Advances in Bioresearch
Adv. Biores., Vol 16 (6) November 2025: 163-180

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.16.6.163180

Advances in Bioresearch

ORIGINAL ARTICLE

Development and Optimization of Orodispersible Tablets for Enhancing Bioavailability of Valsartan for Management of Hypertension

Nilesh S. Mhaske*, Sanjivani Ahire
[1]Department of pharmaceutical quality assurance, Dr. Vithalrao Vikhe Patil Foundation's College of Pharmacy, Ahmednagar, Maharashtra 414111, India.
***Corresponding author's email:** nilesh.2273@gmail.com

ABSTRACT
The present study aimed to develop and optimize Valsartan Orodispersible tablets (ODTs) to enhance solubility, disintegration, and oral bioavailability for improved management of hypertension, particularly in patients with dysphagia. The goal was to create a patient-friendly dosage form with rapid onset of action using a factorial design approach. Kyron T-314 and Sodium Starch Glycolate were added at different proportions to make the formulations via direct compression. For optimizing the formulation, a Central Composite Design (CCD) was used. Precompression parameters, how much time disintegration takes, the amount of drug and the dissolution in an experimental setting were examined. Input parameters were tested by statistical analysis and response surface methodology to determine the optimized batch. The optimized batch (SF10) contained 2.25 mg Kyron T-314 and 12 mg Sodium Starch Glycolate. It demonstrated a disintegration time of 31.23 ± 1.0 s, hardness of 3.23 ± 0.12 kg/cm^2, drug content of 98.8 ± 1.0%, and cumulative drug release of 69.80 ± 0.63 % at 30 minutes. Compared to the marketed conventional tablet (9.98 ± 0.60% at 30 min), the optimized ODT showed nearly tenfold improvement in drug dissolution. Korsmeyer–Peppas kinetics confirmed anomalous transport. Stability studies showed no significant changes over 3 months. The developed Valsartan ODT offers significant advantages in disintegration and dissolution performance, supporting its potential for enhanced patient compliance and faster therapeutic action. The formulation's robust performance and stability suggest strong promise for clinical translation and further in-vivo validation.
Keywords: Valsartan, Orodispersible tablet, Central Composite Design, Hypertension, Solubility enhancement, Bioavailability, Patient compliance.

Received 28.08.2025 Revised 26.10.2025 Accepted 29.11.2025

How to cite this article:
Nilesh S. M, Sanjivani A. Development and Optimization of Orodispersible Tablets for Enhancing Bioavailability of Valsartan for Management of Hypertension. Adv. Biores. Vol 16 [6] November 2025. 163-180

INTRODUCTION

The issue of high blood pressure is found worldwide and it is tied to higher risks of disease, strokes and kidney failures [1]. According to WHO estimates, around 1.28 billion people over the age of 30 have high blood pressure and many of these cases go unnoticed [2]. The costs of care for this condition, along with reduced workforce effectiveness, cost the country billions each year. Because most patients take their antihypertensive drugs once or twice per day, some find it difficult to remember or swallow the medication correctly [3]. Many doctors prescribe valsartan for hypertension since it is a strong angiotensin II receptor blocker, yet its oxygen-containing solubility is not great and a significant part of it is absorbed in the liver [4]. Because of this pharmacokinetic issue, larger doses must be given which increases the chance of unwanted effects. Besides, traditional dosage forms are not appropriate for the elderly or for patients with swallowing difficulties [5]. There is a clear need for new methods of drug delivery that boost bioavailability, bring quick outcomes and help patients stick to their treatment for high blood pressure [6].

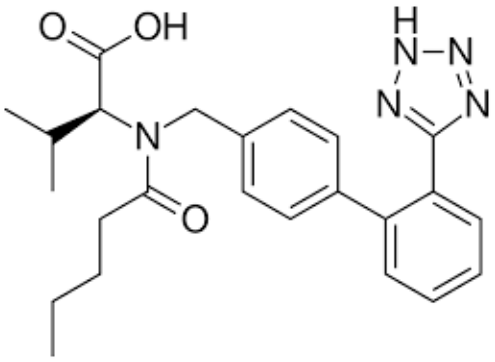

Figure 1: Chemical structure of valsartan

As a highly focused AT1 receptor antagonist, valsartan decreases resistance in the body's arteries without altering heart output [7]. A biphenyl tetrazole structure and a carboxylic acid group make it weakly acidic and dissolve only to some extent in water [8]. Valsartan is a Class II drug under the BCS and is poorly soluble, but it moves easily across membranes, so dissolving it is the main part that limits its absorption. How it works is by stopping angiotensin II from binding to the AT1 receptor, resulting in relaxed blood vessels and lower blood pressure [9]. Tests have confirmed that it effectively lowers both the chances of becoming ill and the risk of death in people having hypertension, heart failure and after myocardial infarction [10]. Yet, because valsartan has low bioavailability and can be inconsistently absorbed, inventing new formulations is necessary. Investigations into nanosizing, complexation and solid dispersions have been conducted. For this reason, dosage forms that people can swallow like candy are attractive since they tend to improve the success of the treatment and make it easier for patients to follow [11].

ODTs which stand for "Orodispersible Tablets", quickly break down in the mouth without water and are useful for both elderly and children [12]. Superdisintegrants and a carefully chosen mix of other ingredients allow the tablets to break down fast and dissolve, aiding fast absorption. Unlike other tablets, ODTs deliver medications faster, are easier for patients to consume and help more of the drug reach the bloodstream especially for drugs such as valsartan that have difficulty being absorbed [13]. Recently, new innovations in direct compression and lyophilization have helped increase the strength and loading abilities of ODTs. Also, adding elements that hide the bitterness makes it easier for patients to take these drugs [14]. The innovative platform is receiving growing acceptance from authorities and generating strong commercial results in chronic therapies. OTDs chosen for valsartan are justified according to its physicochemical properties, intended patient groups and the importance of quick and convenient blood pressure control with a simple dosage [15].

This study works to achieve stable, effective orodispersible tablets loaded with valsartan that have better solubility, fast dissolution and increased oral bioavailability, using a QbD method. The main objectives are to investigate superdisintegrants, tune the formulation for the best results and test performance in both laboratory experiments and real animals. The intention of this work is to make hypertension treatment simpler for patients.

MATERIAL AND METHODS

Materials

The valsartan (USP grade) used was brought from chempure, mumbai. Both Kyron T-314 and Sodium Starch Glycolate were purchased from Corel Pharma Chem (Ahmedabad, India). Both Beta-Cyclodextrin and Eosin were supplied by HiMedia (from Mumbai, India). The mannitol, aspartame and flavoring agent were bought from Loba Chemie (Mumbai, India). SD Fine Chemicals (Mumbai, India) supplied the Magnesium Stearate and MCC (Avicel PH102). The solvents and reagents (analytical/HPLC grade) used came from Merck India, located in Mumbai, India. Distilled water was created using the Milli-Q system. The other chemicals were laboratory grade.

Methods

Calibration curve determination

Valsartan was first dissolved in 100 mL ethanol to make the stock solution. Solutions with 5, 10, 15, 20, 25 and 30 µg/mL of ethanol-diluted drug were prepared with a micropipette. The absorbance of the solutions was measured in a UV-1800 spectrophotometer (Shimadzu, Japan) at 250 nanometers and ethanol was used as a reference. All the measurements were carried out with the sample being at room temperature (25 ± 2 °C) and using quartz cuvettes with 1 cm intervals for the light. With the absorbance

data and concentration ready, a calibration curve was made and regression analysis was used to identify the formula and the correlation coefficient [16,17].

Determination of solubility by solvent saturation method

The solvent saturation method was applied to find out the solubility of valsartan into different solutions. In different screw-capped vials, 10 mL of ethanol, methanol, DMF, DMSO, distilled water, phosphate buffer pH 6.8, chloroform, ethyl acetate, acetone, DCM, sodium hydroxide 0.1 N and phosphate buffer pH 7.4 each contained an excess amount of valsartan. Every vial was put in a water bath orbital shaker (Remi CIS-24BL, India) at 100 rpm and 25 ± 2 °C for two days so that saturation was reached. Following equilibration, the mixtures were kept for 12 hours and then were spun in a laboratory centrifuge (Remi R-8C, India) at 5000 rpm for 15 minutes. To filter the supernatant, a 0.45 µm membrane filter was used and the filtered liquid was diluted as appropriate with suitable solvents. The amount of valsartan was calculated by reading absorbance at 250 nm with a Shimadzu UV-1800 UV-Visible spectrophotometer. Each study used triplicate samples and the average solubility for each solvent was calculated [18,19].

Differential scanning colorimetry

DSC was employed to understand the interactions between valsartan and the excipients as they face heating. About 3–5 mg of pure valsartan and physical mixture were weighed and placed into standard aluminum pans. The DSC analysis was carried out using a DSC-60 Plus instrument (Shimadzu Corporation Japan) in a manner that kept the temperature from 30 °C to 300 °C. During the analysis, dry nitrogen was used as the gas at a flow rate of 50 mL/min. Scientists used an empty aluminum pan as comparison. All samples were turned into fine powders and placed into desiccators to prevent moisture from changing the results. Thermal curves were recorded and the temperatures when the reaction started, reached a maximum and the enthalpy changed were determined. Three replicates of each sample (n=3) were run and these results allowed us to identify changes in any characteristic peaks [20].

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR was used to analyze how valsartan reacts with each of the excipients in the formula. The IR spectra were taken of a single drug, all excipients and the final optimized mixture with an FTIR spectrophotometer (IRAffinity-1S from Shimadzu Corporation) that uses a DTGS detector. We weighed 1 mg of the sample, mixed it with 100 mg of dry potassium bromide and compressed the mixture into a pellet using methods under 10-ton pressure for 2 minutes. Examination of the pellets included 16 spectra each, collected in the spectral range of 4000–400 cm^{-1}. The results were taken at room temperature (25 ± 2°C) and the same spectra were created and measured three different times. Changes or variations in peaks from functional groups were checked and reviewed to notice if the drug is having any interactions with excipients [21,22].

