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ORIGINAL ARTICLE

Novel Fast Disintegrating Tablet of Bisoprolol Fumarate with Its Development and Characterization for Patient Compliances

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ABSTRACT
The study aimed to develop and optimize a fast-disintegrating tablet (FDT) of Bisoprolol Fumarate to enhance patient compliance, particularly for populations with swallowing difficulties, and to ensure rapid therapeutic onset in the management of hypertension. The production of FDTs followed direct compression methods along with a 3^2 full factorial design to optimize Kyron T-314 and sodium starch glycolate concentrations. The evaluation process included tests of disintegration time and in-vitro drug release measurements and wetting time assessments together with mechanical property evaluations. FTIR and DSC assessed drug-excipient compatibility while modeling the drug release kinetics helped identify drug release mechanisms. Results: The optimized batch (VF6) demonstrated a disintegration time of 28.1 sec, in-vitro drug release of 96.94%, and a wetting time of 25 sec, with minimal deviation from predicted values (relative errors < 0.73%). DSC and FTIR studies confirmed compatibility. The release followed the Korsmeyer–Peppas model (R^2 = 0.9844), indicating anomalous transport. MTT assay showed concentration-dependent cytotoxicity with an IC_{50} of 142.20 µg/mL for Bisoprolol. The formulation exhibited excellent mechanical strength, uniformity, and rapid drug release across batches. The optimized Bisoprolol Fumarate FDT offers a clinically promising dosage form with rapid onset, ease of administration, and strong formulation stability. Its favorable pharmacotechnical and safety profile supports further in-vivo studies for potential clinical translation in hypertensive therapy.
KEYWORDS: Bisoprolol Fumarate, fast disintegrating tablet, factorial design, disintegration time, Korsmeyer–Peppas model, MTT assay.

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INTRODUCTION

The global healthcare system lists hypertension as a major problem that causes substantial losses among cardiovascular patients because of illness-related death [1]. The World Health Organization reports that hypertension affects over 1.28 billion adults between 30 and 79 years of age while proper treatment is available for less than half of them [2,3]. Bisoprolol Fumarate serves as a popular type of β1-adrenoceptor blocker which medical professionals use to treat hypertension and angina in addition to heart failure [4]. Ordinary oral dosage forms face issues in elderly and pediatric patients regarding swallowing difficulties and slow medication onset and reduced medication compliance when patients take multiple drugs [5]. The failure to follow prescribed antihypertensive medication creates higher risks for myocardial infarction and stroke that results in increased healthcare costs and disease burden [6]. The United States spends over $100 billion per year due to treating complications which could have been avoided by improved drug adherence rates [7]. New drug delivery strategies focus on patient-centered systems to address existing challenges through more convenient methods and therapeutic results. The ongoing need exists to develop rapidly acting user-friendly formulations which will enhance patient adherence as well as clinical effectiveness [8].

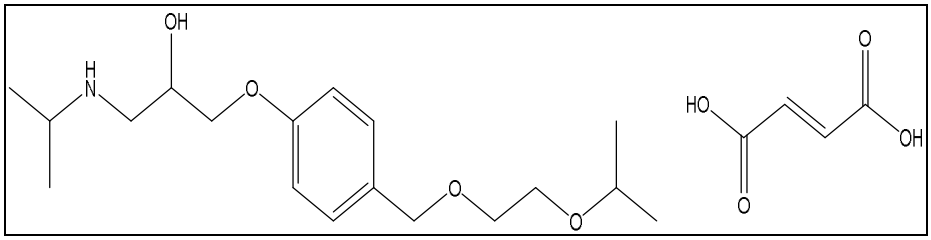

Figure 1: Chemical structure of Bisoprolol Fumarate

The β1-adrenergic receptor blocking agent Bisoprolol Fumarate functions as a cardioselective β1-blocker and offers desirable pharmacokinetic advantages through its long half-life spanning 10 to 12 hours which enables daily administration [9]. Bisoprolol Fumarate competes with β1-adrenergic receptors to decrease heart rate as well as cardiac output and systemic blood pressure. The chemical name for this drug is Bisoprolol Fumarate (±)-1-[4-[[2-(1-Methylethoxy)ethoxy]methyl]phenoxy]-3-[(1-methylethyl)amino]-2-propanol fumarate [10]. It displays moderate lipophilicity in addition to excellent oral bioavailability of approximately 90%. The medical literature has proven that Bisoprolol is effective for essential hypertension and chronic heart failure management while providing better tolerability than traditional beta blockers. The conventional tablet formulation of Bisoprolol Fumarate restricts rapid start of therapy thus it might be suboptimal for specific medical situations demanding quick therapeutic responses [11]. The development of orally disintegrating tablets (ODTs) for similar β-blockers has yielded promising findings regarding faster onset time and improved bioavailability levels. Bisoprolol Fumarate treatment within a fast disintegrating tablet system provides an opportunity to address current dosage restrictions while preserving its therapeutic potency [12].

Fast disintegrating tablets (FDTs) present an advanced method for oral drug delivery because they quickly dissolve or break down in the mouth without requiring water to administer medicines to older patients and children [13]. This format helps patients stay consistent with their medication regimen because of its ease of use and fast dissolving properties particularly helpful for people who have swallowing difficulties or need immediate symptom care [14]. The disintegration process of tablets happens quickly because super disintegrants along with porous matrix structures allow saliva to easily penetrate the formulation for immediate drug release [15]. People prefer FDTs over regular tablets because these drugs start working rapidly while offering better absorption rates and easier tolerance. Several technological advancements in excipient selection direct compression and lyophilization provide pharmaceutical scientists with tools to produce robust FDTs having superior mechanical strength and quick disintegration dynamics. Current research proves the successful implementation of FDT technology to improve therapeutic outcomes for cardiovascular medications including Atenolol and Metoprolol. An FDT system that includes Bisoprolol Fumarate matches contemporary pharmaceutical developments and successfully meets clinical requirements and patient-centered demands [16].

This study aims to develop a novel fast disintegrating Bisoprolol Fumarate tablet which will improve both therapeutic outcomes and patient medicine adherence. The study proposes three primary goals: development through direct compression methods and evaluation of compression stage measurements as well as dissolution rate analysis and drug release pattern assessment. The research examines different methods to improve both mechanical operation and drug release properties of the system.

MATERIAL AND METHODS

MATERIALS

Bisoprolol Fumarate (Ph. Eur. grade, 99.8% w/w, CAS No. 104344-23-2) was obtained from Mangalam Drugs and Organics Ltd. (Valsad, India). Kyron T-314, sodium starch glycolate, microcrystalline cellulose (Avicel PH-102), mannitol, aspartame, magnesium stearate, and talc (all pharmaceutical or analytical grade) were sourced from reputed suppliers including Corel Pharma Chem, HiMedia, Loba Chemie, SRL, Research-Lab Fine Chem, and SD Fine-Chem (India). Potassium bromide (FTIR grade) was from Merck Specialties, and methanol and ethanol (HPLC grade) were procured from Rankem Chemicals (Gurgaon, India). All other reagents used were of analytical grade.

METHODS

Calibration curve determination

A bisoprolol fumarate calibration curve developed in methanol as solvent was used. 10 mg accurately weighed drug were dissolved in 10 mL methanol to prepare a standard stock solution of (1000 µg/mL). The stock was diluted appropriately with methanol in order to get working standard solutions of 2, 4, 6, 8, 10 and 12 µg/mL. Absorbance of each solution was measured at 223 nm as predetermined with a Jasco

V630 UV Visible spectrophotometer (Jasco Inc. Tokyo, Japan) using 1 cm quartz cuvettes. Triplicate analysis was performed for all concentration (n = 3). The absorption versus concentration was plotted and the regression equation of the curve (Y = mX + C) was determined and the correlation coefficient (r^2) between spectral values and quantity [17,18].

Solubility study

The solvent saturation method was used to determine Bisoprolol Fumarate solubility in different solvents. 10 mL of each selected solvent included methanol, water, ethanol, chloroform, acetone, and ethyl acetate were added to each of the vials having a stopper glass and an excess amount of drug was added as well. After dispersion of mixtures, they were sonicated for 15 minutes, then shaken in a mechanical shaker (Remi Instruments, India) at 100 rpm for 24 hours to achieve equilibrium. Also, the undissolved drug was removed by each filtered solution from Whatman filter paper No. 1, after incubation. Appropriate dilutions of the clear filtrate in methanol were analyzed spectrophotometrically at 223 nm in a Jasco V-630 UV-Visible spectrophotometer (Jasco Inc, Tokyo, Japan). The dilution step was performed at standard calibration curve of mg/mL. The mean solubility values were recorded from all measurements carried out in triplicate (n = 3). The results from these studies were carried out according to standard pharmacopeial procedures for assessing the equilibrium solubility [19,20].

