the standards given in IP.

Disintegration Time: The disintegration time of all formulations was found to be in the range of 7.3 to 21.1 sec. The formulation SF9 contains the highest quantity of CCS (8mg) and diluent ratio prosolov: mannitol (3:1).CCS is an internally cross-linked polymer of carboxymethylcellulose sodium; it has a high swelling capacity. This may be due to the substitution of carboxymethyl in CCS increasing the swelling ability and thus faster disintegration. Croscarmellulose also shows wicking action due to their fibrous nature. So both swelling and wicking action is responsible for rapid disintegration[17].In addition, prosolv is chemically composed of silicified MCC, which acts as a diluent. It possesses the ability to improve the disintegration of the tablets since the quantity of the prosolv and CCS is more in SF9. Thus SF9 formulation showed the shortest disintegration time (7.3 sec) as compared to other formulations. The results of disintegration time for all formulations are represented in **Table 5.**

TABLE 5: RESULTS OF POST-COMPRESSION PARAMETERS

Formulation Code	Wetting Time (sec)	Water Absorption Ratio (%)	Drug content (%)	Disintegration Time (sec)
SF1	30 ± 1.2	60	98.9	21.1 ±0.2
SF2	28.2±0.23	65.5	99.3	14.5 ±0.5
SF3	20 ±0.6	70.5	100.1	10.6 ±0.1
SF4	29.3±0.21	60.7	98.8	17 ±0.62
SF5	22.2±0.34	66.6	99.7	11.1 ±0.7
SF6	15.4±0.54	71.4	99.3	9.2 ±0.3
SF7	26.1±0.36	61.5	100.08	12.1 ±0.9
SF8	17.7±0.23	67.2	99.1	9.9 ±0.4
SF9	13.4±0.11	72.06	100.2	7.3 ±0.12

***In-vitro* Dissolution Studies:** All the formulations are subjected to *in-vitro* dissolution studies using dissolution apparatus USP-II. The dissolution media used was pH 6.8 phosphate buffer. The dissolution profiles of all formulations showed more than 80% of drug release within 5 min. The % drug release of 81.52%, 87.3%, 95.1, 87.2, 93.3, 98.51, 91.0, 97.0, 99.8% was observed in

formulations SF1-SF9 respectively at 5 minutes. Among all formulations, SF9 has shown a maximum drug release 99.8% at 5 min. The results show that formulation SF9 contains the highest amount of CCS and diluent prosolv: mannitol (3:1). An increase in the concentration of superdisintegrant and diluent ratio increases the drug release. Drug release profiles of all formulations are illustrated in **Fig. 3.**

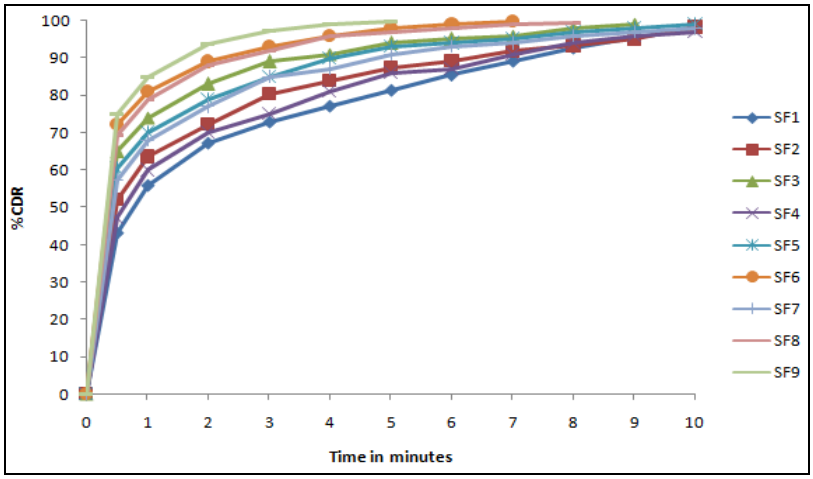

FIG. 3: *IN-VITRO* DRUG RELEASE PROFILE OF SF1 – SF9 FORMULATIONS

Release Kinetic Studies: The results of the release kinetics study showed that all formulations obeyed first-order drug release profile more closely, *i.e.* the release rate depended upon the initial concentration of the drug. The slopes (n) values of Korsmeyer Peppas plot showed that the mechanism was non-fickian. The results of the release kinetic study of all formulations are presented in **Table 6.**