Experimental design

Employing Design-Expert® version 13.0, a Central Composite Design (CCD) was used to optimize Valsartan orodispersible tablets, choosing Kyron T-314 (X_1) and Sodium Starch Glycolate (X_2) as the main factors. Both Kyron T-314 (studied at 0.75 mg and 2.25 mg) and Sodium Starch Glycolate (at 6 mg and 12 mg) were evaluated in the study. Ten experimental runs were carried out which included setting up two center points for better reliability and accuracy of the results. The dependent variables chosen as key quality attributes were hardness (Y_1), disintegration time (Y_2) and percentage drug dissolution at 30 minutes (Y_3). A design was developed to determine both the linear and interacting effects of excipients on the properties of the tablets. Multiple regression analysis was done to understand how the independent and dependent variables were related and the following second-order polynomial equation was used for each response:

$$Y = \beta_0 + \beta_1X_1 + \beta_2X_2 + \beta_{12}X_1X_2 + \beta_{11}X_1^2 + \beta_{22}X_2^2,$$

where Y is the predicted response, β_0 is the intercept, β_1 and β_2 are the linear coefficients, β_{12} is the interaction coefficient, and β_{11} and β_{22} are the quadratic coefficients [23,24]. The detailed experimental runs with factor levels and response outputs are summarized in Table 1.

Table 1: Variables and their levels in central composite design.

Variables	**Levels**	
Independent variables	**Low**	**High**
(A) = Kyron T-314 (mg)	0.75	2.25
(B) = Sodium starch glycolate (mg)	6	12
Dependent variables	**Goals**	
(R_1) = Hardness (Kg/cm^2)	Minimize	
(R_2) = Disintegration time (Sec)	Minimize	
(R_3) = Dissolution at 30 min (%)	Maximize	

Table 2. Composition of Valsartan Orodispersible Tablet Formulations as per Central Composite Design

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Valsartan	40	40	40	40	40	40	40	40	40	40
Kyron T314	2.56	0.75	1.5	2.25	0.4393	1.5	0.75	1.5	1.5	2.25
Sodium starch glycolate	9	12	9	6	9	13.24	6	9	4.75	12
Beta-cyclodextrin	80	80	80	80	80	80	80	80	80	80
Mannitol	10	10	10	10	10	10	10	10	10	10
Aspartame	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6
Flavor	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium stearate	1	1	1	1	1	1	1	1	1	1
Microcrystalline cellulose (q.s to 150) mg	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Precompression Study

All the formulation blends (SF1–SF10) were evaluated using micromeritic methods to check how easily they could be processed and compressed before any compression. The factors studied were the angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio. An angle of repose was measured using the fixed funnel technique to study flow, while the bulk and tapped densities were found using a graduated cylinder. Carr's index and Hausner's ratio were determined from the density values to study the packing and flow of the mixed powders. With the results within pharmaceutical limits, these blend tests helped establish that the mixtures could be successfully used in direct compression [25].

Formulation of Valsartan Orodispersible Tablets

The tablets were prepared using the direct compression method based on the experimental runs designed using Central Composite Design. Table 2 outlines the composition of all ten formulations (SF1–SF10). Exact quantities of Valsartan, Kyron T-314, Sodium Starch Glycolate, Mannitol, Aspartame, and Flavoring agents were sieved through a #40 mesh and blended uniformly in a mortar. Beta-cyclodextrin was incorporated using the kneading technique to form an inclusion complex with Valsartan, thereby enhancing its aqueous solubility. After kneading, the complex was dried and blended with the rest of the excipients. Microcrystalline Cellulose was used as a filler to adjust the total tablet weight to 150 mg, and Magnesium Stearate was added as a lubricant. The final blend was thoroughly mixed and compressed using 6 mm flat-faced punches on a rotary tablet press (Rimek Mini Press-I, Karnavati, India). Each batch was then evaluated for post-compression parameters [26].

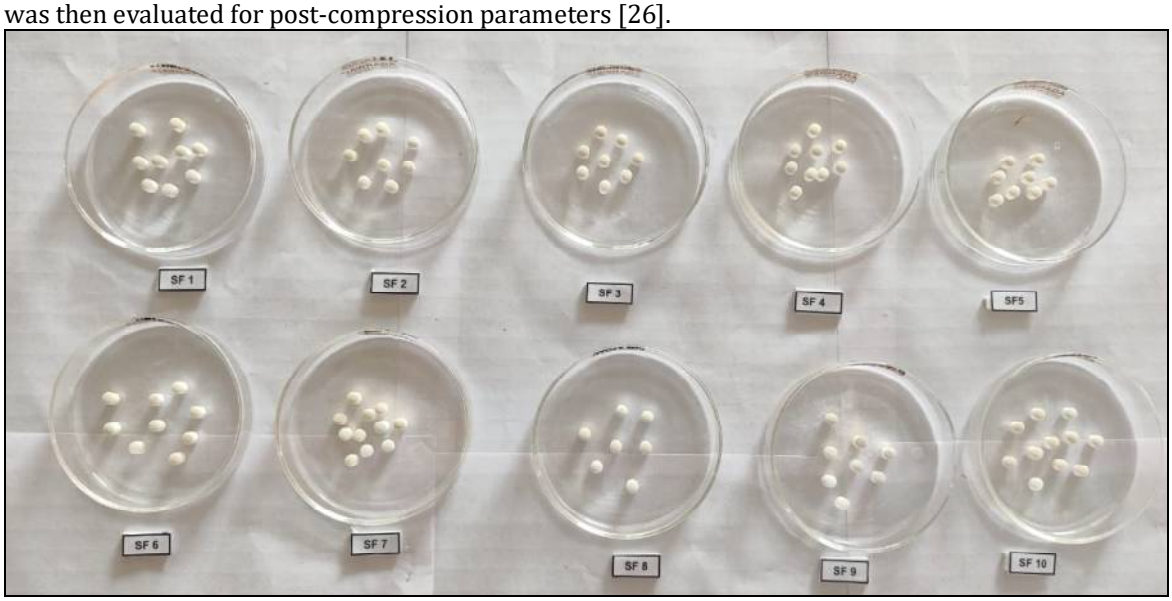

Figure 2: All formulated batches of Orodispersible tablet

Evaluation of Valsartan Orodispersible Tablets

Organoleptic evaluation

After preparing the Valsartan orodispersible tablets, they were checked for attributes such as color, appearance, smell and the feel on their surface. Under natural light, the tablets were examined for color consistency and for cracks, chips or damage. Comparing the shape and surface texture of the items from each batch allowed for checking their uniformity. We carefully sniffed each tablet after opening the packaging to check for unexpected smells. The tests were performed to confirm that the tablets were aesthetically and sensory pleasing [27].

Weight variation

The test was conducted following the guidelines given in the Indian Pharmacopoeia. The manufacturer's instructions directed us to test 20 tablets randomly drawn from every batch and we put each tablet on an electronic Shimadzu balance. The average weight of the tablets was worked out and afterwards was compared with every single tablet's weight. Tablets were measured and compared to the target quantity for each batch to see what the difference was. If a tablet is in the 130-324 mg range, according to the IP, it should not weigh more than 7.5% higher or lower than what is listed. To pass the formulation, each tablet must not exceed 1.5 times the average weight and no tablet should surpass twice the acceptable limit [28].

Tablet Thickness and Diameter

The thickness and diameter of tablets were measured with a digital Vernier caliper (Mitutoyo, Japan) to make sure all batches were the same. The thicknesses and diameters of each tablet were measured for ten tablets chosen from the same batch and then noted in millimeters (mm). The readings were taken by clamping the tablet between the caliper jaws without applying firm pressure to prevent distorting the tablet. Calculating the average and standard deviation served to assess whether the size of the pills remained constant which is crucial for packaging and ensures patients can take them correctly [29].

Tablet hardness

A Monsanto hardness tester from Campbell Electronics (India) was used to measure tablet hardness. For each batch, ten tablets were selected at random. For each tablet, it was wound up through the testing machine between the plunger and anvil, with the required bending force documented and shown as kg/cm^2. For every sample, the procedure was repeated and the overall mechanical strength was set by averaging the hardness value [30].

Tablet friability

An Electrolab Roche friabilator was applied to check how friable the prepared Valsartan orodispersible tablets were. Twenty-five tablets were loaded into the friabilator drum from batches and the run was completed at 25 revolutions per minute for four minutes. After the experiment was done, the tablets were brushed clean and weighed again. The percentage drop in value was calculated with this formula.

$$\%\ Friability = \frac{Initial\ weight - Final\ weight}{Intial\ weight} \times 100$$

According to pharmacopoeial standards, tablets with a friability value of less than 1% are considered to have acceptable mechanical strength [31].

Wetting Time and Water Absorption Ratio

Wetting time and water absorption ratio were used tocheck how quickly and well the Valsartan orodispersible tablets hydrated. We utilized a 6 mL Petri dish with eosin solution (0.1% w/v) in it, positioned a circular tissue paper piece at the dish center to support the tablet and followed up according to the pathology checklist. Every tablet was set down on the wetted tissue and its wetting time was immediately recorded using a stopwatch as the liquid spread over the tablet. A tablet was measured before it was exposed to water (W_1) and then once it had completed absorption (W_2) to find how much water it absorbed. The water absorption ratio (R) was determined with the help of the formula:

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

Three tablets were evaluated from each formulation, and the results were expressed as mean ± standard deviation. These parameters provided valuable insights into the tablets' ability to absorb moisture and disintegrate quickly in the oral cavity [32].

Drug Content Uniformity

Uniformity of drug content in Valsartan orodispersible tablets was checked by testing three tablets from every batch. Each tablet was crushed into powder, with 40 mg of Valsartan carefully measured out and put into a phosphate buffer (pH 6.8) inside a 100 mL volumetric flask. The mixture went through sonication for 15 minutes so that all the drug could be extracted and the samples were filtered with Whatman filter paper No. 41. A UV-visible spectrophotometer (Shimadzu) was used to determine the absorbance of the diluted filtrate at 250 nm. To show the results, data was given as mean + standard deviation after comparing it on a calibration curve [33,34].

Disintegration Time

To determine disintegration time, we used the Electrolab USP disintegration device on prepared Valsartan orodispersible tablets; discs were not employed. Six tablets from each formulation were each put separately in disintegration tubes and exposed to 900 mL of distilled water at 37 ± 0.5°C. The device was used to test each tablet and the time needed for it to be fully dissolved and leave no traces behind

was recorded in seconds. An average disintegration time was found and it was reported with the standard deviation. The requirement for rapid disintegration within 30 seconds for orodispersible tablets was confirmed during this test [35].

