RESEARCH PAPER

Development and Optimization of Chewable Tablet Formulation of Piribedil Using Experimental Design

Mo. Anas Ghanchi[1], Gazala Y. Ansari[2], Jitendra O. Bhangale[3*]

[1] Student, Smt. N. M. Padalia Pharmacy College, Ahmedabad, Gujarat - 382210, India.
Email: anasshalimar03@gmail.com

[2] Associate Professor, Smt. N. M. Padalia Pharmacy College, Ahmedabad, Gujarat - 382210, India.
Email: agazala38@gmail.com

[3*] Professor and Principal, Smt. N. M. Padalia Pharmacy College, Ahmedabad, Gujarat - 382210, India.
Email: jitu2586@gmail.com, ORCID: https://orcid.org/0000-0002-2049-3610 (Corresponding Author)

***Corresponding Author:** Dr. Jitendra O. Bhangale, Email: jitu2586@gmail.com

Received: 20th Feb, 2026 | **Revised:** 4th Mar, 2026 | **Accepted:** 25th Mar, 2026 | **Available Online:** 10th Apr, 2026

ABSTRACT

The present study was undertaken to develop and optimize chewable tablet formulations of Piribedil using experimental design for improved patient compliance and rapid drug release in Parkinson's disease management. Piribedil, a dopamine agonist with low oral bioavailability (<10%) and extensive first-pass metabolism, requires formulation strategies to enhance its therapeutic effectiveness and ease of administration. Preformulation studies confirmed the identity and purity of the drug, with melting point observed in the range of 94–99 °C and λmax at 284 nm. The calibration curve demonstrated excellent linearity (R^2 = 0.9997), validating the analytical method. FTIR studies confirmed compatibility between drug and excipients. Taste masking was achieved using ion-exchange resins, where Tulsion 335 exhibited maximum drug loading (≈91.25%) at a 1:4 drug–resin ratio, indicating superior complexation efficiency. Chewable tablets were prepared using direct compression and evaluated for pre- and post-compression parameters, all of which were within acceptable limits. Among all batches, formulation C9 exhibited the best performance with minimum wetting time (13.31 sec), fastest disintegration time (15.84 sec), highest water absorption ratio (81.49%), and nearly complete drug release (99.25%) within 10 minutes. Thus, the optimized chewable tablet formulation of Piribedil demonstrated effective taste masking, rapid disintegration, and enhanced drug release, offering a promising patient-friendly approach for Parkinson's disease management.

Keywords: Piribedil; Chewable Tablets; Ion-Exchange Resin; Taste Masking.

How to cite this article: Ghanchi MA, Ansari GY, Bhangale JO. Development and Optimization of Chewable Tablet Formulation of Piribedil Using Experimental Design. Int J Drug Deliv Technol. 2026;16(28s):1019-1031. DOI: 10.25258/ijddt.16.28s.119

Source of support: Nil.

Conflict of interest: The authors declare no conflict of interest.

INTRODUCTION

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder that predominantly affects the elderly population and is characterized by motor impairments such as bradykinesia, rigidity, tremors, and postural instability. Effective management of PD largely depends on maintaining consistent dopaminergic stimulation to control symptoms and preserve patients' functional independence. However, conventional oral dosage forms often present challenges in geriatric patients, who frequently suffer from dysphagia, cognitive impairment, and complex medication regimens, ultimately compromising treatment adherence and therapeutic outcomes.[1-2]

Piribedil, a selective dopamine D2/D3 receptor agonist, is widely used in the management of PD either as monotherapy in early stages or as an adjunct to levodopa therapy. Despite its clinical utility, piribedil exhibits certain pharmacokinetic limitations, including extensive first-pass hepatic metabolism and a relatively short elimination half-life, which may lead to fluctuating plasma drug concentrations and inconsistent symptom control. Additionally, the need for repeated dosing can further reduce patient compliance, particularly in elderly populations.[3]

To address these limitations, the development of an alternative, patient-friendly dosage form is warranted. Chewable tablets offer a promising approach by improving ease of administration, especially for patients with swallowing difficulties. These formulations facilitate rapid disintegration in the oral cavity, potentially enhancing the onset of action and promoting more uniform drug dispersion prior to gastrointestinal absorption. Furthermore, the incorporation of taste-masking agents can improve palatability, which is particularly important for long-term therapy.[4]

From a formulation science perspective, achieving an optimal balance between critical quality attributes—such as hardness, disintegration time, mouthfeel, and drug release profile—requires a systematic and scientific approach. The application of experimental design techniques, such as factorial design or response surface methodology, enables efficient identification and optimization of key formulation and process variables. This approach not only reduces the number of experimental trials but also ensures the development of a robust and reproducible formulation.[5-6]

Therefore, the present study is rationally designed to develop and optimize a chewable tablet formulation of piribedil using experimental design, with the aim of enhancing patient compliance, improving drug release characteristics, and ensuring consistent therapeutic performance suitable for clinical application.

MATERIALS AND METHOD

MATERIALS: Tulsion, Kyron T 114, SSG, D-mannitol, Aspartame, SLS, MCC, Magnesium stearate and Talc were obtained from Chemdyes Corporation, Rajkot, Gujarat.

Formulation of Drug Resin Complex

Methods of preparation of resinate:

Preparation of Drug-resin complexes (DRC):

DRC were prepared by adding 100 mg of activated resin that was swollen for 60 min in a beaker containing 50 ml distilled water, 100 mg of drug was added separately into each of the beaker containing the activated resin, to prepare slurry with the aid of magnetic stirrer for 90 min at 60°C. Filter the reaction mixture by Whatmann filter paper. Collect the residue & wash properly. Resins were washed successively with distilled water, 0.1 N HCl and 0.1 N NaOH in separate processes for activation. All resins were dried at room temperature and kept in an amber glass vial. Allow the washed complex for drying on room temperature for 2-3 hrs. From the filtrate 1ml was taken and diluted to 10 ml with distilled water. The unbound drug in the filtrate was estimated spectrophotometrically at 242 nm. The rate of addition of drug to resin slurry had profound effect on the taste masking and free drug concentration of drug-resin complex. Slow addition of drug showed low % of free drug in the mixture and better taste masking while fast addition showed high % of free drug in the mixture and poor taste masking of drug-resin complex. Drug was added with constant time interval of 4-5 minute.[7-8]