Differential scanning colorimetry

Thermal behavior and possible interactions between Bisoprolol Fumarate and excipients were assessed by DSC analysis. Pure drug and their physical mixture were accurately weighed into a standard aluminum pan and analyzed using a differential scanning calorimeter (DSC-60 Plus, Shimadzu, Japan). The samples were heated from 30°C to 300°C at 10°C/min under a dynamic nitrogen atmosphere with a flow rate of 50 mL/min. Reference was made of an empty aluminum pan. Onset temperature, peak shape, and enthalpy change of the physical mixture was examined relative to the pure drug through thermograms to determine potential for compatibility or interaction [21].

Fourier Transform Infrared Spectroscopy

A FTIR analysis was conducted to study any possible bond formation between Bisoprolol Fumarate and its excipients through the evaluation of characteristic functional groups present in both substances. The prepared samples consisted of pure drug, individual excipients and physical mixtures which received potassium bromide (KBr) treatment at 1:100 ratios before undergoing pelletization under hydraulic pressure to generate transparent pellets. The FTIR spectrophotometer (IRAffinity-1S, Shimadzu, Japan) measured samples with spectra between 4000–400 cm^{-1} through 32 scans while operating at 4 cm^{-1} resolution. The spectrums of physical mixture were evaluated to detect any shifts or disappearances or formations of new peaks for drug–excipient interactions [22,23].

Experimental design

A 3^2 full factorial design was used to systematically evaluate the formulation variable contribution to the performance characteristics of Bisoprolol Fumarate fast disintegrating tablets. The concentration of Kyron T-314 (Factor A) was taken as 3,4, 5 %w/w, and of sodium starch glycolate (SSG) (Factor B) was 2, 4, 6 % w/w. Disintegration time (R_1), in vitro drug release (R_2) and wetting time (R_3) were the dependent responses measured. Design matrix and statistical analysis of results obtained were generated and evaluated using Design Expert® software Version 13.0 (Stat-Ease Inc., Minneapolis, USA).

The relationship between the independent and dependent variables was modeled using the following second-order polynomial equation:

$$Y = b_0 + b_1A + b_2B + b_{12}AB + b_{11}A^2 + b_{22}B^2$$

Where: *Y* is the predicted response, b_0 is the intercept, b_1 and b_2 are the coefficients for the main effects of factors A and B, b_{12} is the coefficient for the interaction effect, b_{11} and b_{22} are the coefficients for the quadratic effects [24,25].

Table 1: Variables and their levels in 3^2 full factorial design

Variables	**Levels**		
Independent variables	**Low**	**Medium**	**High**
(A) = Kyron T-314 (%w/w)	2	3.5	5
(B) = Sodium starch glycolate (%w/w)	2	4	6
Dependent variables	**Goals**		
(R_1) = Disintegration time (Sec)	Minimize		
(R_2) = In-vitro drug release (%)	Maximize		
(R_3) = Wetting time (Sec)	Minimize		

Formulation of fast disintegrating tablets

Direct compression method was used to prepare Bisoprolol Fumarate fast disintegrating tablets. It is accurate to weighed out the amount of Bisoprolol Fumarate, Kyron T-314, and sodium starch glycolate

and passed through a #60 mesh sieve. Making homogenous blend with microcrystalline cellulose (MCC) and mannitol, these components were uniformly blended with MCC and mannitol inside a polybag for 10 minutes. The sweetening agent aspartame and also a suitable flavoring agent was incorporated into the mixture and then blended gentle for an extra 5 minutes. That said, magnesium stearate and talc, which had been pre-sieved through a #80 mesh, were then added as lubricants and mixed for 2–3 minutes with minimal shear to avoid over lubrication. The powder blend obtained was then compressed into tablets utilizing a single punch tablet compression machine (Cadm'ach, India) with 6 mm flat faced punches. Formulated tablets were collected and stored in air tight containers under controlled conditions until further evaluation. Table 2 presents detailed composition of all nine formulations (VF1–VF9) [26,27].

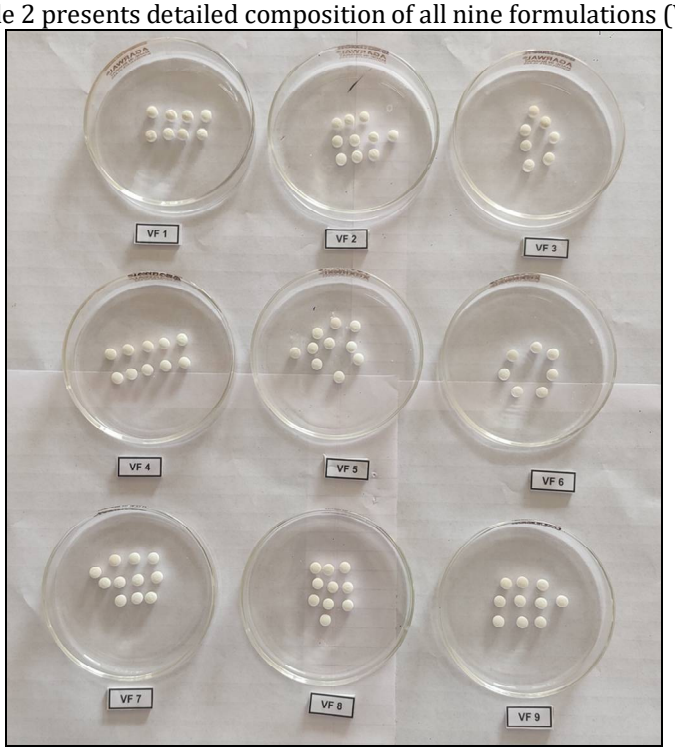

Figure 2: 9 Formulated batches of fast disintegrating tablets.

Table 2: Composition of various formulations (VF1–VF9) of bisoprolol fumarate fast disintegrating tablets

Ingredient	VF1	VF2	VF3	VF4	VF5	VF6	VF7	VF8	VF9
Bisoprolol Fumarate (mg)	10	10	10	10	10	10	10	10	10
Kyron T-314 (% w/w)	3	4	5	3	4	5	3	4	5
Sodium Starch Glycolate (% w/w)	2	2	2	4	4	4	6	6	6
Microcrystalline Cellulose (% w/w)	5	5	5	5	5	5	5	5	5
Magnesium Stearate (% w/w)	2	2	2	2	2	2	2	2	2
Aspartame (% w/w)	3	3	3	3	3	3	3	3	3
Mannitol (q.s to 100 mg)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Organoleptic properties

The tablets were evaluated for color, shape, texture, and odor by a panel of three trained observers under proper lighting. Visual inspection assessed uniformity and surface defects, while odor was checked for any undesirable smell indicating potential drug excipient interaction. Findings were compared with standard expectations [28].

Weight variation

Twenty tablets from each batch were chosen randomly to be weighted using Shimadzu BL-220H digital analytical balance (Japan) at a sensitivity of 0.1 mg. A calculation of average tablet weight was performed followed by percentage deviation assessments between individual weights and the mean. All results were assessed in comparison to the parameters of the Indian Pharmacopoeia (IP) [29].

Tablet thickness and diameter

The physical attributes of tablet diameter and thickness directly affect both uniformity and packaging performance and dose precision of pharmaceutical products. Ten randomly selected tablets were used to determine these dimensions from each batch. Tablets were measured with a digital Vernier caliper (Mitutoyo 500-196-30, Japan) which provided a precision of 0.01 mm. A measurement process of tablet

dimensions involved recording center-based diameter and thickness data for each tested pill through careful positioning. The measurements for tablet dimensions produced average calculations that included standard deviation (n = 10) for mean ± standard deviation. The evaluation process confirmed the tablets met their requirements for manufacturing scale by checking their dimensional uniformity and handling characteristics [30].

Mechanical strength evaluation of tablets

The mechanical strength analysis of tablets involved two tests: hardness testing and friability assessment. A Monsanto hardness tester evaluates ten randomly chosen tablets for their breaking force through force measurements in kg/cm^2. When using the Roche friabilator to measure friability they operated the device by turning tablets (approx. 6.5 g) at a speed of 25 rpm for 4 minutes. After dust removal from the tablets the instrument measured their weight change to determine weight loss percentages. The acceptable limit for the obtained friability value was set at 1% indicating tablets can withstand mechanical stress throughout handling and transport [31].

Drug content uniformity

A set of ten randomly selected tablets received individual powdering before the procedure. A precise measurement of one tablet-equivalent drug powder amount went into a 100 mL volumetric flask with methanol. A 15-minute sonication process occurred to extract all mixture components before filtering through Whatman filter paper No. 1. To determine the drug content in the filtrate scientists added suitable methanol followed by UV-Visible spectrophotometer analysis at 223 nm. Calibration curve was used to calculate the percentage of Bisoprolol Fumarate in each tablet and results were reported as mean ± standard deviation [32].