In-vitro Dissolution Study

An Electrolab TDT-08L (USP Type II bath) apparatus was used to assess the disintegration and dissolution of Valsartan orodispersible tablets. Nine hundred milliliters of phosphate buffer at pH 6.8 were prepared, placed in the incubator to reach 37 ± 0.5°C and the paddle was rotated at a speed of 50 rpm. Five mL was drawn from the dissolution sample after each tablet was put in at different times which were every 5 minutes for the first set, 10 minutes for the second and then again at 15, 20, 25 and 30 minutes. Immediately after taking out the samples, fresh buffer was added to make sure the sink conditions didn't change. After collection, samples that required it were passed through Whatman filter paper No. 41, diluted when necessary and then measured using a UV-visible spectrophotometer (Shimadzu, Japan) at a wavelength of 250 nm. A dissolution test was conducted with the orodispersible tablet and a standard Valsartan tablet to see if there was any better or faster disintegration in the same environment [36].

X-ray Diffraction (XRD) Analysis

A test using XRD analysis was performed to measure the degree of crystallinity in both pure Valsartan and the prepared orodispersible Valsartan tablet drug formulation. Samples were tested with a powder XRD system, functioning under TwoTheta/Theta conditions, in the range of 5° to 50° in normal operating conditions. The diffractograms were examined to determine the appearance or decrease of crystalline peaks. The objective of this study was to discover if producing Valsartan in different forms could cause it to become amorphous instead of crystalline [37].

Drug Release Kinetics

To analyze the drug release data, the values from the optimized Valsartan orodispersible tablet were examined using Zero-order, First-order, Higuchi, Hixson-Crowell and Korsmeyer–Peppas models. The best match for the release behavior was found by looking at the corresponding highest R^2 value. Using the Korsmeyer–Peppas method, the exponential parameter (n) was found to describe the way the drug was released. When making calculations, Microsoft Excel was used all around [38].

Accelerated Stability Study

ICH rules say that the optimized orodispersible tablet should be tested to find out if it remains stable through an accelerated stability study. Aluminum strip packaging was used for the tablets and these were kept in a stability chamber at 40 ± 2°C and 75 ± 5% relative humidity for 3 months. Appearance, hardness, the amount of drug, disintegration time and the amount of drug released from the tablet were checked at 0, 1, 2 and 3 months. All tests used three replicates and the outcomes of each one were checked against the initial test to find out if faster conditions caused any changes [39].

Statistical Analysis

All experiments were expressed with their mean values and standard deviation (3 replicates). The statistical analysis was performed with the program Design-Expert® version 13.0. The ANOVA test was used to determine if each model term was significant ($p < 0.05$). Curves called polynomial equations and response surface plots were created to understand the effect of the different variables. Student's t-test was used to see if the tablet performs as expected [40].

RESULTS AND DISCUSSION

Calibration curve determination

A good linearity was shown by the calibration curve of Valsartan in phosphate buffer pH 6.8, as recorded absorbance at 250 nm was very consistent throughout the concentration range of 5–30 µg/mL. A high correlation between the data points in Figure 3 shows that using linear regression was a reliable method for drug quantification in the following experiments.

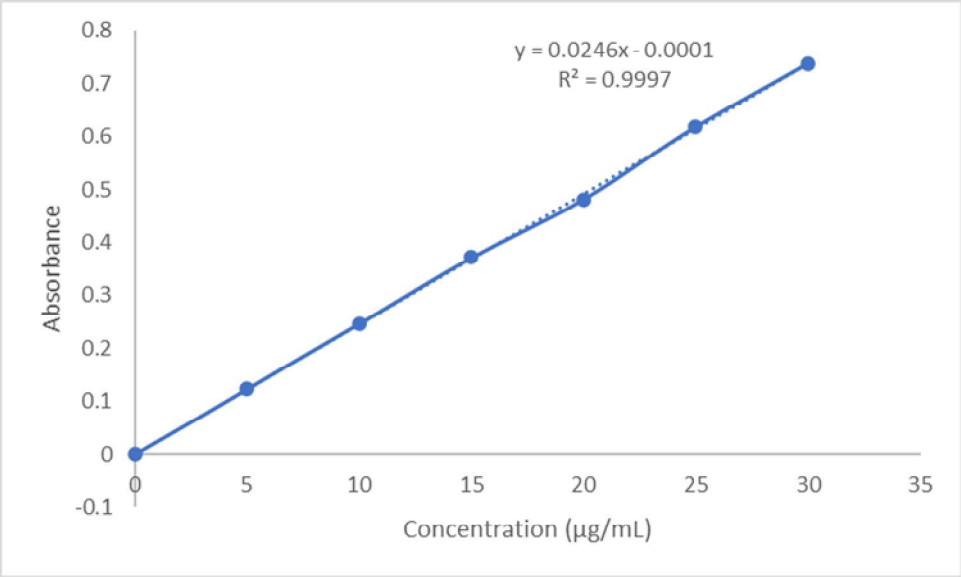

Figure 3: Calibration Curve for Valsartan in Phosphate Buffer (pH 6.8)

Results of solubility determination

The highest solubility of valsartan was recorded in both DMSO and phosphate buffer pH 6.8, showing it was suitable for dissolution testing. Very little of the drug dissolved in water (0.027 ± 0.002 mg/mL) which indicates that it belongs to the BCS Class II group. The data in Table 3 reveal that enhancing aqueous solubility is necessary because the compound exhibits low solubility in many solvents.

Table 3: Determination of solubility in different solvents.

Sr. No.	Solvent	Solubility (mg/mL)	Result
1	Ethanol	30.12 ± 1.3	Freely Soluble
2	Methanol	30.45 ± 1.1	Freely Soluble
3	DMSO	43.55 ± 1.6	Soluble
4	Phosphate buffer pH 6.8	43.53 ± 2.1	Soluble
5	Water	0.027 ± 0.002	Practically Insoluble
6	Phosphate buffer pH 7.4	0.962 ± 0.06	Very Slightly Soluble to Slightly Soluble

All values are expressed as mean ± SD

Differential scanning colorimetry analysis

The DSC thermogram of the pure Valsartan substance showed an obvious peak at 102.28 °C, proving that it has crystals present. The peak in the physical mixture was found at 102.64 °C, suggesting that there was no important drug-excipient interaction. A second peak at 168.15 °C was noticed when the excipient started to melt. The trends in Thermal Analysis (Figure 4) confirm that all components in the formulation are compatible and their stability is not affected.

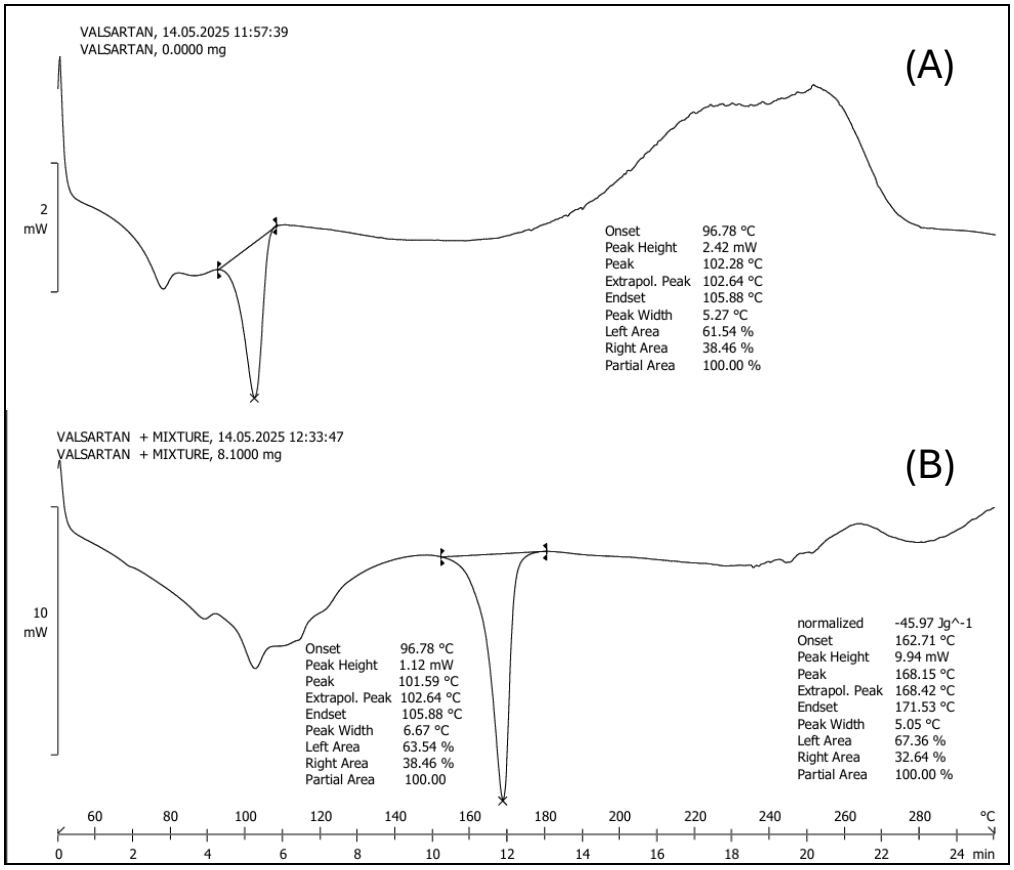

Figure 4: Figure X. DSC Thermograms of (A) DSC thermogram of pure Valsartan. (B) DSC thermogram of physical mixture of Valsartan with excipients.

Fourier Transform Infrared Spectroscopy analysis

Results from FTIR analysis confirmed the presence of Valsartan by finding distinct values at 1722.12 cm^{-1} for C=O stretching, 1591.95 cm^{-1} for C=C stretching in aromatic groups and 1278.57 cm^{-1} for C–N stretching. The excipients did not interact significantly with Valsartan, as shown by the minor shift in peaks to 1684.45 cm^{-1}, 1553.21 cm^{-1} and 1241.64 cm^{-1}. Lastly, there were no new peaks or lost characteristic bands, so the drug was likely stable in the sample we used. Results in Figures 5 and Table 4 prove that Valsartan can be combined with Kyron T-314 and Sodium Starch Glycolate in an orodispersible tablet system.