3^2 Factorial design

A 3^2 full factorial design was employed to investigate the combined influence of formulation variables on the performance of fast disintegrating tablets containing the drug–resin complex. Two independent variables were selected: the amount of drug–resin complex (X_1) and the concentration of superdisintegrant (SSG) (X_2), each evaluated at three levels (−1, 0, +1). The dependent responses studied were *in vitro* disintegration time (Y_1) and percentage cumulative drug release (%CDR, Y_2). Experimental data obtained from nine formulation runs were analyzed using Design-Expert® software, applying ANOVA to assess the significance of model terms. A quadratic polynomial equation was used to describe the relationship between independent variables and responses, incorporating linear, interaction, and quadratic effects. The model enabled systematic evaluation of factor interactions and optimization of formulation parameters. The design matrix included both coded and actual values, where drug–resin ratios (1:4 to 1:6) and SSG concentrations (2–6 mg) were varied across the experimental runs, ensuring a comprehensive assessment of formulation behavior.[9-10]

Formulation of Chewable Tablet of Piribedil by Direct Compression Method

The chewable tablets of Piribedil were formulated using an ion-exchange resin complex across nine different batches (C1–C9) following a factorial design approach as shown in table 1. The quantity of drug–resin complex was varied at three levels, the concentration of Sodium Starch Glycolate (SSG) used as a superdisintegrant, Avicel PH 102 was used as a diluent in all formulations to ensure uniform compressibility. D-mannitol served as a filler and sweetening agent, with its quantity adjusted inversely to maintain a constant total tablet weight of 300 mg. Additional excipients, including aspartame for taste

masking, sodium lauryl sulfate as a wetting agent, talc, and magnesium stearate (2 mg) as lubricants, were kept constant across all batches. This systematic variation in key formulation components enabled the evaluation of their influence on tablet characteristics and optimization of the chewable dosage form.[11-12]

Table 1: Formulation of Chewable Tablet using 3^2 Factorial design

Ingredients (mg)	C1	C2	C3	C4	C5	C6	C7	C8	C9
Drug resin Complex	162.5	198.5	235.0	162.5	198.5	235.0	162.5	198.5	235.0
Avicel PH 102	30	30	30	30	30	30	30	30	30
SSG	2	4	2	4	4	4	6	6	6
D-Mannitol	96.94	58.97	24.425	94.94	58.97	22.425	92.94	56.97	20.425
Aspartame	3	3	3	3	3	3	3	3	3
SLS	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Talc	2	2	2	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2	2	2	2
Total weight	300	300	300	300	300	300	300	300	300

Preformulation Studies of Piribedil

Determination of melting point of Piribedil

The melting point of Piribedil was determined using a melting point apparatus. A small amount of the drug was placed in a thin-walled capillary tube sealed at one end. The capillary tube was then placed in a melting point apparatus with a thermometer, and the temperature range over which Piribedil melted was recorded. The measurements were taken in triplicate.[13]

Estimation of Piribedil by UV-Visible Spectrophotometry

A standard stock solution of Piribedil was prepared by dissolving 10 mg of the compound in 100 ml of phosphate buffer (pH 6.8), yielding a concentration of 100 µg/ml. To identify the λ_{max}, the stock solution was analyzed using a UV-Visible spectrophotometer, scanning wavelengths from 200 to 400 nm, with phosphate buffer (pH 6.8) serving as the blank. Working solutions with concentrations ranging from 5 to 25 ppm were created by transferring 0.5, 1, 1.5, 2, and 2.5 ml aliquots from the 100 ppm stock solution into separate 10 ml volumetric flasks and diluting to the mark. The absorbance of these solutions was measured three times at 242 nm, using phosphate buffer (pH 6.8) as the blank.[14-15]

Determination of drug by FTIR and Compatibility Study of Drug and Excipients

FTIR spectroscopy was used for drug and excipients identification and to evaluate their compatibility. FTIR spectroscopy of pure drug and physical mixture of drug and excipients was carried out to check the compatibility of drug and excipients.[16]

Methods of preparation of resinate:

Optimization of resin concentration for maximum drug loading: Different quantities of activated resins to obtain resin: drug ratios of 1:1, 1:2, 1:3, 1:4 and 1:5 were placed in different beakers containing adequate quantities of distilled water and allowed to swell for 60 min. 100 mg of drug was added and stirred using a magnetic stirrer for 90 min at 60°C. The mixtures were filtered and residues were washed with adequate quantities of distilled water. The drug loading efficiency of the resin was estimated. The ratio of resin: drug revealing maximum loading of drug was the optimized ratio.[17-18]

Optimization of swelling time of resin for maximum drug loading: Separate batches of activated resins were soaked in adequate quantity of distilled water for 60, 90 and 120 min at 60°C. The swelling time required for maximum drug loading was optimized.[17-18]

Optimization of stirring time for maximum drug loading: Separate batches of acid-activated resins were soaked in adequate quantity of distilled water and drug was added and stirred for 60, 90 and 120 min with the aid of a magnetic bead at 60°C. Resin drug loading efficiency was estimated. The time required for maximum drug loading was thus optimized. Depending on the results of resin optimization study; batches of drug-resin mixtures at ratios 1:1, 1:2, 1:3, 1:4 and 1:5 were prepared as previously discussed at optimized conditions for % drug loading capacity. [17-18]

Evaluation Parameters of Chewable Tablet

Pre-Compression parameters

Bulk density: Accurately weighed the powder mixture and transferred to measuring cylinder

carefully measure the volume of powder without compacting. It is expressed as gm/ml.[19]

$$\text{Bulk Density} = \frac{\text{Mass of powder (gm)}}{\text{Bulk Volume of powder (ml)}}$$

Tapped density: Tapped density was measured by placing graduated cylinder containing formulation blend on mechanical tapping apparatus. Tapped volume was measured until constant tapped volume is not achieved. It is expressed as gm/ml. [19]

$$\text{Tapped Density} = \frac{\text{Mass of powder (gm)}}{\text{Tapped Volume of powder (ml)}}$$