Wetting time and water absorption ratio

Water absorption ratio and wetting time was used to test fast disintegrating tablet hydration properties. The petri dish consisting of 6 mL of eosin solution (0.1% w/v) colored water was used to determine wetting time through a circular tissue paper placed at its center. The test required placing a tablet softly in the center of moistened paper after which the stopwatch recorded when dye solution soaked through the tablet completely. The tablet underwent two weight measurements: initial (W_1) followed by weighing after water uptake (W_2) during the wetting procedure. The water absorption ratio (R) calculation followed this equation:

$$R = \frac{W2 - W1}{W1} \times 100$$

Three tablets were tested per batch, and the results were reported as mean ± standard deviation. These tests provided an indication of the tablet's ability to absorb moisture and disintegrate rapidly upon administration [33,34].

Disintegration Time

A USP Type II disintegration test apparatus was used for evaluating disintegration time (Electrolab ED-2L, India). Six tablets were placed into individually the tubes of the basket rack assembly with each with a 10-mesh stainless steel screen at the bottom. In 900 mL of distilled water at 37 ± 2 °C and 30 cycles per minute, the assembly was operated in the immersed condition. The time for each tablet to completely disintegrate, leaving no more than fragments of insoluble excipients that can be palpated on the dissolved surface, was recorded. Disintegration time of all six tablets was recorded and results were presented in mean ± SD [35,36].

***In-vitro* drug release studies**

The in-vitro drug release testing of prepared Bisoprolol Fumarate fast disintegrating tablets was conducted with a USP Type II (paddle) dissolution apparatus (Electrolab TDT-08L from Mumbai, India). The testing utilized 900 mL phosphate buffer (pH 6.8) at 37 ± 0.5°C with a speed of 50 rpm as the dissolution medium. A single tablet from a batch was extracted from the dissolution vessel at predetermined times of 2, 4, 6, 8, 10, 12 and 15 minutes. Subsequently five milliliters of solution were withdrawn. An equal volume of fresh medium received pre-heating to 37°C prior to sample extraction for each withdrawal. The withdrawn volume returned back to the flask and fresh medium reached the sink condition after the withdrawal. The procured samples underwent melting and filtration through a 0.45 µm membrane before testing at 223 nm with a Shimadzu UV-1800 UV-Visible spectrophotometer (Japan). The release profiles for the formulations were calculated by adding their respective time-dependent drug release values. The experimental findings were presented as average values with standard deviation measurements whereas all measurements were carried out in triplicate (n = 3) continuously [37,38].

Drug release kinetics study

For the release data of the optimized Bisoprolol Fumarate fast disintegrating tablet in-vitro release data were fitted into Zero order, First order, Higuchi and Korsmeyer–Peppas model to find out the release

kinetics and mechanism. The zeros order, releases as a constant amount, first order releases as a function of concentration, Higuchi releases in a diffusion-controlled manner, and Korsmeyer–Peppas releases based on their release exponent (n). Microsoft Excel was used to calculate the correlation coefficient (R^2) for each model, and the best-fit model was chosen based on the highest correlation coefficient (R^2) [39].

Biocompatibility study using MTT assay

Cells derived from the human embryonic kidney (HEK-293) were grown in culture using Dulbecco's Modified Eagle Medium (DMEM) with non-essential amino acids (NEAA) added alongside 10% fetal bovine serum (FBS) at 37 °C under a 5% CO_2 humidified environment while the media was changed every 2 to 3 days. A total of one hundred thousand cells per well received incubation in ninety-six well plates over twenty-four hours. The test solution containing 9 concentrations of the test item was added to freshly prepared fresh medium to reach a half confluent cell suspension. After 48 hours of incubation different morphological changes appeared under an inverted microscope. The researchers exchanged media with fresh medium and MTT reagent at 100 µL and 10 µL per well followed by a 4-hour incubation period. The plates received 100 µL of solubilization solution which dissolved the formazan crystals while incubating for one hour. The microplate reader measured the absorbance readings at 570 nm wavelength. The calculation for percent cell viability followed the below mathematical formula:

$$Percentage\ viability = \frac{Absorbance\ of\ test}{Absorbance\ of\ control} \times 100$$

IC_{50} values were derived from log concentration vs. % cell survival plot [40,41].

Stability study

A stability test using optimized formulation tablets underwent accelerated temperature and humidity storage to determine how these conditions affected tablet properties. ICH guidelines directed testing methods to maintain the tablets within aluminium blister packs which were then kept for 3 months in ThermoLab's stability chamber operated at 40 ± 2 °C under 75 ± 5% RH conditions. The researchers used triplicate measurements to assess Physical appearance and drug content alongside disintegration time as well as in-vitro drug release from samples collected at 0, 30, 60, and 90 days. All tests resulted from these measurements were expressed as mean ± standard deviation to determine variations during the storage period [42].

Statistical analysis

The experimental data were analysed utilizing Design Expert® software and Graph Pad Prism® version 10.1.2. Statistical parameters of sequential p-values, adjusted R^2 and predicted R^2 were taken into account for the selection of a quadratic model. Disintegration time, in vitro drug release and wetting time were evaluated with regard to the significance of the formulation variables using ANOVA. For the drug release kinetics regression and modeling, GraphPad Prism was used. Using Design Expert®, contour and 3D surface plots were used to illustrate the variable interactions. Once optimized, the new formulation provided minimal relative errors during model validation, indicating an adequate and predictive accuracy in predicting the system behavior [43,44].

RESULTS

RESULTS

Calibration curve determination

Figure 3 demonstrates the calibration curve of Bisoprolol Fumarate in methanol and displayed excellent linearity over the concentration range of 2 to 12 µg/mL. The spectrophotometric method was used to obtain the regression equation Y = 0.0566X + 0.0007 with r^2 = 0.9998, which indicates a good accuracy and reliability and can be used for further quantitative evaluations.

Solubility study determination

Solubility study results of Bisoprolol Fumarate in water (1032.6 ± 6.2 mg/mL), methanol (1048.4 ± 5.7 mg/mL) and ethanol (1038.1 ± 4.8 mg/mL), were presented in Table 3, showing high solubility in water and methanol, and freely soluble to Chloroform, Glacial Acetic acid and Ethanol. The tablet formulation presented low solubility in acetone and ethyl acetate in accordance to its hydrophilic nature and its suitability for dispersed into fast disintegrating tablet formulations.

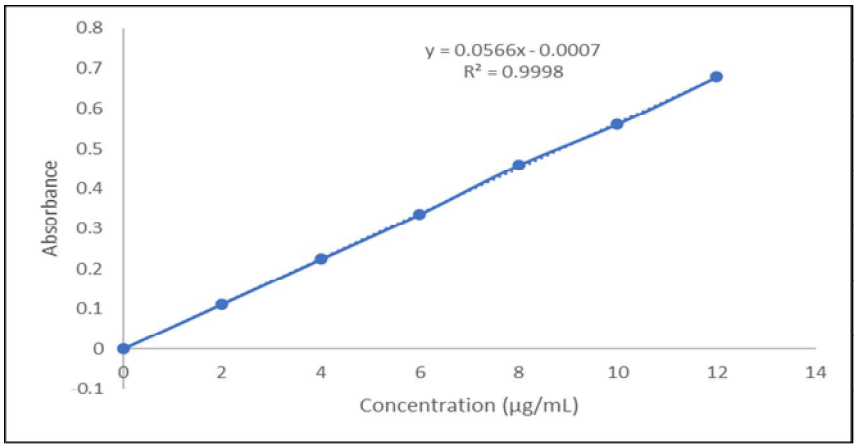

Figure 3: Calibration curve of Bisoprolol Fumarate in methanol.

Table 3: Solubility profile of bisoprolol fumarate in various solvents.

Sr. No.	Solvent	Solubility (mg/mL)	Inference
1	Water	1032.6 ± 6.2	Very soluble
2	Methanol	1048.4 ± 5.7	Very soluble
3	Chloroform	428.7 ± 4.3	Freely soluble
4	Glacial acetic acid	335.2 ± 3.8	Freely soluble
5	Ethanol	265.4 ± 3.1	Freely soluble
6	Acetone	6.7 ± 0.5	Slightly soluble
7	Ethyl acetate	4.3 ± 0.4	Slightly soluble

All values are expressed as mean ± standard deviation (n = 3).

Differential scanning colorimetry

DSC thermograms of pure Bisoprolol Fumarate are shown on Figure 4, in which a sharp endothermic peak was found at 103.67 °C, corresponding to the melting point which indicated pure Bisoprolol Fumarate was crystalline. The drug peak was slightly shifted to 105.63 °C in the physical mixture with excipients and an additional peak at 166.12 °C, which is an attribute to excipients. No strong interaction or incompatibility of Bisoprolol Fumarate and the selected excipients is indicated by the absence of any significant shift, broadening and disappearance of the main drug peak, indicating thermal compatibility for direct compression formulation.