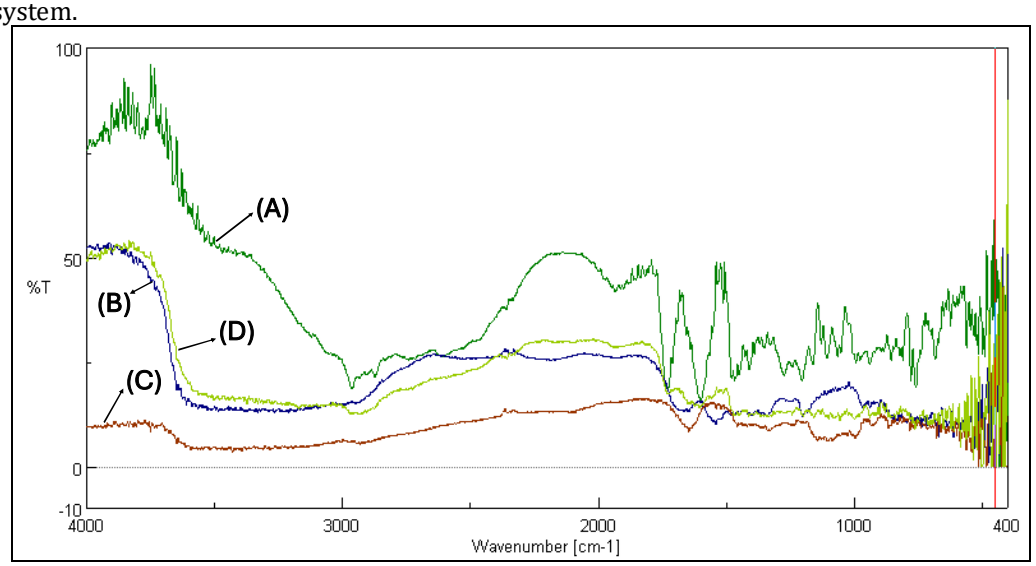

Figure 5: FTIR Spectra of (A) pure Valsartan, (B) Kyron T-314, (C) Sodium Starch Glycolate, and (D) Physical mixture of Valsartan with excipients.

Table 4: FTIR Spectral Interpretation Showing Functional Groups of Valsartan, Excipients, and Physical Mixture for Compatibility Assessment

Functional Group	Standard Wavelength (cm^{-1})	Observed in Pure Drug	Observed in Kyron	Observed in Starch	Observed in Physical Mixture
O–H stretching (broad)	3200–3600	–	–	–	–
C–H stretching (alkyl)	2850–3000	2964.05, 2877.38	–	–	–
C=O stretching (acid/carboxylic)	1700–1725	1722.12	1672.95	–	1684.45
Aromatic C=C stretching	1450–1600	1591.95	1543.74	–	1553.21
C–N stretching	1250–1350	1278.57	1408.45	–	1241.64
Aromatic C–H bending	700–900	754.99	–	–	–
COO^- asymmetric stretching	1540–1600	–	1543.74	–	1553.21

Results of precompression study

All ten experimental batches were found to have good flow and were suitable for direct compression. The flow of the material is excellent to good, since the angle of repose varied between 26.74° and 29.58°. All Carr values were from 12.24% to 15.22% and Hausner ratios from 1.14 to 1.18 which fit the accepted range. The blend uniformity is confirmed by the complete micromeritic parameters shown in Table 5.

Table 5. Precompression Parameters of Valsartan Orodispersible Tablet Powder Blends.

Batch	Angle of Repose (°)	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner's Ratio
SF1	28.36 ± 0.42	0.41 ± 0.01	0.48 ± 0.02	14.58 ± 0.37	1.17 ± 0.02
SF2	27.45 ± 0.35	0.43 ± 0.01	0.49 ± 0.01	12.24 ± 0.41	1.14 ± 0.01
SF3	29.01 ± 0.48	0.40 ± 0.01	0.47 ± 0.02	14.89 ± 0.39	1.17 ± 0.01
SF4	26.89 ± 0.36	0.42 ± 0.01	0.48 ± 0.01	12.50 ± 0.35	1.14 ± 0.01
SF5	28.76 ± 0.39	0.41 ± 0.02	0.47 ± 0.02	12.76 ± 0.42	1.15 ± 0.01
SF6	27.23 ± 0.41	0.43 ± 0.01	0.49 ± 0.01	12.24 ± 0.36	1.14 ± 0.01
SF7	29.58 ± 0.40	0.39 ± 0.02	0.46 ± 0.01	15.22 ± 0.34	1.18 ± 0.01
SF8	27.89 ± 0.33	0.42 ± 0.01	0.48 ± 0.01	12.50 ± 0.38	1.14 ± 0.01
SF9	28.15 ± 0.36	0.41 ± 0.01	0.47 ± 0.01	12.76 ± 0.30	1.15 ± 0.01
SF10	26.74 ± 0.37	0.43 ± 0.01	0.49 ± 0.01	12.24 ± 0.31	1.14 ± 0.01

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

Results of organoleptic evaluation

All the Valsartan orodispersible tablets tested were white, had a round edge, a flat face, a smooth surface and did not have any clear defects. All tablets smelled the same and appeared similarly from batch to batch, showing that they were physically the same. The sensory and aesthetic acceptability of the samples has been confirmed, as stated in Table 6.

Table 6: Organoleptic Evaluation of Valsartan Orodispersible Tablets.

Batch	Color	Shape	Surface Texture	Odor	Appearance Uniformity
SF1	White	Circular, flat-faced	Smooth	Odorless	No visible defects
SF2	White	Circular, flat-faced	Smooth	Odorless	No visible defects
SF3	White	Circular, flat-faced	Smooth	Odorless	No visible defects
SF4	White	Circular, flat-faced	Smooth	Odorless	No visible defects
SF5	White	Circular, flat-faced	Smooth	Odorless	No visible defects
SF6	White	Circular, flat-faced	Smooth	Odorless	No visible defects
SF7	White	Circular, flat-faced	Smooth	Odorless	No visible defects
SF8	White	Circular, flat-faced	Smooth	Odorless	No visible defects
SF9	White	Circular, flat-faced	Smooth	Odorless	No visible defects
SF10	White	Circular, flat-faced	Smooth	Odorless	No visible defects

Results of weight variation, thickness, diameter and hardness

All formulations (SF1–SF10) complied with weight variation limits, with average weights ranging from 149.84 ± 1.22 mg to 151.07 ± 1.26 mg. Tablet thickness ranged between 2.77 ± 0.04 mm and 2.83 ± 0.05 mm, and diameters varied from 6.07 ± 0.03 mm to 6.12 ± 0.03 mm. Hardness values were between 2.63 ± 0.12 kg/cm^2 and 4.54 ± 0.12 kg/cm^2. Detailed results are presented in Table 7, confirming dimensional consistency and mechanical strength.

Table 7: Fourier Transform Infrared Spectroscopy.

Batch	Avg. Weight (mg)	Thickness (mm	Diameter (mm)	Hardness (kg/cm^2)
SF1	150.35 ± 1.09	2.83 ± 0.05	6.07 ± 0.03	3.90 ± 0.12
SF2	149.90 ± 1.09	2.80 ± 0.04	6.10 ± 0.03	2.95 ± 0.12
SF3	150.45 ± 1.15	2.80 ± 0.03	6.11 ± 0.02	3.84 ± 0.12
SF4	151.07 ± 1.26	2.77 ± 0.04	6.10 ± 0.04	4.45 ± 0.12
SF5	149.84 ± 1.22	2.79 ± 0.03	6.10 ± 0.02	3.46 ± 0.12
SF6	150.65 ± 1.37	2.78 ± 0.05	6.12 ± 0.03	2.63 ± 0.12
SF7	150.49 ± 1.41	2.81 ± 0.06	6.08 ± 0.04	4.10 ± 0.12
SF8	149.92 ± 1.32	2.79 ± 0.04	6.11 ± 0.03	3.86 ± 0.12
SF9	150.71 ± 1.39	2.82 ± 0.03	6.09 ± 0.02	4.54 ± 0.12
SF10	150.12 ± 1.24	2.80 ± 0.05	6.10 ± 0.03	3.23 ± 0.12

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

Results of Friability, Wetting Time, Water Absorption Ratio, Drug Content Uniformity and disintegration time.

All formulations exhibited friability below 1%, ranging from 0.27 ± 0.01% (SF9) to 0.38 ± 0.02% (SF6), indicating acceptable mechanical strength. Wetting time varied from 14.9 ± 0.7 s (SF9) to 24.3 ± 1.2 s (SF6), while water absorption ratios ranged between 76.5 ± 1.8% and 86.7 ± 1.1%. Drug content uniformity was within 97.9 ± 1.4% to 99.8 ± 0.7%, and disintegration times ranged from 24.81 ± 0.6 s to 31.52 ± 1.3 s, all meeting pharmacopeial requirements. Complete data are presented in Table 8.

Table 8. Evaluation of Friability, Wetting Time, Water Absorption Ratio, Drug Content Uniformity and disintegration time.

Batch	Friability (%)	Wetting Time (sec)	Water Absorption Ratio (%)	Drug Content (%)	Disintegration time (sec)
SF1	0.29 ± 0.01	18.4 ± 0.8	82.3 ± 1.5	99.2 ± 0.9	28.89 ± 0.8
SF2	0.34 ± 0.02	21.7 ± 1.0	79.6 ± 1.4	98.7 ± 1.1	29.72 ± 1.0
SF3	0.30 ± 0.01	17.6 ± 0.9	83.4 ± 1.3	99.5 ± 0.8	27.65 ± 0.9
SF4	0.28 ± 0.01	15.2 ± 0.7	85.9 ± 1.2	99.8 ± 0.7	26.23 ± 0.7
SF5	0.36 ± 0.02	22.9 ± 1.1	77.2 ± 1.6	98.3 ± 1.2	27.09 ± 1.1
SF6	0.38 ± 0.02	24.3 ± 1.2	76.5 ± 1.8	97.9 ± 1.4	31.52± 1.3
SF7	0.31 ± 0.01	16.8 ± 0.8	84.1 ± 1.4	99.0 ± 0.9	25.18 ± 0.8
SF8	0.30 ± 0.01	17.4 ± 0.9	83.2 ± 1.5	99.3 ± 0.8	27.65 ± 0.9
SF9	0.27 ± 0.01	14.9 ± 0.7	86.7 ± 1.1	99.7 ± 0.6	24.81 ± 0.6
SF10	0.33 ± 0.02	20.6 ± 1.0	80.2 ± 1.3	98.8 ± 1.0	31.23 ± 1.0