Carr's index: Compressibility index is a ratio of difference of tapped density and bulk density to tapped density. It is expressed in percentage (%).[20-21]

$$\text{Compressibility Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Hausner's ratio: Hausner's ratio is a ratio of tapped density to bulk density. Generally, Glidant were added to improve the powder flow of the material. [20-21]

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Angle of repose: Angle of repose was determined by funnel method. Powder blend was poured from funnel that can be raised vertically until it reaches maximum cone height (h) was obtained. Radius (r) of the pile was measured. Angle of repose was measured by following formula. [20-21]

$$\theta = \tan^{-1}\frac{h}{r}$$

Where, θ = Angle of repose, h = Height of pile and r = Radius of pile

Post compression parameters

Thickness: Thickness of tablets was important for uniformity of tablet size. The thickness of tablets were determined with the help of Vernier caliper. The average diameter and thickness of the tablet was calculated.[22]

Weight variation: 20 tablets selected at random were weighed and the average weight was calculated.[22]

Hardness: The hardness of tablet is an indication of its strength. Measuring the force required to break the tablet across tests it. The force is measured in kg and the hardness of about 3-5 kg/cm^2 is considered to be satisfactory for uncoated tablets. The crushing strength of tablets was measured by using Monsanto type hardness tester. [23]

Friability: The friability of tablets was measured by Roche type friabilator. 20 tablets were initially weighed and then tablets were placed in friabilator at 25 rpm for 4 min then tablets were deducted and weighed again. Loss in weight should not be more than 1%. friability determined by using following equation.[23]

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

Drug content: The amount of drug present in 50 mg equivalent amount of Drug resin complex was determined by dissolving the powder mixture in 100 ml of pH 6.8 phosphate buffer and suitably diluted with pH 6.8 phosphate buffer. The solution was filtered through 0.45 mm membrane filter and UV absorbance was measured at 242 nm. Drug concentration was determined from standard graph. [24]

Wetting Time and Water Absorption Ratio: The wetting time of the tablets was measured using a simple procedure. A filter paper (10 cm diameter) was placed in a petri dish having a diameter of 10 cm. One milliliter of amaranth (a water-soluble dye) solution was added to a petri dish. A pre-weighed tablet was carefully placed on the filter paper. The time taken by water to reach the upper surface of the tablet was noted as a wetting time.

The wetted tablet was then reweighed for determination of water absorption ratio using the formula: [24]

$$\text{Water Absorption Ratio} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

In Vitro Disintegration test: This test performed on six tablets using digital tablet disintegration test apparatus. 500 ml Phosphate buffer (pH 6.8) at 37 ± 0.5°C was used as a disintegration media and time in sec. was recorded for complete disintegration of tablet with no residue remaining in apparatus. [25]

Cumulative Drug release study: % drug release of Piribedil Chewable Tablets was determined by USP type II (paddle type) dissolution apparatus. This test performed using 900 ml of phosphate buffer (pH 6.8) at 37 ± 0.5 °C at 50 rpm. 5 ml samples were withdrawn at regular time intervals and the same quantity of sample was replaced with fresh dissolution media. The sample was filtered through 0.45µm membrane filter. Absorbance of these samples was analyzed by using UV spectrophotometer at 242 nm.[25]

Stability study of optimized batch: In the present study, stability study of optimized batch was carried out at 40 ± 2 °C/ 75 ± 5 % RH for time period of 1 month by wrapping the formulation in aluminum foil to prevent the formulation from exposure to light

under the 40 ± 2 °C/ 75 ± 5% RH for 1 month as prescribed by ICH guidelines for accelerated stability study. After completion of 30 days tablets were evaluated for various parameters.[26]

RESULTS AND DISCUSSION

Preformulation Study

Determination of Melting point of Piribedil: The reported melting point range is 96–100°C, while the observed values were 94–97°C, 96–99°C, and 96–98°C. The results were found to be in close agreement with the reported range, with only minor variation likely due to experimental conditions. Therefore, the melting point analysis confirms the identity and suitability of Piribedil for further formulation and research work.

Estimation of drug by UV overlay spectra: The overlay spectra of drug were obtained by scanning different concentrations of solutions viz., 5, 10, 15, 20 and 25 ppm showed maximum absorption at 242 nm as shown in figure 1. Reported λmax of Piribedil is 242 nm. So, it can be concluded that the given drug was Piribedil. Calibration curve of prepared working solutions of Piribedil was constructed by plotting a graph between concentration and absorbance shown in figure 2 and regression analysis from the calibration curve of Piribedil is shown in table 2 and table 3.

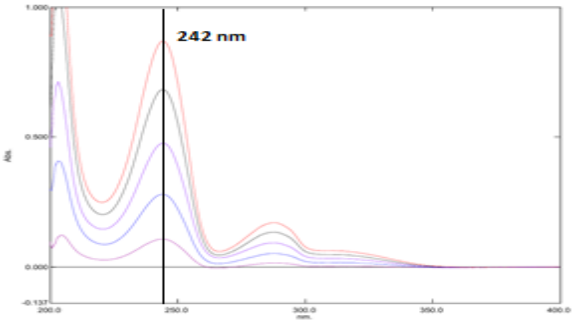

Figure 1: Overlay Spectra of Piribedil

Table 2: Absorbance of different concentration of Piribedil in phosphate buffer at pH 6.8

Sr. No.	Concentration (ppm)	Absorbance			Mean Absorbance ± S.D.
		I	II	III	
1.	5	0.110	0.109	0.112	0.110 ± 0.0015
2.	10	0.279	0.278	0.282	0.280 ± 0.0021
3.	15	0.477	0.475	0.475	0.476 ± 0.0012
4.	20	0.677	0.676	0.68	0.678 ± 0.0021
5.	25	0.872	0.875	0.876	0.874 ± 0.0021