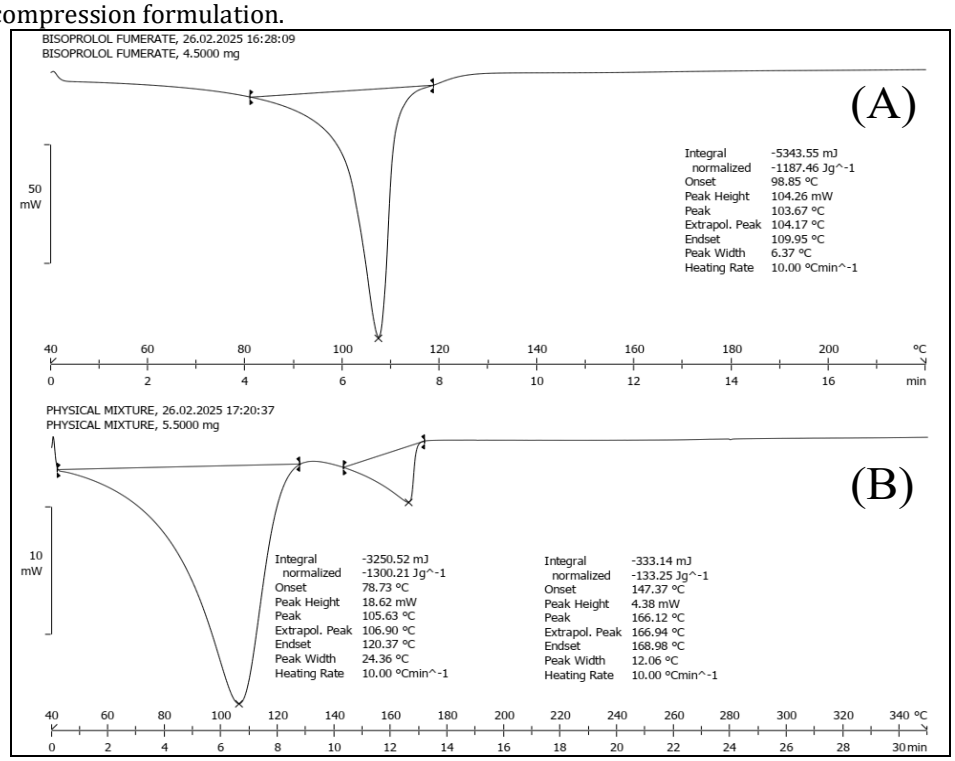

Figure 4: Differential scanning calorimetry (DSC) thermograms of (A) pure bisoprolol fumarate (103.67 °c) and (B) bisoprolol fumarate with excipients (105.63 °c and 166.12 °c).

Fourier transform infrared spectroscopy

FTIR spectra in Figure 5 showed the presence of characteristic functional groups of Bisoprolol Fumarate with the O–H stretching peak at 3580.63 cm^{-1}, C–H stretching at 2922.37 cm^{-1} and C–N stretching at 1065.73 cm^{-1}. As shown in Table 4, in the physical mixture with excipients, these key peaks were retained without shifts or disappearance. This proves that there is no chemical interaction and all selected excipients can be used for the formulation.

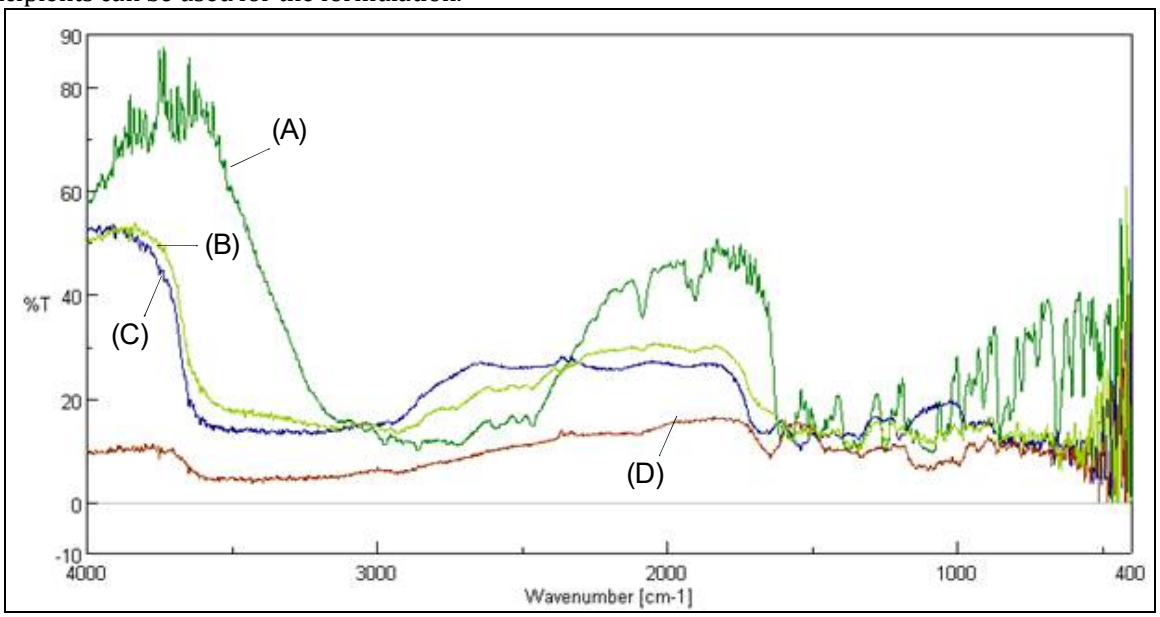

Figure 5: FTIR spectra of (A) pure bisoprolol fumarate, (B) kyron t-314, (C) sodium starch glycolate, and (D) their physical mixture.

Table 4: FTIR spectral interpretation of bisoprolol fumarate, individual excipients, and their physical mixture

Functional Group	Standard Wavelength (cm^{-1})	Observed in Pure Drug (cm^{-1})	Kyron T-314 (cm^{-1})	SSG (cm^{-1})	Physical Mixture (cm^{-1})
O–H Stretch (alcohol/acid)	3200–3600	3580.63	–	–	Broad (3100–3500) (weak)
C–H Stretch (aliphatic)	2850–2950	2922.37	–	–	–
C=O Stretch (carboxylic)	1650–1750	–	1672.95	1642.09	1564.95
Aromatic C=C Stretch	~1600	1611.23	1543.74	–	1564.95
C–O–C Stretch (ether/ester)	1200–1300	1250.61	1385.64	1328.71	1244.66
C–N Stretch (amine)	1020–1250	1065.73	–	–	1352.86
C–O Stretch (starch/polymer)	1000–1100	–	–	996.946	–
Fingerprint Region	600–900	–	–	–	849.49, 647.00, 445.47

Characterization of formulation

Organoleptic evaluation

All of the nine batches of Bisoprolol Fumarate fast disintegrating tablets were uniformly white, flat faced, round, with a smooth surface texture and with no cracks or chipping as seen in Table 5. The results are consistent and acceptable in terms of appearance and no undesirable odour was detected showing that there was no interaction nor degradation during formulation. The fact that these turned out to be satisfactory in terms of aesthetic and sensor qualities for patient compliance confirms the premises.

Table 5: Organoleptic Properties of Bisoprolol Fumarate Fast Disintegrating Tablets

Batch Code	Color	Shape	Surface Texture	Appearance	Odor
VF1	White	Flat-faced, round, uniform	Smooth, no cracks or chipping	Acceptable, consistent	Odorless
VF2	White	Flat-faced, round, uniform	Smooth, no cracks or chipping	Acceptable, consistent	Odorless
VF3	White	Flat-faced, round, uniform	Smooth, no cracks or chipping	Acceptable, consistent	Odorless
VF4	White	Flat-faced, round, uniform	Smooth, no cracks or chipping	Acceptable, consistent	Odorless
VF5	White	Flat-faced, round, uniform	Smooth, no cracks or chipping	Acceptable, consistent	Odorless
VF6	White	Flat-faced, round, uniform	Smooth, no cracks or chipping	Acceptable, consistent	Odorless
VF7	White	Flat-faced, round, uniform	Smooth, no cracks or chipping	Acceptable, consistent	Odorless
VF8	White	Flat-faced, round, uniform	Smooth, no cracks or chipping	Acceptable, consistent	Odorless
VF9	White	Flat-faced, round, uniform	Smooth, no cracks or chipping	Acceptable, consistent	Odorless

Results of weight variation, thickness, and diameter of bisoprolol fumarate FDT's

Table 6 shows that all nine batches of the Bisoprolol Fumarate fast disintegrating tablets were within the limits of weight variation, thickness, diameter according to pharmacopeia standards. The tablet weight ranged 99.7 ± 1.5mg to 100.8 ± 1.3 mg, and with a deviation percentage of well within ±0.8%, therefore showing good weight uniformity. Tablets were found to be between 2.87 ± 0.05 mm and 2.96 ± 0.03 mm thick, and 6.00 ± 0.02 mm in diameter regardless of batch. The results confirm the physical uniformity and dimensionality accuracy of the formulated tablets.