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

Result of *In-vitro* Drug Dissolution Profile

Table 9. *In-vitro* Drug Dissolution Profile

Time (min)	SF1	SF2	SF3	SF4	SF5	SF6	SF7	SF8	SF9	SF10
1 min	8.32 ± 0.43	9.01 ± 0.45	7.93 ± 0.42	8.67 ± 0.47	7.64 ± 0.41	10.94 ± 0.49	8.53 ± 0.44	7.68 ± 0.40	9.34 ± 0.46	9.87 ± 0.48
5 min	24.26 ± 0.59	25.61 ± 0.56	23.18 ± 0.55	24.79 ± 0.54	22.17 ± 0.51	28.83 ± 0.63	24.43 ± 0.53	22.02 ± 0.48	25.35 ± 0.60	26.73 ± 0.62
10 min	41.58 ± 0.57	43.72 ± 0.55	39.93 ± 0.54	42.84 ± 0.52	38.01 ± 0.50	48.76 ± 0.60	41.03 ± 0.51	37.68 ± 0.47	44.55 ± 0.59	46.91 ± 0.58
15 min	53.41 ± 0.52	55.66 ± 0.48	50.38 ± 0.47	53.42 ± 0.46	48.07 ± 0.45	61.92 ± 0.62	52.14 ± 0.49	48.19 ± 0.46	56.02 ± 0.51	58.63 ± 0.54
20 min	60.33 ± 0.54	62.90 ± 0.50	56.84 ± 0.51	59.14 ± 0.52	54.02 ± 0.48	67.82 ± 0.59	58.49 ± 0.50	54.23 ± 0.49	62.12 ± 0.55	64.41 ± 0.56
25 min	63.12 ± 0.50	65.20 ± 0.52	59.23 ± 0.49	61.38 ± 0.50	57.11 ± 0.47	70.18 ± 0.61	61.42 ± 0.48	57.02 ± 0.46	64.65 ± 0.53	67.83 ± 0.55
30 min	65.40 ± 0.70	66.60 ± 0.65	62.50 ± 0.48	64.60 ± 0.55	61.10 ± 0.52	71.62 ± 0.74	63.90 ± 0.58	61.69 ± 0.62	66.40 ± 0.54	69.80 ± 0.63

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

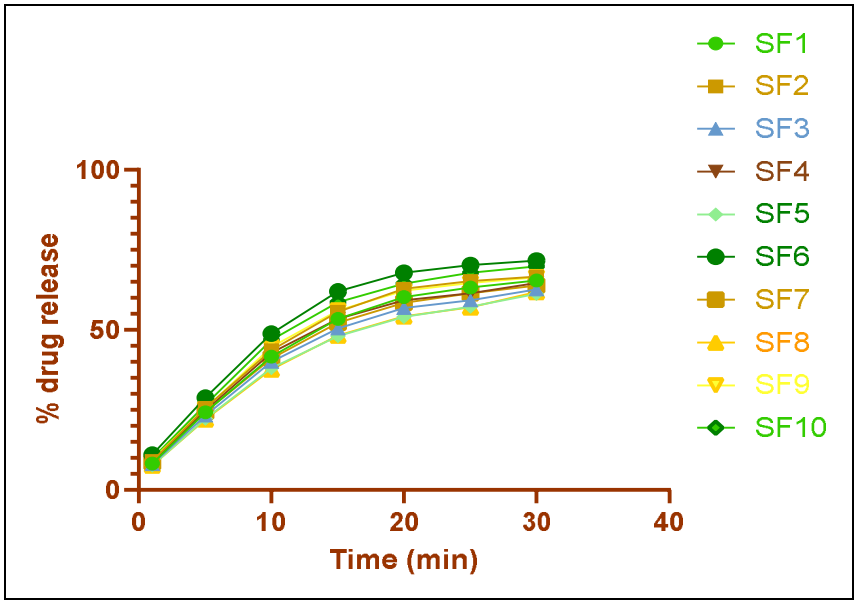

Figure 6: Cumulative % drug release profile of Valsartan Orodispersible tablets

XRD analysis

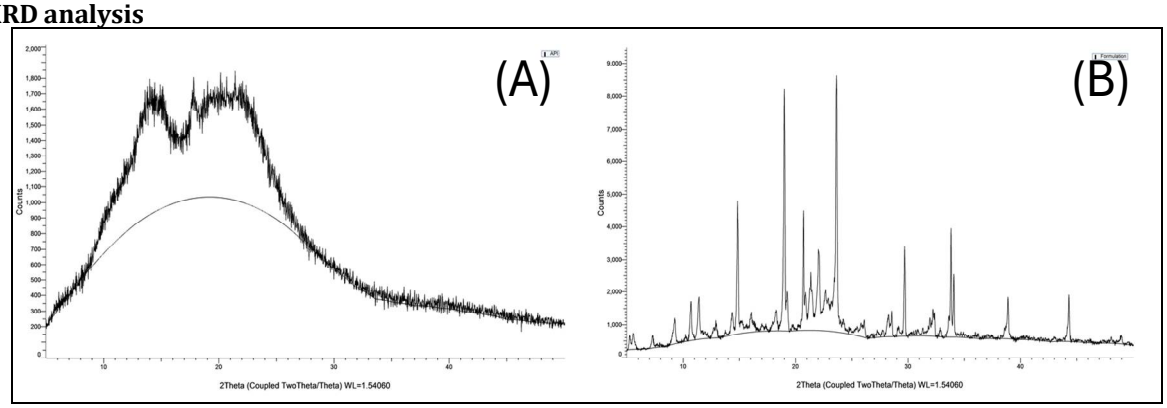

Figure 7: X-ray diffraction (XRD) patterns of (A) pure Valsartan and (B) optimized Valsartan orodispersible tablet formulation.

Optimization

Tablet Hardness (Y_1)

The model created for tablet hardness was established as statistically significant by the p-value found in Table 10. There is a very strong correlation between what was measured and what the model predicted, since the Adjusted R^2 is 0988 and the Predicted R^2 is 0.9646. Table 11 reveals through ANOVA that Sodium Starch Glycolate (Factor B) played the greatest role, as its F-value was 733.41 ($p < 0.0001$), while Kyron T-314 (Factor A) was following closely with an F-value of 45.48 ($p = 0.0025$). B^2 played an important role ($p = 0.0150$), but AB and A^2 did not make a significant difference.

The final polynomial equation derived from regression analysis was:

Hardness (Y_1) = 3.85 + 0.156532 * A + -0.62859 * B + -0.0175 * AB + -0.070625 * A^2 + -0.125625 * B^2

This means that both linear and squared terms of Sodium Starch Glycolate greatly affected the hardness of the tablets. Figure 8A and 8B show that additional Sodium Starch Glycolate made the hardness higher, but Kyron T-314 had relatively little effect. A close look at the 3D plot makes it obvious that Factor B has a significant effect on the outcome, like the ANOVA analysis showed.

Disintegration Time (Y_2)

The fit of the disintegration time model was very good, as was reported by the low p-value in Table 10 (< 0.0001). It was clear from the model that Adjusted R^2 and Predicted R^2 are both 1.0000 and 0.9999, therefore the model was very accurate. From Table 11, it is clear that both formulation factors had strong influences: Sodium Starch Glycolate (Factor B) came out as F-value of 442484.39 ($p < 0.0001$) which was the highest of any effect and Kyron T-314 (Factor A) followed with a value of 31760.96 ($p < 0.0001$). Both the interaction term AB ($p < 0.0001$) and the quadratic effects of A^2 and B^2 ($p < 0.0001$) were found to be important, implying that the variables affected each other and the relationship was curved.

The derived polynomial equation was:
Disintegration Time (Y_2) = 27.65 + 0.636948 * A + 2.37742 * B + 0.1125 * AB + 0.1725 * A^2 + 0.26 * B^2
This equation reflects the major role of Sodium Starch Glycolate in increasing disintegration time, especially at higher concentrations. As shown in Figures 8C and 8D, the disintegration time significantly increased with increasing amounts of both excipients, with Sodium Starch Glycolate exerting a dominant influence. The 3D surface plot confirmed a strong interaction between A and B, visualized as a steep incline across both axes.

% Drug Dissolution at 30 Minutes (Y_3)

Analysis showed that the quadratic model explaining drug dissolution at 30 minutes was very significant, as it had a p-value of 0.0003. The values of Adjusted R^2 (0.9789) and Predicted R^2 (0.9432) prove the model has excellent accuracy and no signs of overfitting. There is no evidence of a lack of fit since the p-value from the test is high (p = 0.6949). Quoting ANOVA, Sodium Starch Glycolate significantly affected the results (F=119.86, p = 0.0004), while Kyron T-314 (p = 0.0020) came in second with an F-value of 51.13. B^2 was strongly significant among the quadratic terms (F = 227.46, p = 0.0001), while A^2 (p = 0.0597) and the interaction AB (p = 0.0645) were close to significance.
The regression equation was:
% Drug Dissolution (Y_3) = 62.095 + 1.24764 * A + 1.91027 * B + 0.625 * AB + 0.60125 * A^2 + 3.48125 * B^2
This polynomial model indicates a nonlinear effect of both excipients, particularly highlighting the pronounced curvature effect of Sodium Starch Glycolate. While both linear terms positively influenced dissolution, the strong negative coefficient of B^2 reveals that excess starch may reduce drug release at higher concentrations. The response surface plots showed a sharper gradient along the B-axis, emphasizing the dominant role of Sodium Starch Glycolate in modulating dissolution performance, while the slope along the A-axis was comparatively mild.