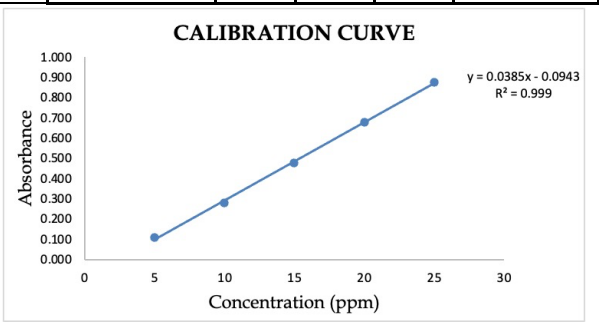

Figure 2: Calibration curve of Piribedil in phosphate buffer at pH 6.8

Table 3: Regression Analysis of Piribedil in phosphate buffer at pH 6.8

Sr. No.	Parameters	Result
1.	Regression equation	y = 0.0385x - 0.0943
2.	Correlation coefficient	R^2 = 0.999
3.	Calibration curve range	5 – 25 ppm

FTIR Study of Piribedil: The FTIR spectrum of Piribedil showed clear and characteristic absorption peaks corresponding to its functional groups, which were consistent with reported reference data, thereby confirming the identity and purity of the drug. No additional peaks or noticeable spectral changes were observed, suggesting the absence of impurities or degradation. In addition, the FTIR spectra of Piribedil when mixed with the selected excipients retained all the key drug peaks without any significant shift in position, change in intensity, or appearance of new peaks. This indicates that there were no chemical interactions between the drug and excipients. Overall, the study confirms that Piribedil is pure and compatible with the excipients used, supporting its suitability for the formulation of chewable tablets.

Preparation of Drug-resin complexes (DRC): Taste masking done by using ion exchange resin with batch method. IER are solid and suitably insoluble high molecular weight polyelectrolytes that can exchange their mobile ions of equal charge with the surrounding medium. Being high molecular weight water insoluble polymers, the resins are not absorbed by the body and are therefore inert. Weak cationic exchange resins of Tulsion 335 and Kyron T 159 were tried in different ratios drug and resins respectively. After complexing

it was evaluated for % drug loading capacity. Then this DRC transferred into compression blend.

Optimisation of resin concentration for maximum drug loading: From the different DRC, the one was selected on the basis of % drug loading capacity. The Drug resin complexes were prepared by batch method which characterized maximum drug loading. The amount of drug loaded onto the resin was higher with increasing resin concentration; the maximum amount of drug loaded was found to be 91.25 in the ratio 1:4 for Tulsion 335 resin and for Kyron T159 shows 75.08. When comparing both drug loading capacity it noticed that Tulsion 335 show high drug loading as compared to Kyron T 159 as shown in below table 4. This can be explained by the stoichiometric nature of the exchange reaction between drug and resin in solution.

Table 4: The drug loading based on drug: resin ratio

Drug resin ratio	% of drug bound to resin (Tulsion 335)	% of drug bound to resin (Kyron T 159)
1:1	82.63	68.25
1:2	84.26	65.97
1:3	86.48	69.24
1:4	91.25	75.08
1:5	90.36	73.63

Optimization of swelling time & stirring time of resin for maximum drug loading:

The swelling and hydration properties of resin is significantly affects the rate of the exchange reaction. These type of reaction is greatly affected by stirring time where the % of loaded drug was increased by increasing stirring time and rate of addition of drug is slow (4-5min). The optimized % drug loading (w/w) was found to be 91.25 and 75.08 at swelling time of 90 min and stirring time also 90 min for Tulsion 335 and Kyron T 159 respectively. When comparisons were made between this two resins then obtained results showed that Tulsion 335 is good candidate than Kyron T 159 for taste masking of Piribedil as shown in table 5. Therefore, for further study DRC of Tulsion 335 was used.

Table 5: The drug loading based on swelling time and stirring time

Batch	Stirring time (min)	Swelling time (min)	% of drug bound to resin (Tulsion 335)	% of drug bound to resin (Kyron T 159)
F1	60	60	85.25	63.25
F2	90	60	87.26	67.25
F3	120	60	86.26	69.18
F4	60	90	89.26	69.56
F5	90	90	92.36	73.216
F6	120	90	90.05	72.50
F7	60	120	87.09	70.44
F8	90	120	85.63	74.26
F9	120	120	92.93	72.63

Results of Chewable Tablets of Piribedil

Precompression Parameters: Precompression parameters were evaluated to assess the flow properties, compressibility, and overall suitability of the powder blends for direct compression, ensuring uniform die filling and consistent tablet quality and results as shown in table 6.

Table 6: Bulk density, Tapped density, Carr's index, Hausner's ratio and Angle of Repose data

Batch	Bulk density (gm/ml)	Tapped density (gm/ml)	Hausner's Ratio	Carr's index (%)	Angle of repose (°θ)
C1	0.82 ± 0.04	0.86 ± 0.06	1.05 ± 0.02	4.42 ± 2.15	27.78 ± 1.06
C2	0.50 ± 0.00	0.56 ± 0.00	1.11 ± 0.00	10.00 ± 0.00	27.16 ± 0.60
C3	0.50 ± 0.01	0.54 ± 0.00	1.09 ± 0.03	8.58 ± 2.13	26.76 ± 0.34
C4	0.53 ± 0.01	0.58 ± 0.01	1.09 ± 0.02	8.44 ± 2.02	28.18 ± 0.37
C5	0.85 ± 0.02	0.95 ± 0.02	1.11 ± 0.04	10.19 ± 3.22	28.83 ± 0.38
C6	0.84 ± 0.02	0.98 ± 0.04	1.16 ± 0.07	13.41 ± 5.64	27.98 ± 0.72

C7	0.53 ± 0.01	0.57 ± 0.01	1.08 ± 0.03	7.73 ± 2.33	27.56 ± 0.35
C8	0.50 ± 0.01	0.54 ± 0.00	1.09 ± 0.03	8.58 ± 2.13	26.76 ± 0.34
C9	0.88 ± 0.02	1.12 ± 0.03	1.27 ± 0.05	21.14 ± 3.15	30.24 ± 0.85

The **Bulk Density** values ranged from 0.50 ± 0.01 to 0.88 ± 0.02 g/ml, while **tapped density** varied between 0.54 ± 0.00 and 1.12 ± 0.03 g/ml. The relatively small difference between bulk and tapped densities in most batches indicates good packing ability of the powder blends.