TABLE 6: RELEASE KINETICS OF SF1-SF9 FORMULATIONS

Formulation code	Zero order R^2	First order R^2	Higuchi R^2	Korsmeyers-Peppas R^2	Korsmeyer-Peppasn value
SF1	0.392	0.961	0.769	0.288	0.628
SF2	0.512	0.990	0.775	0.214	0.661
SF3	0.452	0.921	0.698	0.311	0.652
SF4	0.465	0.973	0.721	0.293	0.634
SF5	0.399	0.890	0.758	0.267	0.732
SF6	0.425	0.936	0.772	0.253	0.713
SF7	0.490	0.981	0.739	0.199	0.671
SF8	0.531	0.974	0.717	0.274	0.683
SF9	0.485	0.984	0.770	0.296	0.736

Statistical Analysis: Statistical analysis is performed by regression analysis using Systat software 13.2. Nine batches were prepared. The concentration of Croscarmellose Sodium (X1) and diluents ratio (Prosolv: Mannitol) (X2) were selected as independent variables, which were varied at 3 levels. Three dependent variables (Response) were selected friability (Y1), disintegration time (Y2), and *in-vitro* dissolution (Y3), and a polynomial equation was derived for desired responses.

TABLE 7: RESULTS OF STATISTICAL ANALYSIS

Response	R^2 value	Factors	Tolerance	p-values	Significance
Friability	0.893	Factor 1	1.000	0.060	Non-significant
		Factor 2	1.000	0.001	Significant
Disintegration	0.915	Factor 1	1.000	0.003	Significant
		Factor 2	1.000	0.001	Significant
In-vitro dissolution at 5 min.	0.920	Factor 1	1.000	0.002	Significant
		Factor 2	1.000	0.001	Significant

Effect of Formulation Variables on Friability (Y_1): In regression coefficient analysis of friability, the p-value for factor 1 (Crosscarmellose sodium) was found to be 0.06, and for factor 2 (diluents ratio-Prosolv: Mannitol) was found to be 0.001, Here p-value for factor 1 is > than 0.05 thus no significant effect on friability and p-value for factor 2 is < than 0.05 thus significant effects on friability and the results of statistical analysis are tabulated in **Table 7.** The 3D response surface graph of Friability v/s Factor-1(X1), Factor-2(X2), as depicted in **Fig. 4A**, showed that as the diluents ratio increases, percentage friability increases, and no significant effect was observed with an increase in the concentration of croscarmellose sodium. The polynomial equation was generated by using the regression analysis was given below for response variable friability (Y_1)