Table 10. Model Fit Summary for Response Variables

Response Variable	Model	Sequential p-value	Lack of Fit p-value	Adjusted R^2	Predicted R^2	Remark
Hardness	Quadratic	0.0359	0.1369	0.9888	0.9646	Suggested
Disintegration Time	Quadratic	< 0.0001	–	1.0000	0.9999	Suggested
% Drug Dissolution	Quadratic	0.0003	0.6950	0.9789	0.9432	Suggested

Table 11: ANOVA results for quadratic models of response variables

Source	Sum of Squares	df	Mean Square	F-value	p-value	Remark
Hardness (Y_1)						
Model	3.432	5	0.6864	159.26	0.0001	Significant
A – Kyron T-314	0.1960	1	0.1960	45.48	0.0025	Significant
B – Sodium starch glycolate	3.1610	1	3.1610	733.41	< 0.0001	Significant
AB	0.0012	1	0.0012	0.28	0.6222	NS
A^2	0.0228	1	0.0228	5.29	0.0829	NS
B^2	0.0721	1	0.0721	16.74	0.0150	Significant
Disintegration Time (Y_2)						
Model	48.8432	5	9.7686	95593.85	< 0.0001	Significant
A – Kyron T-314	3.2456	1	3.2456	31760.96	< 0.0001	Significant
B – Sodium starch glycolate	45.2171	1	45.2171	442484.39	< 0.0001	Significant
AB	0.0506	1	0.0506	495.41	< 0.0001	Significant
A^2	0.1360	1	0.1360	1331.15	< 0.0001	Significant
B^2	0.3090	1	0.3090	3024.09	< 0.0001	Significant
Drug Release at 30 min (Y_3)						
Model	103.05	5	20.61	84.62	0.0004	Significant
A – Kyron T-314	12.45	1	12.45	51.13	0.0020	Significant
B – Sodium starch glycolate	29.19	1	29.19	119.86	0.0004	Significant
AB	1.56	1	1.56	6.42	0.0645	NS
A^2	1.65	1	1.65	6.78	0.0597	NS
B^2	55.40	1	55.40	227.46	0.0001	Significant

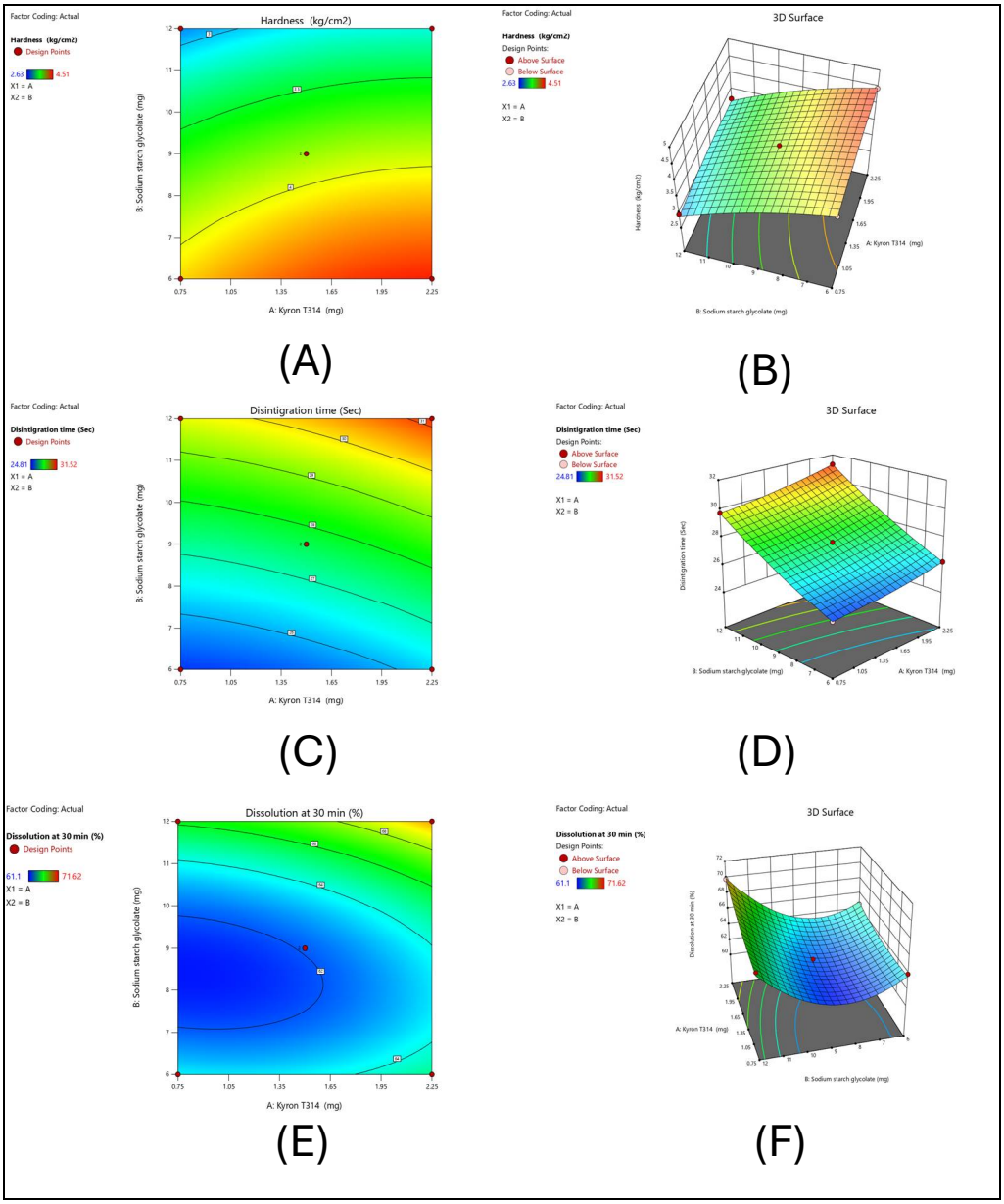

Figure 8: Response surface methodology-based contour and 3D surface plots illustrating the influence of formulation variables on key quality attributes of Valsartan orodispersible tablets. (A–B) Effect of Kyron T-314 and Sodium Starch Glycolate concentrations on tablet hardness; (C–D) Combined influence of independent variables on disintegration time; (E–F) Effect of formulation composition on cumulative drug release at 30 minutes, derived from Central Composite Design analysis.

Statistical optimization of formulation

The statistically optimized formulation (SF10), composed of 2.25 mg Kyron T-314 and 12 mg Sodium Starch Glycolate, showed strong agreement between predicted and experimental values. Predicted hardness was 3.162 kg/cm^2 versus experimental 3.23 kg/cm^2; disintegration time predicted at 31.009 s matched closely with 31.22 s observed; drug release at 30 min was 69.401% predicted and 69.8% experimental. These results confirm model validity (Table 12).

Table 12: Statistical optimization of formulation

F. Code	Composition	Amount (mg)	Response	Predicted Value	Experimental Value	Relative Error (%)
SF10	Kyron T-314	0.75	Hardness (kg/cm^2)	3.162	3.23	2.15
	Sodium Starch Glycolate	6	Disintegration Time (sec)	31.009	31.22	0.68
			In-vitro Drug Release (%)	69.401	69.8	0.57

In-vitro Drug Release Comparison Between Optimized Orodispersible and Marketed Conventional Valsartan Tablet

The optimized orodispersible tablet (SF10) showed significantly enhanced drug release compared to the marketed conventional tablet. At 1 min, SF10 released 9.87 ± 0.48%, whereas the marketed tablet released only 1.82 ± 0.43%. At 30 min, SF10 achieved 69.80 ± 0.63% release versus 9.98 ± 0.60% for the marketed product. This marked improvement in dissolution is illustrated in Figure 9 and detailed in Table 13.

Table 13. Comparative In-vitro Drug Dissolution Profile of Optimized Orodispersible Tablet (SF10) and Marketed Conventional Valsartan Tablet

Time (min)	Optimized Orodispersible Tablet (SF10)	Marketed Conventional Tablet
1	9.87 ± 0.48	1.82 ± 0.43
5	26.73 ± 0.62	3.47 ± 0.51
10	46.91 ± 0.58	5.92 ± 0.58
15	58.63 ± 0.54	7.04 ± 0.61
20	64.41 ± 0.56	8.25 ± 0.59
25	67.83 ± 0.55	9.31 ± 0.56
30	69.80 ± 0.63	9.98 ± 0.60

All values are expressed as mean± SD (n=3)

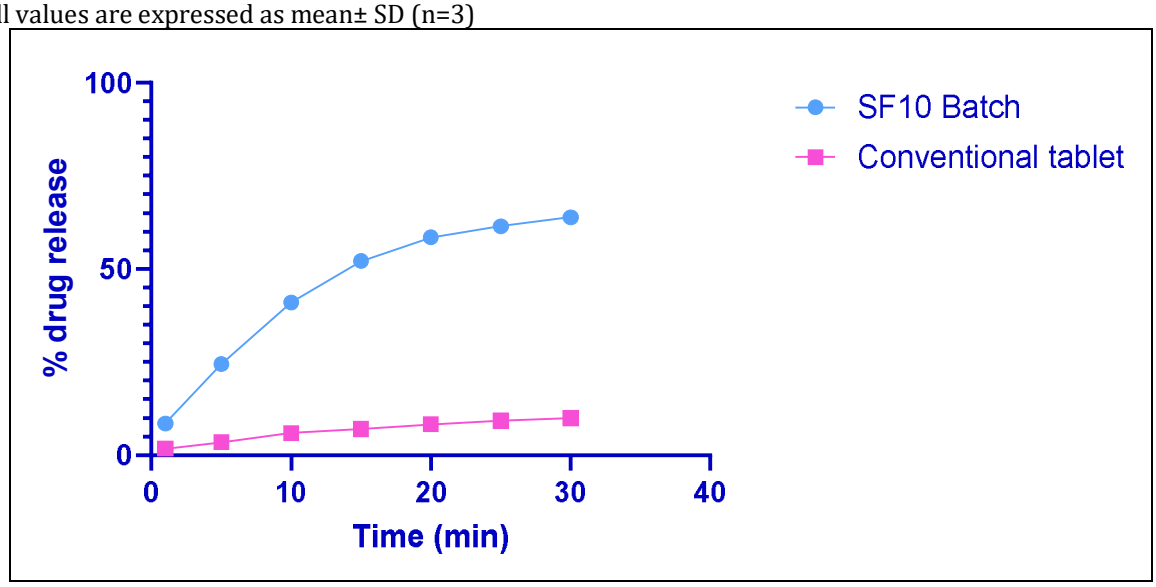

Figure 9: Comparative in-vitro drug release profile of the optimized Valsartan Orodispersible tablet (SF10) and the marketed conventional tablet.

Results of release kinetics study

The in-vitro drug release kinetics of the optimized Valsartan orodispersible tablet (SF10) were evaluated using various mathematical models. Among all, the Korsmeyer-Peppas model demonstrated the best fit with the highest R^2 value of 0.9744, indicating a controlled release mechanism governed by anomalous (non-Fickian) transport. The Higuchi model also showed a strong linear relationship (R^2 = 0.9732), suggesting diffusion as a key mechanism. Comparatively, the First-order model exhibited a good correlation (R^2 = 0.9476), whereas the Zero-order (R^2 = 0.9218) and Hixson-Crowell (R^2 = 0.9275) models showed relatively lower but acceptable fits. These findings confirm that the drug release follows a complex mechanism, primarily diffusion-controlled with contributions from erosion or swelling processes.