Table 6: Tablet evaluation results of weight variation, thickness, and diameter of bisoprolol fumarate FDT's

Batch Code	Avg Weight (mg)	% Deviation	Thickness (mm)	Diameter (mm)
VF1	100.2 ± 1.1	0.2%	2.95 ± 0.03	6.01 ± 0.01
VF2	99.9 ± 1.1	0.1%	2.91 ± 0.02	5.99 ± 0.01
VF3	100.3 ± 1.2	0.3%	2.87 ± 0.05	6.03 ± 0.01
VF4	100.8 ± 1.3	0.8%	2.91 ± 0.05	5.99 ± 0.02
VF5	99.9 ± 1.3	0.1%	2.95 ± 0.04	6.01 ± 0.02
VF6	100.5 ± 1.4	0.5%	2.96 ± 0.03	6.00 ± 0.02
VF7	99.7 ± 1.5	0.3%	2.93 ± 0.04	6.02 ± 0.03
VF8	100.4 ± 1.6	0.4%	2.89 ± 0.03	6.04 ± 0.01
VF9	100.0 ± 1.2	0.0%	2.92 ± 0.02	6.00 ± 0.02

Average tablet weight values are expressed as mean ± standard deviation (n = 20); thickness and diameter values are expressed as mean ± standard deviation (n = 10).

Results of disintegration time and mechanical strength evaluation of bisoprolol fumarate fast disintegrating tablets

As indicated in Table 7, the disintegration time of Bisoprolol Fumarate fast disintegrating tablets was 27.7 ± 1.2 sec (VF5) to 38.4 ± 1.5 sec (VF1), keeping fairly recorded and indicating quick breakdown for FDTs. The mechanical strength, and resistance to handling stress was within acceptable limits, i.e. hardness value (2.5–3.2 kg/cm^2) and friability (0.40–0.48%).

Table 7: Disintegration time and mechanical strength evaluation of bisoprolol fumarate fast disintegrating tablets

Batch Code	Disintegration Time (sec)	Hardness (kg/cm^2)	Friability (%)
VF1	38.4 ± 1.5	3.2 ± 0.3	0.48 ± 0.04
VF2	35.2 ± 1.3	3.0 ± 0.4	0.45 ± 0.03
VF3	32.5 ± 1.7	2.8 ± 0.2	0.43 ± 0.05
VF4	28.73 ± 1.4	2.6 ± 0.3	0.41 ± 0.04
VF5	27.7 ± 1.2	2.5 ± 0.2	0.40 ± 0.03
VF6	28.1 ± 1.3	2.6 ± 0.3	0.41 ± 0.04
VF7	31.0 ± 1.5	2.8 ± 0.4	0.43 ± 0.05
VF8	34.2 ± 1.6	3.0 ± 0.3	0.46 ± 0.03
VF9	36.4 ± 1.4	3.1 ± 0.3	0.47 ± 0.04

Values are expressed as mean ± standard deviation (n = 3 for disintegration; n = 10 for hardness and friability).

Results of drug content uniformity, wetting time and water absorption ratio of bisoprolol fumarate fast disintegrating tablets

Bisoprolol Fumarate fast disintegrating tablets active ingredients content were between 96.11 ± 0.2 and 97.91 ± 0.3 % meaning that the active ingredient was uniformly distributed in all batches, as presented in Tab. 8. Results from wetting time ranged from 24.72 ± 0.9 to 30.8 ± 0.7 seconds which indicate a rapid tablet hydration. This resulted in an efficient moisture uptake of 68.9 ± 1.3 to 81.6 ± 1.2 of water absorption ratio. The findings are consistent with the formulations of rapid wetting and effective hydration.

Table 8: Drug content uniformity, wetting time and water absorption ratio of bisoprolol fumarate fast disintegrating tablets

Batch Code	Drug Content (%)	Wetting Time (sec)	Water Absorption Ratio
VF1	97.37 ± 0.4	30.8 ± 0.7	76.1 ± 1.3
VF2	96.11 ± 0.2	29.1 ± 0.7	68.9 ± 1.3
VF3	96.62 ± 0.3	27.2 ± 0.8	81.6 ± 1.2
VF4	97.19 ± 0.3	25.4 ± 0.8	75.6 ± 1.0
VF5	96.47 ± 0.3	24.72 ± 0.9	73.5 ± 1.0
VF6	96.54 ± 0.2	25.0 ± 0.8	78.9 ± 1.4
VF7	97.63 ± 0.3	26.9 ± 0.9	72.3 ± 1.1
VF8	96.98 ± 0.4	28.4 ± 0.6	70.5 ± 1.3
VF9	97.91 ± 0.3	29.8 ± 0.8	74.2 ± 1.0

Drug content values are expressed as mean ± SD (n = 10); Wetting time and water absorption ratio values are expressed as mean ± SD (n = 3).

Results of *In-vitro* drug release profiles of bisoprolol fumarate fast disintegrating tablets

As shown in Table 9 and Figure 6, the in-vitro drug release profiles of Bisoprolol Fumarate fast disintegrating tablets were fast and highly efficient with all the formulations. In all batches, 94 % of the drug was released in the first 15 min, or more than 55 % of the total drug within the first 6 min. A release of 97.60 ± 0.9 % was found in VF4, while even the lowest (VF9) released a minimum of 94.58 ± 0.8 %, indicating that the formulations are capable of expediting and stabilizing the drug release to great extent.

Table 9: *In-vitro* drug release profiles of bisoprolol fumarate fast disintegrating tablets

Time (min)	VF1	VF2	VF3	VF4	VF5	VF6	VF7	VF8	VF9
2	19.2± 0.6	20.6 ± 0.8	18.4 ± 0.5	22.1 ± 0.7	21.5 ± 0.6	20.3 ± 0.7	20.0 ± 0.6	21.2 ± 0.8	18.9 ± 0.5
4	34.5 ± 0.9	36.9 ± 1.0	33.1 ± 0.8	38.6 ± 1.1	37.4 ± 0.9	39.2 ± 1.0	35.2 ± 0.9	36.1 ± 1.0	33.9 ± 0.8
6	52.2 ± 1.0	54.7 ± 1.1	51.3 ± 0.9	56.2 ± 1.2	55.8 ± 1.0	54.3 ± 1.1	53.4 ± 0.9	54.1 ± 1.0	51.9 ± 0.9
8	68.7 ± 1.1	71.5 ± 1.2	66.9 ± 1.0	72.9 ± 1.3	71.7 ± 1.1	64.7 ± 1.2	69.2 ± 1.0	69.8 ± 1.2	67.4 ± 1.0
10	80.1 ± 1.0	83.0 ± 1.1	78.5 ± 0.9	85.0 ± 1.2	83.2 ± 1.0	76.6 ± 1.1	81.1 ± 1.0	81.7 ± 1.1	79.6 ± 0.9
12	89.4 ± 0.9	92.6 ± 1.0	87.9 ± 0.8	94.2 ± 1.1	92.8 ± 0.9	85.1 ± 1.0	90.3 ± 0.9	90.8 ± 1.0	88.5 ± 0.8
15	96.13 ± 0.7	96.84 ± 0.9	97.41 ± 0.8	97.60 ± 0.9	97.25 ± 0.7	96.76 ± 0.8	96.02 ± 0.7	95.39 ± 0.9	94.58 ± 0.8

Values are expressed as mean ± SD of cumulative % drug release (n = 3).

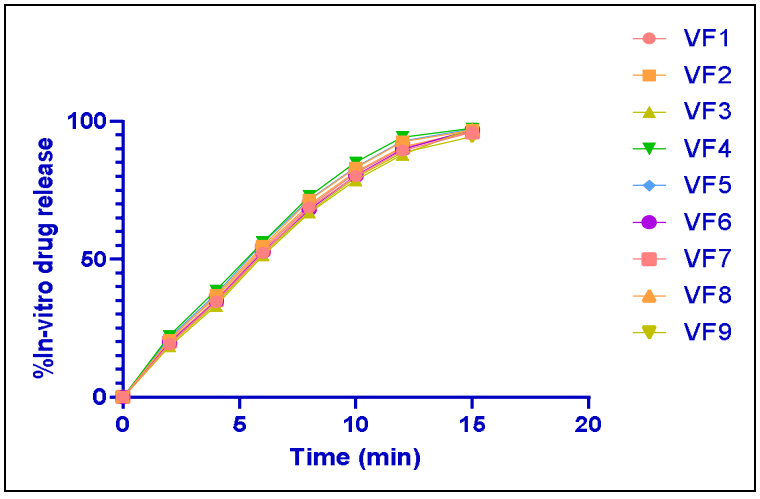

Figure 6: In-vitro Drug Release Profiles of Bisoprolol Fumarate Fast Disintegrating Tablets Over Time

Optimization of formulations

Disintegration time (Y_1)

An excellent model fit by the quadratic model applied for disintegration time was indicated by the adjusted R^2 of 0.9563 and predicted R^2 of 0.9877 while statistically significant with a sequential p value of 0.0005 (Table 10). The overall model significance (F = 129.46, p = 0.0011) was confirmed by ANOVA results (Table 11). In a linear fit analysis, sodium starch glycolate (Factor B) showed a significant linear effect (F = 18.43, p = 0.0232) and between Kyron T-314 and sodium starch glycolate (AB) interaction effect was highly significant for effect on disintegration time (F = 174.37, p = 0.0009). Other terms such as A, A^2, and AC did not prove to be statistically significant (p > 0.05), while the quadratic term B^2 (sodium starch glycolate) was also strongly significant (F = 453.07, p = 0.0002). These results suggest that B and AB are the major determinants of disintegration behavior.