Hausner's ratio values were found in the range of 1.05 ± 0.02 to 1.27 ± 0.05. Batches C1, C3, C4, C7, and C8 exhibited Hausner's ratio values below 1.10, indicating excellent to good flow properties. However, batch C9 showed a comparatively higher value (1.27 ± 0.05), suggesting relatively poorer flow characteristics.

Carr's index values ranged from 4.42 ± 2.15% to 21.14 ± 3.15%. Most batches demonstrated compressibility index values below 15%, indicating good flow and compressibility suitable for direct compression. Batch C9 showed the highest Carr's index (21.14 ± 3.15%), reflecting comparatively higher compressibility and reduced flowability.

The angle of repose values were observed between 26.76 ± 0.34° and 30.24 ± 0.85°, which fall within the acceptable range for good flow properties. Batches C3 and C8 exhibited comparatively lower angle of repose values, indicating better flow behavior, whereas C9 showed the highest value (30.24 ± 0.85°), correlating with its relatively higher compressibility index and Hausner's ratio.

Overall, the precompression evaluation indicates that most of the formulations possess satisfactory to good flow properties and are suitable for direct compression. Although batch C9 exhibited comparatively inferior flow characteristics, its values remain within acceptable limits. Therefore, the prepared blends were considered appropriate for further compression into chewable tablets.

Post Compression Parameters: The compressed chewable tablets of Piribedil (C1–C9) were evaluated for post-compression parameters including weight variation, thickness, hardness, and friability to assess their mechanical integrity and compliance with pharmacopoeial standards as shown in table 7 and 8.

Table 7: Weight variation, Thickness, Hardness and Friability data

Batch	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)
C1	299.15 ± 1.39	3.30 ± 0.35	3.83 ± 0.58	0.42
C2	299.55 ± 1.61	3.57 ± 0.12	3.67 ± 0.29	0.46
C3	299.95 ± 1.61	3.33 ± 0.40	3.50 ± 0.87	0.48
C4	299.50 ± 1.47	3.53 ± 0.15	3.50 ± 0.87	0.53
C5	300.00 ± 1.56	3.43 ± 0.31	3.17 ± 0.29	0.57
C6	300.15 ± 1.31	3.27 ± 0.21	3.33 ± 0.29	0.56
C7	299.15 ± 1.31	3.07 ± 0.38	2.83 ± 0.76	0.61
C8	300.70 ± 1.38	3.30 ± 0.44	3.00 ± 0.87	0.59
C9	299.40 ± 1.64	3.30 ± 0.35	2.67 ± 0.76	0.65

(n=3)

The **average tablet weight** for all batches was found to be in the range of 299.15 ± 1.39 mg to 300.70 ± 1.38 mg, which is very close to the theoretical weight of 300 mg. The minimal standard deviation observed across batches indicates uniform die filling and consistent compression, confirming compliance with the IP limits for weight variation.

The **thickness** of the tablets varied between 3.07 ± 0.38 mm and 3.57 ± 0.12 mm. The slight variation in thickness among batches may be attributed to differences in powder packing and compression force; however, the values remained within acceptable limits, indicating uniform compression and dimensional consistency.

The **hardness** of the tablets ranged from 2.67 ± 0.76 kg/cm² to 3.83 ± 0.58 kg/cm². Batch C1 exhibited the highest hardness, while batch C9 showed comparatively lower hardness. Since chewable tablets are intended to be chewed rather than swallowed whole, moderate hardness is desirable to ensure mechanical strength without compromising chewability. All batches demonstrated adequate hardness suitable for chewable formulations.

Friability values were observed between 0.42% and 0.65%, which are well below the pharmacopoeial limit of 1%. This indicates good mechanical resistance and the ability of the tablets to withstand handling, packaging, and transportation without significant weight loss.

Overall, the post-compression evaluation confirms that all formulated batches meet acceptable quality standards in terms of uniformity, mechanical strength, and durability. The prepared chewable tablets of Piribedil were found to possess satisfactory post-compression characteristics and were considered suitable for further *in vitro* evaluation studies.

Table 8: Wetting time, *In-vitro* disintegration time, Water absorption ratio and Drug Content Data

Batch	Wetting time (sec.)	*In-vitro* Disintegration time (sec.)	Water absorption ratio	Drug content (%)
C1	38.29 ± 1.36	40.83 ± 1.23	44.34 ± 0.31	98.77 ± 0.43
C2	34.53 ± 1.18	37.07 ± 1.05	49.65 ± 0.28	98.83 ± 0.40
C3	30.72 ± 1.49	33.25 ± 1.29	53.20 ± 0.10	98.57 ± 0.58
C4	25.10 ± 0.64	30.45 ± 0.55	55.18 ± 0.66	99.04 ± 0.75
C5	22.32 ± 0.98	26.39 ± 0.45	69.25 ± 0.72	98.65 ± 0.65
C6	23.85 ± 0.53	27.63 ± 0.52	59.85 ± 0.59	98.94 ± 0.54
C7	15.64 ± 0.58	20.23 ± 0.86	73.77 ± 0.59	98.88 ± 0.91
C8	17.69 ± 0.76	21.79 ± 0.78	71.79 ± 0.61	99.25 ± 0.80
C9	13.31 ± 0.20	15.84 ± 0.29	81.49 ± 0.81	99.04 ± 0.28

(n=3)

The prepared chewable tablets (C1–C9) were evaluated for wetting time, *in vitro* disintegration time, water absorption ratio, and drug content to assess their performance characteristics and uniformity.

The **wetting time** was observed in the range of 13.31 ± 0.20 sec to 38.29 ± 1.36 sec. Batch C1 exhibited the highest wetting time, whereas batch C9 showed the lowest value, indicating rapid penetration of water into the tablet matrix. A decreasing trend in wetting time from C1 to C9 suggests improved hydrophilicity and better wicking action of excipients in later batches.

The ***in vitro*** **disintegration time** varied between 15.84 ± 0.29 sec and 40.83 ± 1.23 sec. Batch C9 demonstrated the fastest disintegration, while batch C1 showed the slowest. The reduction in disintegration time correlates well with decreased wetting time, confirming efficient water uptake and rapid tablet breakup. All batches showed satisfactory disintegration suitable for chewable formulations.