Friability (Y_1) = $0.7485+0.014X_1+0.041X_2$

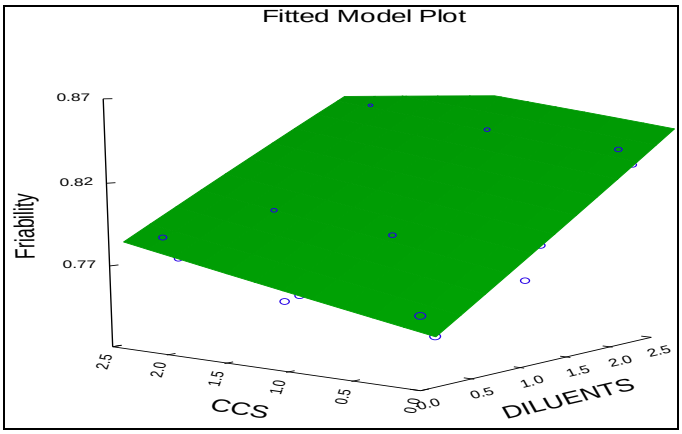

FIG. 4A: 3D RESPONSE SURFACE GRAPH OF FRIABILITY

Effect of Formulation Variables on Disintegration Time (Y_2): In regression coefficient analysis of disintegration time, the p-value for factor 1 (Croscarmellose Sodium) was found to be 0.003 and for factor 2 (diluents ratio-Prosolv: Mannitol) was found to be 0.001. the p-value for factors 1 and 2 is < 0.05; thus, both factors significantly affect disintegration time, and the statistical analysis results are tabulated in **Table 7.** In 3D response surface graph of disintegration v/s Factor-1(X_1), Factor-2(X_2), as depicted in **Fig. 4B.** Showed that as crossmellose sodium and diluents ratio increases, disintegration time decreases. Thus both factors were affected significantly. The polynomial equation was generated by using the regression analysis was given below for response variable disintegration time (Y_2)

Disintegration time (Y_2) = $12.133-2.717X_1-3.917X_2$

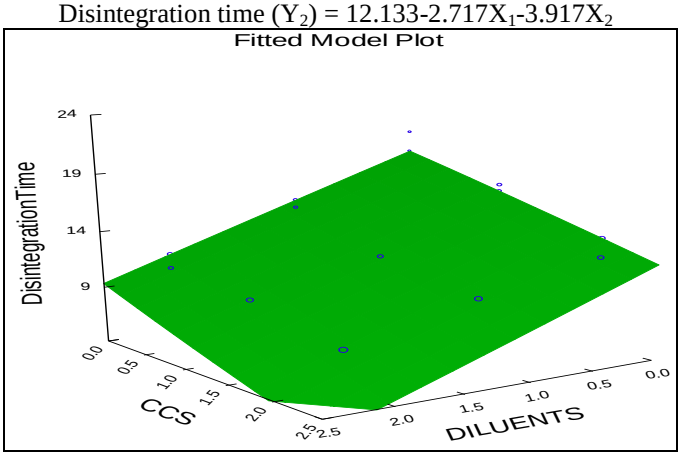

FIG. 4B: 3D RESPONSE SURFACE GRAPH OF DISINTEGRATION

Effect of Formulation Variables on *In-vitro* Dissolution Study (Y_3): In regression coefficient analysis of *in-vitro* drug release, the p–value for factor 1 (Crosscarmellose sodium) was found to be 0.002 and for factor 2 (diluents ratio-Prosolv: Mannitol) was found to be 0.001.p–value for factor 1 and factor 2 is <0.05 thus both factors effects significantly on *in-vitro* dissolution and the results of statistical analysis are tabulated in **Table 7.** In 3D response surface graph of *in-vitro* dissolution v/s Factor-1(X_1), Factor-2(X_2) as depicted in **Fig. 4C.** showed that as the concentration ofcrosscarmellose sodium and diluents ratio (prosolov: mannitol) increases, % CDR increases. Thus both factors were effected significantly. The polynomial equation was generated by using the regression analysis was given below for response *in-vitro* dissolution (Y_3)

In-vitro dissolution (Y_3) = $90.704+2.263X_1+2.758X_2$

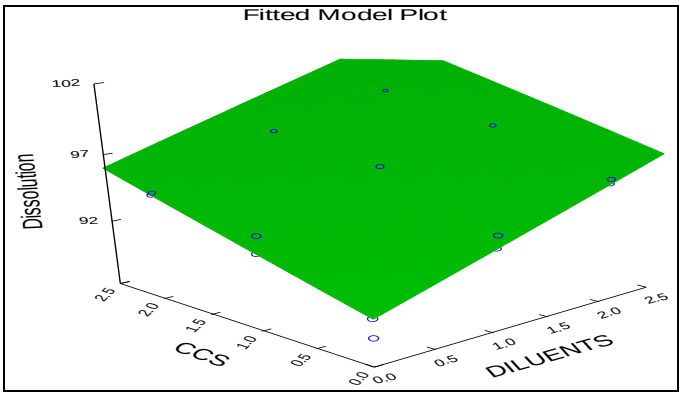

FIG. 4C: 3D RESPONSE SURFACE GRAPH OF DISSOLUTION

CONCLUSION: The orodispersible tablets of Bisoprolol fumarate were prepared by direct compression method. Among all formulations, SF9 showed less disintegration time and the highest percentage of drug release at 5 min; hence it can be chosen as an optimized formulation. 3^2 factorial design revealed that amount of superdisintegrant and diluent ratio affect the disintegration time and % drug release.