Disintegration time = 28.0733 + -0.188333 * A + -0.75 * B + 2.825 * AB + 0.155 * A^2 + 6.44 * B^2

The large positive quadratic coefficient for B^2 and the positive coefficient of the interaction term AB indicate that sodium starch glycolate disintegration time is very sensitive to amount at high amounts. The shortest disintegration times were observed, as shown in Fig. A and B, through the contour and 3D surface plots, when the temperature and the sodium starch glycolate concentration were moderate and Kyron T-314 concentration was lower. High B values areas in the design space displayed rapid disintegration time increases, in agreement with the curvature in the B^2 response. A strong Factor B interaction with A combined with a non linear behavior were further supported by the distinct ridge in the 3D plot.

In-vitro drug release (Y_2)

As table 10 shows, the quadratic model applied to in vitro drug release gave a p value for assigned sequential 0.0016, strong adjusted r squared of 0.9450, and predicted r squared of 0.9879, thus supporting this model. Table 11 shows ANOVA results which indicate that the overall model is highly significant (F = 131.82; p = 0.0010). Sodium starch glycolate (Factor B) had a highly significant linear effect (F = 277.96, p = 0.0005) and it interacted substantially with Kyron T- 314 (AB) (F = 160.06, p = 0.001). Additionally, a high degree of curvature was indicated by the strong significance of the quadratic term B^2 (F = 215.17, p = 0.0007). Results from regressions indicate that Factor A and its quadratic term did not achieve statistical significance (p > 0.05) and accordingly, Kyron T-314 played a less role as an individual.

In-vitro Drug Release = 97.2367 + -0.0933333 * A + -0.731667 * B + -0.68 * AB + -0.09 * A^2 + -1.115 * B^2

The negative signs on coefficients B, AB and B^2 imply that increasing sodium starch glycolate concentrations have negative effects on the drug release rate. Both contour and 3D surface plots (see Figure C, D) demonstrated that the highest value of drug release (greater than 97%) occurred at low to moderate levels of sodium starch glycolate, and then their values got declined. The 3D plot showed a clear downward curvature as can be seen, indicating the suppressive effects of excessive B to release. The interaction of A and B was slightly concave, as expected of an antagonistic interaction (negative coefficient of AB), and curvature due to B^2.

Wetting time (Y_3)

The statistical significance of the quadratic model for wetting time was apparent with sequential p-value equal to 0.0004, adjusted R^2 equal to 0.9729 and predicted R^2 equal to 0.9904 (Table 10). The summary of the fit of the model (Table 11) showed that the fit was significant (F = 165.61, p = 0.0007). The factors among the various factors included in the study were sodium starch glycolate (Factor B) as these factors showed significant (F = 14.43, p = 0.0320), interaction (F = 228.68, p = 0.0006) and quadratic (F = 580.042, p = 0.0002) effects. In contrast to wetting time, the square term of Kyron T-314 (Factor A) and its outer product were statistically insignificant (p>0.05), indicating limited effect on wetting time alone.

Wetting time = 24.9667 + -0.183333 * A + -0.333333 * B + 1.625 * AB + 0.11 * A^2 + 3.66 * B^2

In accordance with the model equation, the wetting time increases significantly with the increase in sodium starch glycolate concentration, especially because of positive B^2 and AB coefficients. The contour and 3D surface plots (Figure E, F) support them visibly by showing a steady increase of wetting time for higher B concentration. The response surface produced in the interaction region (AB) is convex, meaning that when one increases both A and B together, the wetting time increases synergistically. Wetting characteristics are more expressed and dominated by quadratic effect of sodium starch glycolate in B due to the curvature.

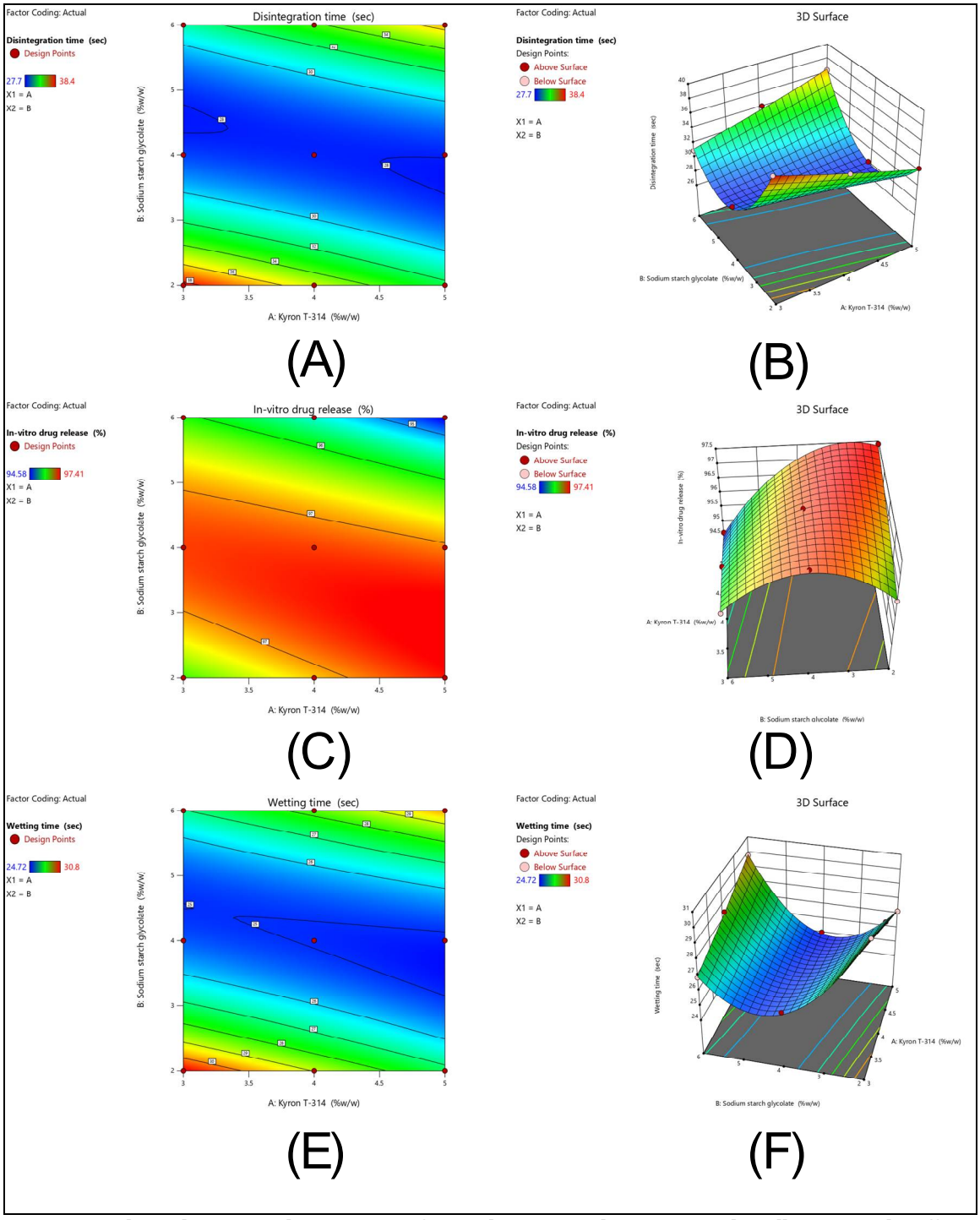

Figure 7: Three-dimensional response surface and corresponding contour plots illustrating the effects of formulation variables on critical quality attributes of bisoprolol fumarate fast disintegrating tablets. (A) 2d contour plot and (B) 3d response surface plot showing the influence of kyron t-314 and sodium starch glycolate concentrations on disintegration time; (C) 2d contour plot and (D) 3d response surface plot demonstrating the interactive effects of kyron t-314 and sodium starch glycolate concentrations on in-vitro drug release; (E) 2d contour plot and (F) 3d response surface plot depicting the effect of formulation variables on wetting time.