The **water absorption ratio** ranged from 44.34 ± 0.31 to 81.49 ± 0.81, with batch C9 exhibiting the highest value. Increased water absorption indicates enhanced swelling and capillary action within the tablet matrix, which directly contributes to faster disintegration. Batches C7, C8, and C9 demonstrated significantly higher water absorption ratios, supporting their improved performance.

Drug content analysis revealed values between 98.57 ± 0.58% and 99.25 ± 0.80%, indicating uniform distribution of Piribedil in all batches. The results fall within acceptable pharmacopoeial limits (90–110%), confirming content uniformity and consistency of the formulation process.

Overall, the evaluation results indicate that all batches comply with the required quality parameters. Among them, batches C7, C8, and C9 exhibited comparatively better performance in terms of wetting time, disintegration time, and water absorption ratio, while maintaining satisfactory drug content. Therefore, these batches may be considered more suitable for further *in vitro* dissolution and optimization studies.

The ***in vitro*** **drug release study** of Piribedil chewable tablets (C1–C9) was carried out to evaluate the dissolution performance and comparative release behavior of all formulated batches. The cumulative drug release (% CDR) was recorded at predetermined time intervals up to 16 minutes. Results are demonstrated in table 9 and figure 3.

Table 9: % drug release of batches C1 to C9

Time (min.)	C1	C2	C3	C4	C5	C6	C7	C8	C9
0	0	0	0	0	0	0	0	0	0
2	33.48	36.44	39.26	39.87	45.68	42.26	47.22	46.85	49.26
4	48.4	50.6	53.2	59.2	64.2	61.2	72.1	69.6	76.2

	6	9	6	1	8	2	8	4	6
6	54.56	58.96	61.93	65.28	71.15	68.28	78.93	73.46	82.26
8	63.48	64.24	65.47	70.69	75.35	72.63	83.26	78.46	90.56
10	73.48	76.26	80.26	84.26	90.95	85.26	96.05	93.56	99.25
12	78.82	80.93	82.84	86.26	92.24	88.98	99.37	98.15	-
14	81.95	83.24	85.15	98.19	99.24	98.86	-	-	-
16	97.06	98.86	99.64	-	-	-	-	-	-

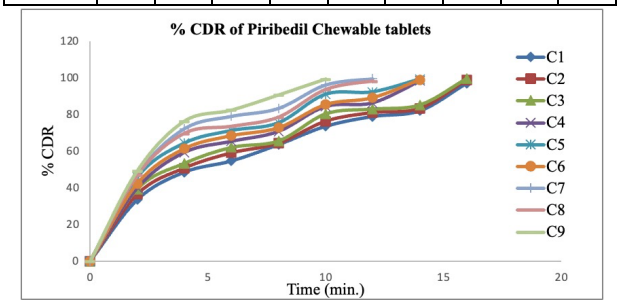

Figure 3: *In-vitro* drug release of Batches C1 to C9

At the initial 2-minute interval, drug release ranged from **33.48% (C1)** to **49.26% (C9)**, indicating rapid onset of dissolution in all formulations. Batch C9 exhibited the highest initial release, suggesting improved wettability and faster drug diffusion from the tablet matrix. At 6 minutes, the % CDR values increased significantly, ranging between **54.56% (C1)** and **82.26% (C9)**. A progressive increase in drug release was observed from C1 to C9, demonstrating formulation-dependent enhancement in dissolution rate. Batches C7, C8, and C9 showed comparatively faster release profiles. By 10 minutes, cumulative drug release was found in the range of 73.48% (C1) to 99.25% (C9). Batch C9 achieved nearly complete drug release within 10 minutes, whereas earlier batches such as C1 and C2 exhibited comparatively slower release behavior. At 14 minutes, batches C4 and C5 achieved approximately 98–99% drug release, while batches C7 and C8 crossed 98% release by 12 minutes. The final readings at 16 minutes showed that batches C1, C2, and C3 reached 97.06%, 98.86%, and 99.64%, respectively, confirming complete drug release within the study period. The dissolution graph demonstrates a consistent and gradual increase in % CDR for all formulations, with no evidence of dose dumping or irregular release patterns. The faster dissolution observed in batches C7, C8, and C9 correlates well with their lower wetting time, reduced disintegration time, and higher water absorption ratio, indicating improved tablet performance.

STATISTICAL ANALYSIS

Statistical Analysis for *In-vitro* Disintegration Time: The effect of independent variables, **X_1 (Drug resin complex)** and **X_2 (SSG)**, on *in vitro* disintegration time (Y_1) was evaluated using a quadratic model generated by Design-Expert® software. The final coded equation obtained for the response was: $\mathbf{Y_1 = 28.40 - 2.46\ B_1 - 8.88\ B_2 + 0.7975\ B_{12} - 0.3733\ B_1^2 + 0.0117\ B_2^2}$. The negative coefficients of both the drug–resin complex (X_1) and sodium starch glycolate (SSG, X_2) indicate that increasing their concentrations leads to a decrease in disintegration time, with SSG showing a more pronounced effect, highlighting its key role as a superdisintegrant. The positive interaction term suggests a slight combined effect between the two variables, while the quadratic terms reflect minor non-linear behavior, particularly at higher levels of the drug–resin complex. The contour plot (figure 4) showed a gradual reduction in disintegration time with increasing levels of both variables, and the relatively parallel contour lines indicate a moderate interaction between them. This observation is further supported by the three-dimensional surface plot (figure 5), which illustrates a consistent decline in disintegration time as both factors increase. In addition, the predicted versus actual plot (figure 6) demonstrated a close agreement between experimental and predicted values, confirming the reliability of the model. Overall, the results indicate that both variables significantly influence disintegration time, with SSG playing a dominant role, and the model can be effectively used for optimization of the formulation.