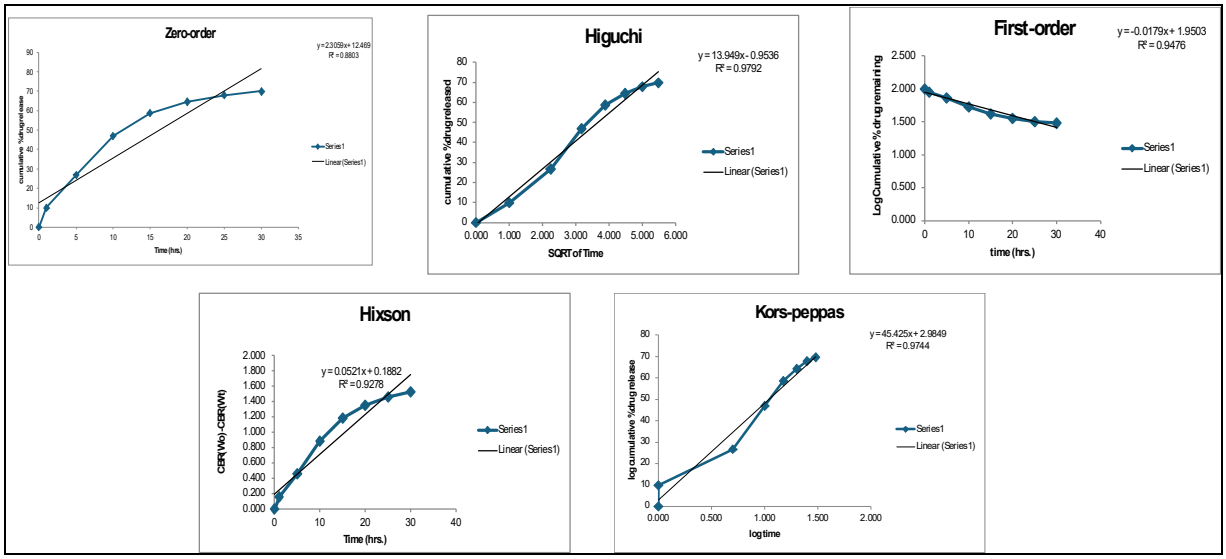

Figure 10: Release kinetics graphs of the optimized Valsartan Orodispersible tablet formulation

Results of accelerated stability study

This formulation (SF10) remained unchanged during 3 months of conditions used to accelerate stability testing (40 °C, 75% RH). We did not notice any changes in the way the sample looked. The hardness of the samples fell slightly from 4.10 ± 0.12 to 4.06 ± 0.10 kg/cm^2 and the time required for disintegration increased by 0.85 seconds from 25.18 ± 0.8 to 26.03 ± 0.9 s. The drug content remained very high (98%) and drug release at half an hour was constant. The statistics are presented in Table 14.

Table 14. Accelerated Stability Study of Optimized Batch SF10 (40 ± 2°C / 75 ± 5% RH)

Parameter	Initial (0 Month)	1 Month	2 Months	3 Months
Appearance	White, circular, smooth	No change	No change	No change
Hardness (kg/cm^2)	4.10 ± 0.12	4.08 ± 0.10	4.07 ± 0.11	4.06 ± 0.10
Disintegration Time (sec)	25.18 ± 0.8	25.67 ± 0.9	25.89 ± 0.8	26.03 ± 0.9
Drug Content (%)	99.0 ± 0.9	98.9 ± 1.0	98.7 ± 1.2	98.6 ± 1.1
% Drug Release at 30 min	69.80± 0.63	69.10 ± 0.71	68.92± 0.68	67.78 ± 0.69

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

DISCUSSION

A QbD approach was used to successfully make and enhance an ODT containing Valsartan that resolves its low aqueous solubility and low oral absorption. The creation of the linear calibration curve (Figure 3) provided solid evidence for the method's dependability in subsequent drug quality and dosage evaluations. Valsartan displayed high solubility in DMSO (43.55 ± 1.6 mg/mL) and phosphate buffer pH 6.8 (43.53 ± 2.1 mg/mL), a small amount in water (0.027 ± 0.002 mg/mL) and low solubility in other solvents, all consistent with its Class II in the BCS. DSC experiments revealed that while the melting endotherm for Valsartan fell at 102.28 °C alone, it was seen at 102.64 °C in the blend and an extra peak appeared at 168.15 °C related to the inert ingredients [41]. The FTIR results of the mixture (Figure 5, Table 4) confirmed that the tablet's ingredients did not react with Valsartan, showing its stability. Tests before compression indicated good powder blending, since angles of repose were between 26.74° and 29.58° and the Carr's Index sat between 12.24% and 15.22%. The results match previous data on compressibility for ODTs. According to organoleptic observations (Table 6), all tablets appeared alike, were without a smell and had no physical issues, making them suitable for older users, mainly because of patient compliance [42].

Measurements using dimensional analysis (Table 7) showed that the tablets were uniform in weight, their thickness and the diameter. Hardness of the tablets were 2.63–4.54 kg/cm^2, fulfilling the strength standards for use and packaging [43]. Table 8 confirms that every batch was proved robust because the friability values were below the 1% limit for pharmacopoeia. Wetting was completed within seconds, taking 14.9 to 24.3 seconds and disintegration time was between 24.81 and 31.52 seconds, according to standards for ODT performance [44]. All formulations contained at least 97% of their drug content, showing the blend was regular in every batch. Using Central Composite Design, it was shown that Sodium Starch Glycolate strongly affected all three main quality traits: hardness, disintegration time and how

much drug dissolves in water. According to the regression model equations, B (Sodium Starch Glycolate) showed higher performance than A (Kyron T-314) through graphical analysis as seen in Figures 8A–8F. As expected, according to previous findings, crosslinked polymers positively contribute to breakup in On-Demand Therapy systems [45]. Formulated SF10 with Kyron T-314 (2.25 mg) and Sodium Starch Glycolate (12 mg) had almost the same as predicted values for hardness (3.23 kg/cm^2), disintegration time (31.22 s) and the percentage of drug release (69.8%), according to Table 12. The results confirm the usefulness of the statistical model and the suitability of the chosen design space [46].

Tests in the laboratory showed that the improved orodispersible tablet (SF10) has a faster and more complete release than the marketed conventional tablet (Table 13, Figure 9). At 30 minutes, the SF10 formulation had released almost all of its drug; the marketed tablet had not released even 10% in the same time. Enhancing the release profile depends on the substance being better wetted, more efficiently disintegrating and being dissolved by Beta-cyclodextrin [47]. Drug release from the MCG was illustrated by a first order model in the drug release kinetics analysis (Figure 10). Such kinetics indicate that the delivery performs well in the human body and match earlier reported processes of polymer ODT formulations. During 3 months accelerated testing, the optimized batch maintained its physical and chemical stability, as seen in Table 14. Nothing in the formulation's appearance changed and the hardness, disintegration time, amount of drug and rate of dissolving all stayed suitable, showing it can be stored safely [48]. Combined, these results verify that the Valsartan ODTs can be made effective using hydrophilic excipients and superdisintegrants in a design chosen by statistics. If these improvements are sustained, both adherence to treatment and patient outcomes may improve for populations who have trouble swallowing. The results harmonize well with what is required by regulators for rapid-dissolving forms and provide a firm background for going further with animal experiments.

CONCLUSION

The study developed and improved a Valsartan orodispersible tablet using quality by design which resulted in higher solubility, faster disintegration and improved dissolution. In comparison, the optimized formulation (SF10) disintegrated much faster (31.22 s), had higher drug uniformity (98.8 ± 1.0 %) and released more drug (69.80% at 30 minutes) than the marketed product. These characteristics could provide faster start of treatment and better availability, making treatment easier for hypertensive patients with difficulties in swallowing or following medication. Tests on stability showed that the paint could stand up well to speeding up the aging process. The good results suggest that this formulation is a suitable replacement for current antihypertensive approaches. More in vivo studies should be done to confirm that the optimized orodispersible tablet is both effective and has therapeutic benefits for patients.

Abbreviations

ANOVA: Analysis of Variance; FTIR: Fourier-transform infrared spectroscopy; UV: Ultra-violet spectroscopy; DSC: Differential Scanning Calorimetry; ODT: Orodispersible Tablet; QbD: Quality by Design; CCD: Central Composite Design; API: Active Pharmaceutical Ingredient; SD: Standard Deviation; RPM: Revolutions Per Minute; USP: United States Pharmacopeia; XRD: X-ray Diffraction; HPLC: High Performance Liquid Chromatography; DMSO: Dimethyl Sulfoxide; DMF: Dimethylformamide; DCM: Dichloromethane; MCC: Microcrystalline Cellulose; NaOH: Sodium Hydroxide; MW: Molecular Weight; R^2: Coefficient of Determination; Df: Degree of Freedom.

Acknowledgement

The authors deeply thank Dr. Vithalrao Vikhe Patil Foundation's College of Pharmacy in Ahmednagar for enabling this research through their necessary facilities. At the conclusion we thank the members of the Department of Pharmaceutical Quality Assurance who continuously supported us with their guidance during every step of this work.

Authors contribution

All authors contributed equally.

Conflict of interest

The authors declare no conflict of interest.