The results indicate that the presence of crosscarmellulose and diluent ratio enhanced the or dispersion and improved the drug release rate. Thus a satisfactory orodispersible tablet of bisoprololfumarate for large-scale production is feasible.

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CONFLICTS OF INTEREST: Authors declare no conflict of interest.

REFERENCES:

1. Kadam SV, Rane NU and Magdum CS: Formulation and evaluation of orodispersible tablets of levamisole hydrochloride. Asian J Pharm Tech 2019; 9(2): 63-68.
2. Gholve S, Kaware A, Thonte S, Kaudewar D and Bhusnure O: Orodispersible tablets: a systematic review. World J Pharm Res 2018; 7(6): 152-165.
3. Heba AF and Alaa AR: Effect of different and binder types on the preparation of bisoprololfumarate as tablet dosage form. Iraqi J Pharm Sci 2013; 22(1): 32-39
4. Masum M, Ripon MA, Bhowmik DR and Amin MT: Formulation development and evaluation of bisoprolol sustained release tablets. J Sci Res 2021; 13(1): 209-219.
5. Padamwar PA and Phasate PP: Formulation and evaluation of fast dissolving oral film of bisoprolol fumarate. Int J Pharm Sci Res 2015; 6(1): 135-142.
6. Panati D, Varlakshmi C, Prakash Reddy PK and Pamula Reddy B: *In-vitro* and *in-vivo* studies of oral thin film containing bisoprolol fumarate. Asian J Chem 2011; 23(9): 4148-4150.
7. Malakar J, Nayak A and Goswami S: Use of response surface methodology in the formulation and optimization of bisoprolol fumarate matrix tablets for sustained drug release. ISRN Pharmaceutics 2012; 1-10.
8. Sharannavar B and Khedekar S: A comparative solubility enhancement and dissolution study of ranolzine using different techniques. Int J Pharm Sci Res 2021; 12(5): 2692-2699
9. Panda S, Nodagala H, Panchagunala US and Baratam SR: Formulation and evaluation of orodispersible tablets of diclofenac sodium by using superdisintegrant from natural origin. Int J App Pharm 2019; 11(6): 190-197.
10. Jawed R and Wajid A: Formulation and evaluation of orodispersible tablet of cefiximetrihydrate by using fenugreek mucilage as a superdisintegrant. Research Journal of Pharmaceutical Dosage Forms and Technology 2022; 14(1): 23-28.
11. Baghel P, Roy A, Chandrakar S, Bahadur S and Bhairam M: Formulation optimization and evaluation of quick dispersible tablets of sumatriptan. J Appl Pharm Res 2019; 7(3): 9-16.
12. Kaur M, Mittal A, Gulati M, Sharma D and kumar R: Formulation and *in-vitro* evaluation of fast dissolving tablets of febuxostat using co-processed excipients. Recent Pat. Drug Deliv Formul 2020; 14: 48-62.
13. Kanathe P, Jain R, Jain N and Jain S: Formulation and evaluation of orodispersible tablet of fluvastatin sodium. J Drug Deliv Ther 2021; 11(1): 42-47.
14. Dawadi S, Pandey B, Nepal S and Gurau Y: Formulation and evaluation of orally disintegrating tablet of metoclopramide hydrochloride. World J Curr Med Pharm Res 2020; 2(6): 322-329.
15. Sivadasan D, Sultan MH, Madkhali O, Javed S and Jabeen A: Formulation and in vitro evaluation of orodispersible tablets of fexofenadine hydrochloride. Trop J Pharm Res 2020; 19(5): 919-925.
16. Rao YS, Kamala Kumari PV: Formulation and evaluation of orodispersible tablets of donepezil hydrochloride. Int J Curr Pharm Res 2020; 12(4): 45-51.
17. Kumar A and Saharan VA: A comparative study of different proportions of superdisintegrants: Formulation and evaluation of orally disintegrating tablets of salbutamol sulphate. Turk J Pharm Sci 2017; 14(1): 40-48.

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