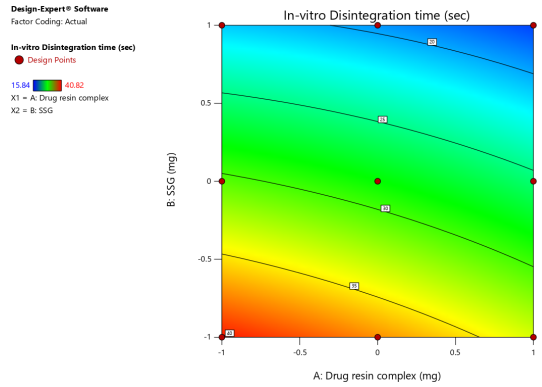

Figure 4: Contour plot showing the effect of Drug resin complex (X_1) and SSG (X_2) on *In-vitro* Disintegration time

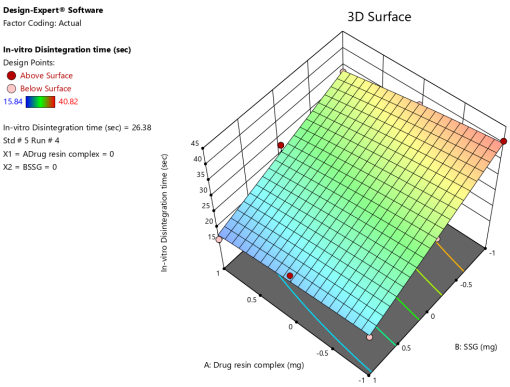

Figure 5: 3D surface plot showing the effect of Drug resin complex (X_1) and SSG (X_2) on *In-vitro* Disintegration time

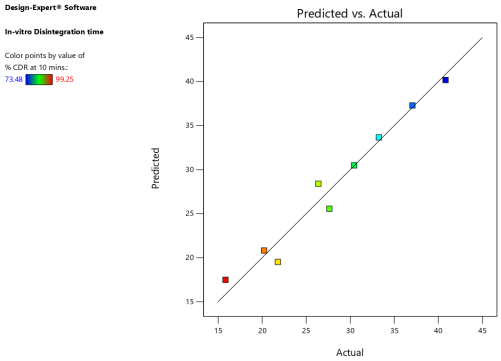

Figure 6: Graph of Actual value vs Predicted value of *In-vitro* Disintegration Time

Statistical Analysis for % CDR: The effect of independent variables, **X_1 (Drug resin complex)** and **X_2 (SSG)**, on percentage cumulative drug release at 10 minutes (Y_2) was evaluated using Design-Expert® software. The final quadratic equation obtained in terms of coded factors was**: $Y_2 = 87.87 + 2.37\ B_1 + 9.81\ B_2 - 0.8950\ B_{12} + 0.0400\ B_1^2 - 1.42\ B_2^2$.** The positive coefficients of both the drug–resin complex (X_1) and sodium starch glycolate (SSG, X_2) indicate that increasing their concentrations enhances the drug release at 10 min, with SSG showing a more pronounced effect due to its higher coefficient value. The negative interaction term suggests a slight antagonistic interaction between the two variables at combined higher levels. The quadratic terms reveal a minimal curvature effect for X_1, whereas a comparatively stronger negative quadratic effect for X_2 indicates that excessively high levels of SSG may not proportionally increase drug release. The contour plot (figure 7) demonstrates a progressive increase in % cumulative drug release with increasing levels of both variables, while the three-dimensional surface plot (figure) further confirms this trend by showing an ascending response surface. Additionally, the predicted versus actual plot (figure 9) indicates a good agreement between experimental and predicted values, as the data points closely follow the line of identity, confirming the adequacy and reliability of the model. Overall, the findings suggest that both variables significantly influence early drug release, with SSG playing a dominant role, and the model can be effectively utilized for optimization of the formulation.

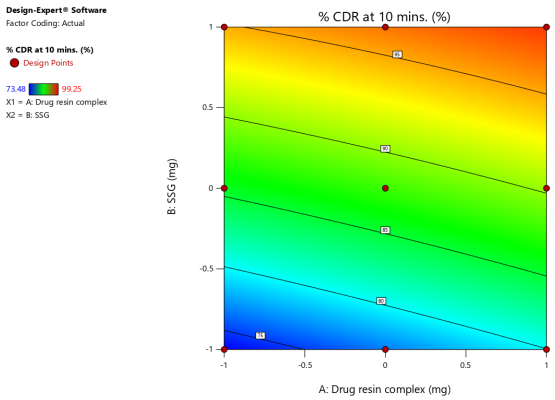

Figure 7: Contour plot showing the effect of Drug resin complex (X_1) and SSG (X_2) on % CDR at 10 mins

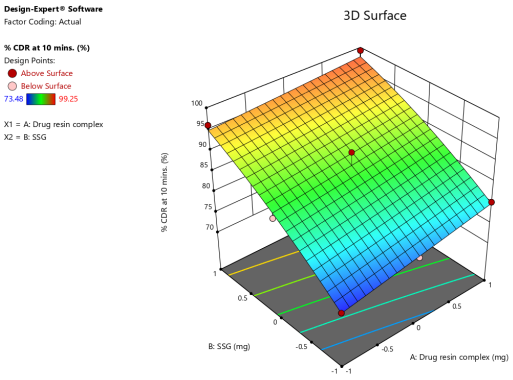

Figure 8: 3D surface plot showing the effect of Drug resin complex (X_1) and SSG (X_2) on % CDR at 10 mins