Table 10: Model fit summary for response variables of bisoprolol fumarate fast disintegrating tablets

Response Variable	Model	Sequential p-value	Lack of Fit p-value	Adjusted R^2	Predicted R^2
Disintegration Time	Quadratic	0.0005	0.9877	0.9563	0.9877
In-vitro Drug Release	Quadratic	0.0016	0.9879	0.9450	0.9879
% Drug Release (at 15 min)	Quadratic	0.0004	0.9904	0.9729	0.9904

Table 11: ANOVA results for quadratic models of response variables

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Disintegration time (Y1)						
Model	118.51	5	23.70	129.46	0.0011	significant
A-Kyron T-314	0.2128	1	0.2128	1.16	0.3599	Not significant
B-Sodium starch glycolate	3.38	1	3.38	18.43	0.0232	significant
AB	31.92	1	31.92	174.37	0.0009	significant
A^2	0.0481	1	0.0481	0.2625	0.6438	Not significant
B^2	82.95	1	82.95	453.07	0.0002	significant
In-vitro drug release (Y2)						
Model	7.62	5	1.52	131.82	0.0010	significant
A-Kyron T-314	0.0523	1	0.0523	4.52	0.1234	Not significant
B-Sodium starch glycolate	3.21	1	3.21	277.96	0.0005	significant
AB	1.85	1	1.85	160.06	0.0011	significant
A^2	0.0162	1	0.0162	1.40	0.3217	Not significant
B^2	2.49	1	2.49	215.17	0.0007	significant
Wetting time (Y3)						
Model	38.25	5	7.65	165.61	0.0007	significant
A-Kyron T-314	0.2017	1	0.2017	4.37	0.1278	
B-Sodium starch glycolate	0.6667	1	0.6667	14.43	0.0320	significant
AB	10.56	1	10.56	228.68	0.0006	significant
A^2	0.0242	1	0.0242	0.5239	0.5215	Not significant
B^2	26.79	1	26.79	580.04	0.0002	significant

Statistical optimization of formulation

Finally, in Table 12, the formulation of the formulation is statistically optimized as summarized, which predicted minimal relative error between predicted and experimental values and selected VF6 as the optimized batch. The experimental value (28.1 sec) and the predicted disintegration time (27.97 sec) had relative error of 0.46%. In the same manner, the in vitro release of drug and the wetting time showed negligible differences between the predicted values of 97.36 % and 24.82 sec, and experimental values of 96.94 % and 25 sec. This confirms the reliability and accuracy of the quadratic model applied for predicting the performance of the formulation.

Table 12: Statistical optimization of formulation

F. Code	Composition	Amount (%w/w)	Response	Predicted Value	Experimental Value	Relative Error (%)
VF6	Kyron T-314	5.00	Disintegration Time (sec)	27.97	28.1	0.46
	Sodium Starch Glycolate	4	In-vitro Drug Release (%)	97.36	96.94	0.43
			Wetting Time (sec)	24.82	25	0.73

Results of release kinetics

The optimized Bisoprolol Fumarate fast disintegrating tablet drug release kinetics, that was analysed by using Zero order, First order, Higuchi and Korsmeyer–Peppas models, is given in Figure 8. The Korsmeyer – Peppas model yielded the best fit with a correlation coefficient (R^2) = 0.9844 showing that the transport mechanism is anomalous (non Fickian). This implies control over drug release by both diffusion and erosion, an advantageous situation for ensuring rapid and predictable drug delivery in fast disintegrating tablet formulations.

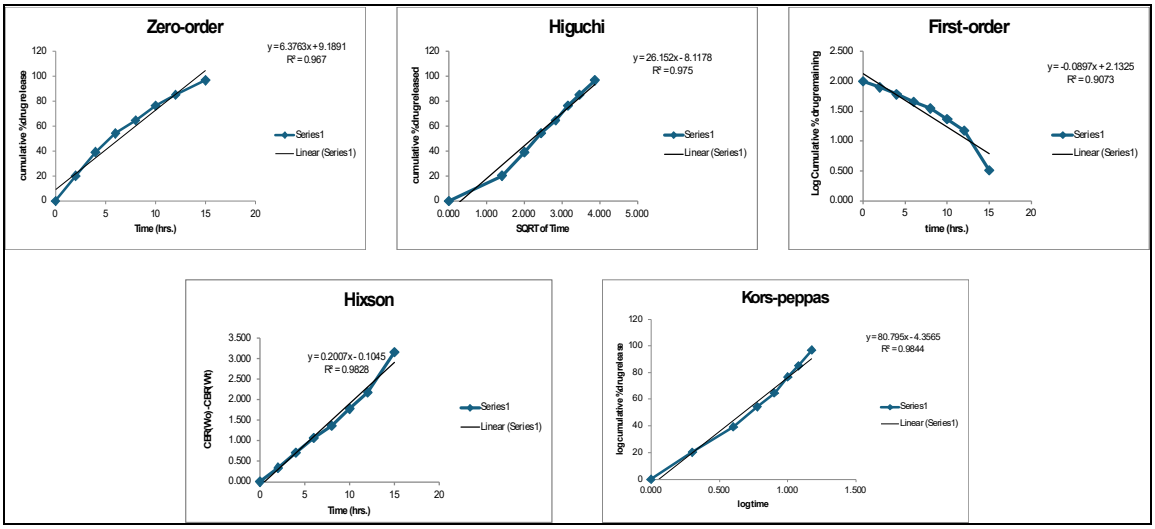

Figure 8: Kinetic modeling of drug release from optimized bisoprolol fumarate fast disintegrating tablet

MTT assay results

The cytocompatibility of Bisoprolol was assessed using an MTT assay on HEK-293 cells, revealing a concentration-dependent reduction in cell viability. Compared to the standard drug (STD), Bisoprolol demonstrated a higher IC_{50} value of 142.20 µg/mL versus 94.23 µg/mL, suggesting lower cytotoxic potential at equivalent doses (Table 13, Figure 9). These findings indicate that Bisoprolol is less harmful to normal cells within the studied concentration range. Complementary morphological evaluation (Figure 10) supported these results, with minimal cellular changes observed at lower concentrations and more prominent alterations only at higher doses, further confirming the acceptable biological safety of Bisoprolol for in vitro use.

Table 13: Comparative MTT assay results showing percent cell survival of bisoprolol and STD on HEK-293 cells at varying concentrations

Concentration (µg/mL)	Bisoprolol % Cell Survival	STD % Cell Survival
Control	100.00 ± 3.90	100.00 ± 1.67
1	85.71 ± 0.24	91.21 ± 0.68
5	87.72 ± 0.31	80.07 ± 1.67
25	80.07 ± 1.58	81.37 ± 0.51
50	92.23 ± 7.91	84.30 ± 4.53
100	79.12 ± 0.00	70.14 ± 2.00
250	58.78 ± 4.08	55.92 ± 0.63
500	69.34 ± 3.12	67.57 ± 1.64
IC_{50} Value (µg/mL)	142.20	94.23
Log IC_{50} Value	2.153	1.974

All values are expressed as mean ± standard deviation (n = 3).

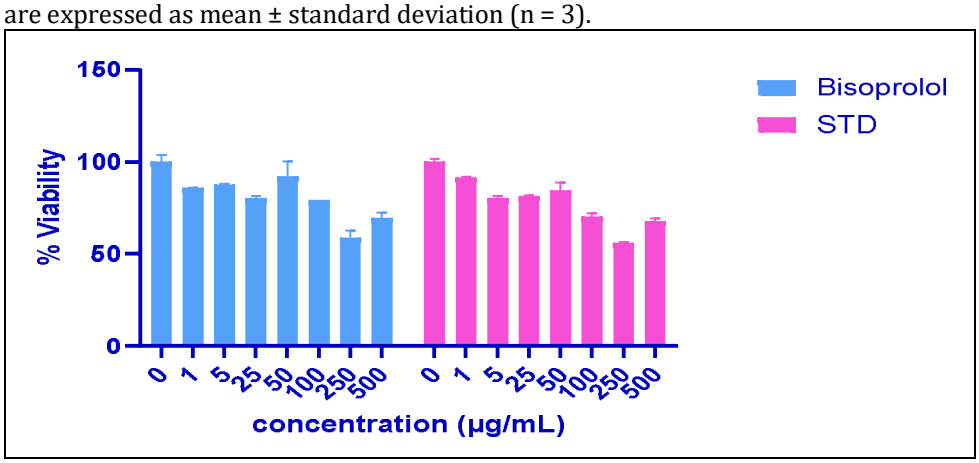

Figure 9: Comparative Cytotoxicity of Bisoprolol and STD on HEK-293 Cells Assessed by MTT Assay.