Funding

Nil

REFERENCES

1. Fuchs, F.D. & Whelton, P.K. (2020). High blood pressure and cardiovascular disease. Hypertension, 75:285–292.
2. Zhou, B., Perel, P., Mensah, G.A. & Ezzati, M. (2021). Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. Nat. Rev. Cardiol., 18:785–802.
3. Asanga, D.E. (2023). The prevalence of high blood pressure in adult and elderly: Implication and remedies. Int. J. Adv. Res., 7:1–6.
4. Chen, A., Mocumbi, A.O., Ojji, D.B., Waite, L., Chan, Y.-K., Beilby, J. et al. (2024). Projected burden and distribution of elevated blood pressure levels and its consequence among adolescents in sub-Saharan Africa. J. Glob. Health, 14:04136.
5. Kothavale, A., Puri, P. & Yadav, S. (2022). The burden of hypertension and unmet need for hypertension care among men aged 15–54 years: A population-based cross-sectional study in India. J. Biosoc. Sci., 54:1078–1099.
6. Farhadi, F., Aliyari, R., Ebrahimi, H., Hashemi, H., Emamian, M.H. & Fotouhi, A. (2023). Prevalence of uncontrolled hypertension and its associated factors in 50–74 years old Iranian adults: A population-based study. BMC Cardiovasc. Disord., 23:318.
7. Kario, K. & Williams, B. (2022). Angiotensin receptor–neprilysin inhibitors for hypertension—hemodynamic effects and relevance to hypertensive heart disease. Hypertens. Res., 45:1097–1110.
8. Ramirez-Hernandez, D., Lezama-Martinez, D., Velazco-Bejarano, B., Valencia-Hernandez, I., Lopez-Sanchez, P., Fonseca-Coronado, S. et al. (2024). The beneficial effects of swimming training preconditioning on reducing vascular reactivity in chronic myocardial infarction: Independent of NO production. J. Renin Angiotensin Aldosterone Syst., 25:14703203241294029.
9. Nasrallah, D., Abdelhamid, A., Tluli, O., Al-Haneedi, Y., Dakik, H. & Eid, A.H. (2024). Angiotensin receptor blocker-neprilysin inhibitor for heart failure with reduced ejection fraction. Pharmacol. Res., 204:107210.
10. Sahana, U., Wehland, M., Simonsen, U., Schulz, H. & Grimm, D. (2023). A systematic review of the effect of vericiguat on patients with heart failure. Int. J. Mol. Sci., 24:11826.
11. Brignone, J., Assersen, K.B., Jensen, M., Jensen, B.L., Kloster, B., Jønler, M. et al. (2021). Protection of kidney function and tissue integrity by pharmacologic use of natriuretic peptides and neprilysin inhibitors. Pflüg. Arch. Eur. J. Physiol., 473:595–610.
12. Biswas, R., Mondal, S. & Ansari, M.A. (2024). Orodispersible tablets: A novel approach to combat dysphagia. Int. J. Pharm. Sci. Rev. Res., 84:12–16.
13. Patel, J. (2021). Formulation development and evaluation of orally disintegrating antiretroviral pediatric tablet. M. Pharm. Thesis, Gujarat Technological University.
14. Roy, D., De, A., Biswas, S., Pramanick, N., Das, A. & Mondal, S. (2023). An overview on mouth dissolving tablets. Pharm. Innov. J., 50:21–28.
15. Cornilă, A., Iurian, S., Tomuţă, I. & Porfire, A. (2022). Orally dispersible dosage forms for paediatric use: Current knowledge and development of nanostructure-based formulations. Pharmaceutics, 14:1621.
16. Ali, M.S. & Elsaman, T. (2021). Development and validation of the UV spectrophotometric method for simultaneous determination of paracetamol and pseudoephedrine in bulk and combined tablet dosage form. Pharm. Chem. J., 54:1306–1310.
17. Abu Shawish, H.M., Saadeh, S.M. & Al-Kahlout, S.T. (2022). PVC membrane, coated-wire, and carbon-paste electrodes for potentiometric determination of vardenafil hydrochloride in tablet formulations and urine samples. Sens. Int., 3:100175.
18. Shakeel, F., Haq, N., Alsarra, I. & Alshehri, S. (2021). Solubility data, solubility parameters and thermodynamic behavior of an antiviral drug emtricitabine in different pure solvents: Molecular understanding of solubility and dissolution. Molecules, 26:746.
19. Annisa, V., Saifullah Sulaiman, T.N., Kharis Nugroho, A. & Endro Nugroho, A. (2022). Determination of saturated ketoconazole solubility using spectrophotometry UV-Vis method. Res. J. Pharm. Technol., 15:4795–4800.
20. Aswathy, K.N., Asdaq, S.M.B., Saritha, C.K., Thomas, L., Haridas, N., Viswanad, V. et al. (2022). Formulation and in-vitro characterization of fast-disintegrating herbal extract sublingual immunotherapy tablet for peanut-induced allergic asthma. Saudi J. Biol. Sci., 29:1283–1297.
21. van Haaren, C., De Bock, M. & Kazarian, S.G. (2023). Advances in ATR-FTIR spectroscopic imaging for the analysis of tablet dissolution and drug release. Molecules, 28:4705.
22. Jadhav S, Dighe P, Kumbhare M. (2025). Synthesis In Vitro Evaluation and Molecular Docking Studies of Novel Pyrazoline Derivatives as Promising Bioactive Molecules. J Pharm Sci Comput Chem;1.
23. Verma, V. (2018). Formulation and evaluation of orodispersible tablet of Montelukast sodium and Desloratadine. Int. J. Pharm. Sci., 5:1–6.
24. M., Agrawal, S. & Khan, A. (2018). Formulation and evaluation of nanosuspension of valsartan. Int. J. Curr. Pharm. Res., 10(2):68–72.
25. Pandey, A.K., Tyagi, C.K., Shah, S.K., Tiwari, S.M., Rawat, P.K. & Sahu, G.D. (2023). Formulation development and evaluation of directly compressed polyherbal tablets for the management of infections caused by helminthes. Mater. Today Proc., 80:3532–3539.
26. Vlad, R.-A., Antonoaea, P., Todoran, N., Rédai, E.-M., Bîrsan, M., Muntean, D.-L. et al. (2022). Development and evaluation of cannabidiol orodispersible tablets using a 2^3-factorial design. Pharmaceutics, 14:1467.
27. Elshahat, A., Hasan, A.A., Elghamry, H.A. & Balata, G.F. (2024). Formulation and optimization of olanzapine-carboxylic acid cocrystals orodispersible tablets: In-vitro/In-vivo study. J. Drug Deliv. Sci. Technol., 100:106093.

28. Alalaiwe, A., Alsenaidy, M.A., Almalki, Z.S. & Fayed, M.H. (2023). Development and optimization of sildenafil orodispersible mini-tablets (ODMTs) for treatment of pediatric pulmonary hypertension using response surface methodology. Pharmaceutics, 15:923.
29. Ali, A.T., Nasir, F., Fazli, H., Hidayatullah, T., Pervez, S., Sadia, R. et al. (2025). Quality by design formulation approach for the development of orodispersible tablets of dexlansoprazole. Drug Des. Devel. Ther., 19:4163–4181.
30. Dash, G.S., Murthy, P.N. & Chowdary, K.A. (2022). Selection and optimization of most efficient superdisintegrant for the formulation of dispersible tablets of tramadol hydrochloride. Int. J. Pharm. Pharm. Sci., 14(7):21–26.
31. Kinani, A.A.Y. & Taghi, H.S. (2022). Formulation and characterization of orodispersible tablet of glimepiride. J. Adv. Pharm. Technol. Res., 13:252.
32. Mankar, S.D., Satpute, A., Siddheshwar, S.S., Bhawar, S.B. & Dighe, S.B. (2023). Design, development and optimization of mouth dissolving tablet of ambrisentan using design expert software. Int. J. Appl. Pharm., 15(4):282–290.
33. Kumar Thummala, U., Guptha Maddi, E. & Rani Avula, P. (2022). Orodispersible films of Ledipasvir and Sofosbuvir combination: Formulation optimization and development using design of experiments. Asian J. Pharm. Res., 12(1):11–18.
34. Prohit P, Pakhare P, Pawar V, Dandade S, Waghmare M, Shaikh F, et al. (2025). Formulation and Comparative Evaluation of Naproxen-Based Transdermal Gels. J Pharm Sci Comput Chem;1. https://doi.org/10.48309/jpscc.2025.522940.1009
35. Anonymous. (2024). Formulation and evaluation of domperidone orodispersible tablets. Res. Gate Preprint, accessed May 23, 2025.
36. Pandey, P., Pal, R., Bharath, K., Akilandeshwari, A., Koli, M. & N., N. et al. (2023). Design of experiments (DoE) manipulation in the formulation and optimization of a traditional Ayurvedic medicine derived from dried extract of Senegalia catechu enhanced through statistical analysis. J. Pharmacogn. Phytochem., 12(6b):159–169.
37. Tafere, C., Yilma, Z., Abrha, S. & Yehualaw, A. (2021). Formulation, in vitro characterization and optimization of taste-masked orally disintegrating co-trimoxazole tablet by direct compression. PLoS ONE, 16:e0246648.
38. Singh, S., Khare, E., Srivastava, S., Rajput, H.S. & Singh, L.K. (2022). Design, formulation, and optimization of novel mouth dissolving tablet of drug ketorolac using special super disintegrate. Asian J. Pharm., 16:371.
39. González-González, O., Ramirez, I.O., Ramirez, B.I., O'Connell, P., Ballesteros, M.P. & Torrado, J.J. et al. (2022). Drug stability: ICH versus accelerated predictive stability studies. Pharmaceutics, 14:2324.
40. Kumar, G., Bhatt, M. & Dhyani, A. (2025). Formulation and optimization of fast dissolving thin strips of Desvenlafaxine HCl by using quality by design (QbD) approach. Indian J. Pharm. Educ. Res., 59:913–922.
41. Ahire, P.P., More, Y.M. & Kothawade, V.R. (2024). Formulation, development and evaluation of famotidine orodispersible tablets. Res. J. Pharm. Dos. Forms Technol., 16(4):317–324.
42. Khare, E. (2022). Design, formulation, and optimization of novel mouth dissolving tablet of drug ketorolac using special super disintegrate. Asian J. Pharm., 16:1–6.
43. Salam, S., Fathima, R., Sreelekha, P.P., Kavya, M. & Anjali, E. (2023). Statistical optimization of fast dissolving tablet contains isosorbide dinitrate for the treatment of angina pectoris. Biosci. Biotechnol. Res. Asia, 20:1373–1381.
44. Gharat, S.N., Bhongade, Y.M. & Sawkare, A.D. (2024). Formulation and optimization of fast-dissolving film containing rizatriptan benzoate. Int. J. Pharm. Sci., 10:1–6.
45. Kaur, L., Bala, R., Kanojia, N., Nagpal, M. & Dhingra, G.A. (2024). Formulation development and optimization of fast dissolving tablets of aceclofenac using natural superdisintegrant. Res. Pharm. Technol., 11:1–7.
46. Borse, L.B., Bendale, A.R., Borse, S.L., Naphade, V.D. & Jadhav, A.G. (2022). Formulation and evaluation of mouth dissolving tablet rivaroxaban and its validation. Biosci. Biotechnol. Res. Asia, 19:943–954.
47. Sharma, S. & Gupta, G.D. (2024). Development and optimization of fast-dissolving tablets of promethazine theoclate using vacuum drying technology by 3-factor, 3-level response surface full factorial design. Int. J. Pharm. Sci., 12:1–8.
48. Ghumman, S.A., Hameed, H., Noreen, S., Al-Hussain, S.A., Kausar, R. & Irfan, A. et al. (2023). In vitro/in vivo evaluation of clomipramine orodispersible tablets for the treatment of depression and obsessive-compulsive disorder. Pharmaceuticals, 16:265.