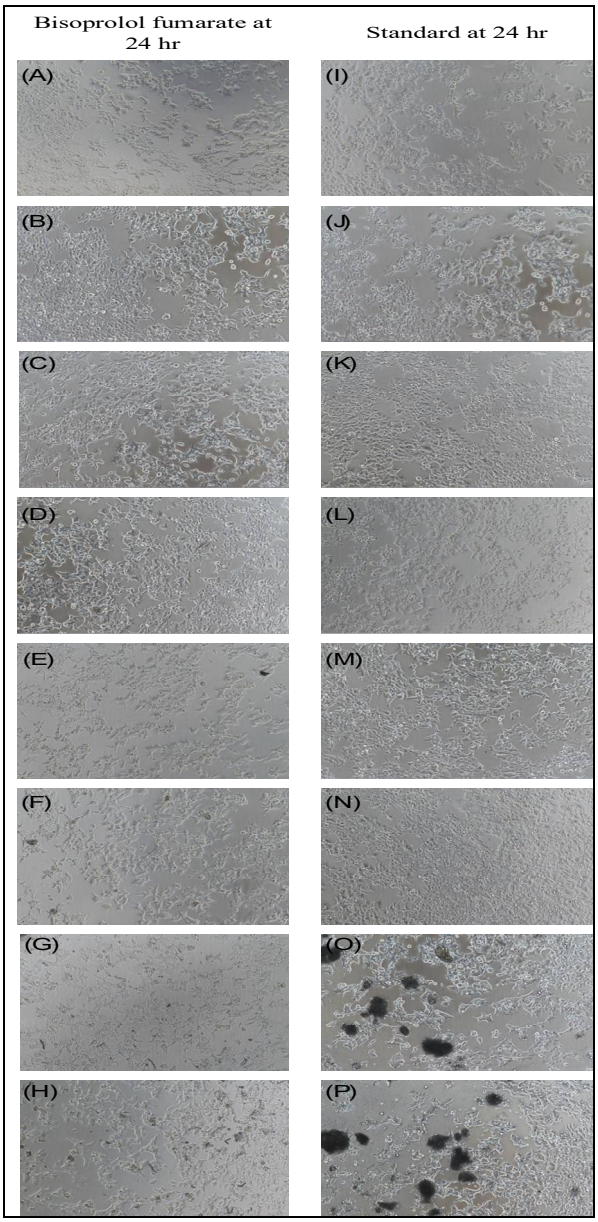

Figure 10. Morphological observations of HEK-293 cells treated with Bisoprolol and STD after 24 hours. (A) Control group for Bisoprolol; (B–H) increasing Bisoprolol concentrations from 1 to 500 µg/mL. (I) Control group for STD; (J–P) increasing STD concentrations from 1 to 500 µg/mL.

DISCUSSION

The main purpose of this research involved developing an optimized fast disintegrating tablet (FDT) formulation of Bisoprolol Fumarate which should provide swift medication absorption while increasing patient obedience and simplifying pill consumption. The 3^2 full factorial design represented a systematic investigation that evaluated how Kyron T-314 and sodium starch glycolate (SSG) levels affected the critical quality measures disintegration time in addition to in-vitro drug release and wetting time [45]. The validated quantification method for Bisoprolol Fumarate measurement consisted of a calibration curve that demonstrated linearity from 2 to 12 µg/mL concentrations with Y = 0.0566X + 0.0007 regression and 0.9998 r^2 value as shown in Figure 3. The drug quantification method demonstrates reliability through these results that will be used for future analysis. The solubility testing of Bisoprolol Fumarate (Table 3) revealed high dissolution rates exceeding 1032.6 ± 6.2 mg/mL in water and 1048.4 ± 5.7 mg/mL in methanol as well as free dissolution in ethanol, chloroform, and glacial acetic acid making the substance suitable for use in immediate-release FDTs. The drug demonstrates hydrophilic properties due to its poor solubility when exposed to non-polar solvents including ethyl acetate and acetone [46].

Both DSC and FTIR Spectroscopy techniques showed findings that supported the stability of the designed formulation during physicochemical compatibility investigations. The DSC thermograms (Figure 4) of the

drug substance alongside the physical mixture displayed only minor modifications in the melting peak (from 103.67 °C to 105.63 °C) without any signs of new peaks or peak broadening to indicate strong thermal interactions. The physical mixture showed no significant peak movement in FTIR spectra (Figure 5, Table 4) which indicated that the drug showed no chemical incompatibility with excipients [47]. The evaluation of the tablet formulations from initial to final compression stages proved their manufacturing consistency and product quality. The tablets maintained parallel characteristics in color production, shape attributes, and odor occasion between all manufacturing batches (Table 5) as weight limitations alongside thickness and diameter parameters remained in authorized boundaries (Table 6). Testing for mechanical strength showed tablets achieved hardness between 2.5–3.2 kg/cm^2 with low friability values below 1% (Table 7) which demonstrates good physical durability when handled. The disintegration time of the tablets fluctuated from 27.7 ± 1.2 sec (VF5) to 38.4 ± 1.5 sec (VF1) which meets the required time limits for FDTs. Drug analysis found uniformity between all produced batches with results between 96.11 ± 0.2% to 97.91 ± 0.3% (Table 8) for ensuring equivalent dosage distribution. The wetting time and water absorption ratio further proved the rapid hydration and disintegration capabilities of the formulations through optimal results achieved by VF5 and VF6 [48].

The in-vitro drug release studies presented in Table 9 accompanied by Figure 6 revealed quick drug release of Bisoprolol Fumarate exceeding 50% during the first 6 minutes and reaching 94% during fifteen minutes across all developed formulations. The formulation VF4 displayed the maximum drug release percentage at 97.60 ± 0.9% thus validating the excipients' combined potential and formulation method for fast dissolution. Sodium starch glycolate (Factor B) demonstrated greater impact than Kyron T-314 (Factor A) on disintegration time along with drug release and wetting time according to statistical analysis of the formulation. All models demonstrate the need for clear determination of SSG concentration because of both the significant (AB) interaction term and (B^2) quadratic term [49]. The results from optimized batch VF6 indicated low variations between computed values and experimental findings for disintegration time (27.97 vs. 28.1 sec) and drug release (97.36% vs. 96.94%) as well as for wetting time (24.82 vs. 25 sec) which can be found in Table 12 showing the model's credibility. The Korsmeyer–Peppas model showed the most fitting pattern to represent drug release kinetics from the optimized formulation with an R^2 value of 0.9844 because it combines erosion alongside diffusion in a non-Fickian transport process (Figure 8). Drug liberation in the FDT occurs through a combination of fast hydration processes and matrix breakdown events in line with its physical design [50].

The biological compatibility of Bisoprolol was evaluated using the MTT assay on HEK-293 cells, demonstrating a concentration-dependent effect on cell viability. The IC_{50} value for Bisoprolol was found to be 142.20 µg/mL, compared to 94.23 µg/mL for the standard drug (STD), indicating that Bisoprolol exhibits lower cytotoxicity at equivalent concentrations (Table 13, Figure 9). This suggests a better safety profile for Bisoprolol within the tested range. Morphological assessment under microscopy (Figure 10) further corroborated these results, showing intact cell morphology at lower concentrations and noticeable cellular changes only at higher doses, reinforcing the compound's favorable cytocompatibility for potential pharmaceutical applications [51].

CONCLUSION

The research developed an optimized fast disintegrating Bisoprolol Fumarate tablet formula through a 3^2 factorial design which led to quick tablet dissolution along with uniform drug content and efficient drug release performance. The optimized batch (VF6) presented outstanding compatibility along with appropriate mechanical toughness and release kinetics under the Korsmeyer–Peppas model that indicated both diffusion and erosion release mechanisms. The evaluated formulation demonstrated low toxicity toward HEK-293 cells while maintaining optimal morphology which supports its safety potential. The formulation demonstrates capabilities to promote patient adherence through accelerated drug effects and simple application processes which benefit elderly patients alongside those experiencing swallowing difficulties. Additional in-vivo testing should be conducted to confirm bioavailability and drug response performance because these findings will strengthen its clinical worth for hypertension control.

ABBREVIATIONS

ANOVA: Analysis of Variance; FTIR: Fourier-Transform Infrared Spectroscopy; UV: Ultraviolet Spectroscopy; DSC: Differential Scanning Calorimetry; FDT: Fast Disintegrating Tablet; IC_{50}: Inhibitory Concentration 50%; MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; SSG: Sodium Starch Glycolate; MCC: Microcrystalline Cellulose; R^2: Correlation Coefficient; SD: Standard Deviation; USP: United States Pharmacopeia; API: Active Pharmaceutical Ingredient.

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Authors contribution
All authors contributed equally.

Conflict of interest
The authors declare no conflict of interest.

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