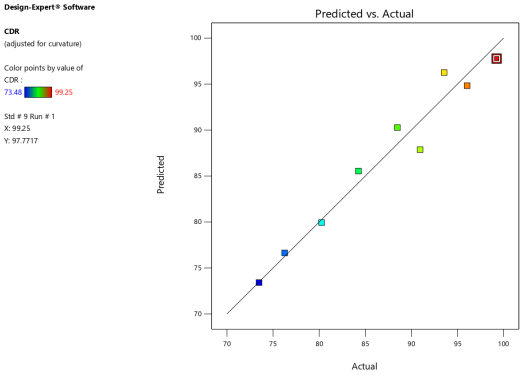

Figure 9: graph of Actual value vs Predicted value of % CDR at 10 mins

Result of Stability Study: Based on the overall evaluation of formulation parameters, batch C9 was selected as the optimized formulation due to its good surface characteristics, sufficient mechanical strength, and uniform drug content. The stability of this batch was further assessed under accelerated conditions at 40° ± 2 °C and 75 ± 5 % RH for one month and the results are demonstrated in table 10. After the storage period, the formulation was re-evaluated for key quality attributes, including hardness, wetting time, *in vitro* disintegration time, and drug content. Only minor variations were observed, with hardness showing a slight increase (from 2.67 ± 0.76 to 2.93 ± 0.31 kg/cm^2), while wetting time (13.31 ± 0.20 to 13.16 ± 0.09 s), disintegration time (15.84 ± 0.29 to 15.76 ± 0.42 s), and drug content (99.04 ± 0.28% to 99.19 ± 0.28%) remained essentially unchanged. Similarly, the *in vitro* drug release profile showed no meaningful difference after stability, with % cumulative drug release at 10 min remaining comparable (99.25% initially and 98.19% after one month) and the results are demonstrated in table 11 and figure 10. Overall, these results indicate that the optimized formulation remained stable under accelerated conditions, with no significant changes in its physicochemical properties or drug release performance.

Table 10: Result of the Stability study

Sr. No.	Evaluation parameter	Results of optimized batch C9	Result after 1 month at 40° ± 2 °C and 75 ± 5 % RH
1	Hardness (kg/cm^2)	2.67 ± 0.76	2.93 ± 0.31
2	Wetting Time (sec.)	13.31 ± 0.20	13.16 ± 0.09
3	*In-vitro* Disintegration Time (sec.)	15.84 ± 0.29	15.76 ± 0.42
4	Drug Content (%)	99.04 ± 0.28	99.19 ± 0.28

Table 11: *In-vitro* Drug Release Study of Stability Batch

Time (Min.)	% CDR of Optimized Batch C9 (%)	% CDR of batch C9 After Time Period of 1 Month (%)
0	0	0
2	49.26	49.02
4	76.26	75.85
6	82.26	81.26
8	90.56	90.01
10	99.25	98.19

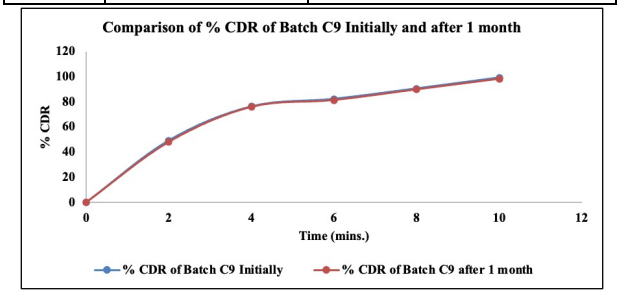

Figure 10: Comparison of *In-vitro* Drug Release study of Optimized batch and Stability batch

Conclusion: The present study successfully developed and optimized Piribedil chewable tablets using a systematic experimental design approach. Preformulation studies confirmed the identity, purity, and suitability of the drug, while FTIR analysis established its compatibility with the selected excipients. The use of an ion-exchange resin proved effective in masking the inherent bitterness of Piribedil, thereby improving the overall palatability of the formulation. Among the resins studied, Tulsion 335 showed superior drug loading efficiency (≈91.25%) at the optimized drug–resin ratio, contributing to both effective taste masking and formulation performance. The application of a 3^2 factorial design provided a clear understanding of the influence of formulation variables on key parameters such as disintegration time and drug release. Among all batches, formulation C9 was identified as the optimized formulation, demonstrating rapid wetting, fast disintegration, high water uptake, and nearly complete drug release within 10 minutes. Statistical

analysis further confirmed the significant role of sodium starch glycolate in enhancing tablet performance and supported the reliability of the developed model. In addition, the optimized formulation remained stable under accelerated conditions, with no significant changes in physicochemical properties or drug release behavior. Overall, the developed chewable tablet formulation of Piribedil offers a practical and patient-friendly dosage form with improved taste, rapid onset of action, and consistent performance, making it a promising option for effective management of Parkinson's disease.

ACKNOWLEDGEMENT

The authors are grateful to Smt. N. M. Padalia Pharmacy College, Ahmedabad, for encouragement and for providing the necessary facilities to carry out this research work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Bernhardt R, and Schulze-Hentrich J. "A multi-dimensional view on the etiology of Parkinson's disease." *Nature Partner Journals Parkinson's Disease*. **2025**; *11(1)*:150–165.
2. Tanaka M. "Parkinson's Disease: Bridging gaps, building biomarkers, and reimagining clinical translation." *Cells*. **2025**; *14*:1161.
3. Sohi H, Sultana Y and Khar R, "Taste masking technologies in oral pharmaceuticals: Recent developments and approaches." *Drug Development and Industrial Pharmacy*. **2004**; *30(5)*: 429-448.
4. Rohini Harikrushna K, "Formulation and development of taste masked dispersible tablet of Cephalexin monohydrate using ion exchange fibers and resins." *International Journal of Pharmaceutical, Chemical and Biological Sciences.* **2014**; *4(3)*: 537-544.
5. Monika, Pragi, Varun Kumar, Amit Kumar, Deepak Garg, Preeti, and Ashok Kumar. "A narrative review on formulation and quality attribute considerations for chewable tablets." *International Journal of Current Pharmaceutical Review and Research*. **2023**; *15(9)*:178–189.
6. Vaishnavi Bakka, Annie Vijetha, and M. Sunitha Reddy. "Chewable tablets as a patient-friendly drug delivery system: a comprehensive review." *International Journal of Pharmaceutical Sciences*. **2025**; *3(9)*:822–830.
7. Rahul G, Gulshan C, Kamla P, Harish B and Anil K, "To formulate and evaluate taste masked chewable tablet of Levocetirizine dihydrochloride and Montelukast sodium using ion exchange resin as a drug carrier." *The Pharma Innovation Journal.* **2017**; *6(7)*: 27-32
8. Divya S and Arti H, "Taste Masked Orodispersible Formulation of Fexofenadine Hydrochloride Using Ion Exchange Resins." *Indian Journal of Pharmaceutical Sciences*. **2015**; 550-555.
9. Kimaro E, Tibalinda P, Shedafa R, Temu M, and Kaale E. "Formulation development of chewable albendazole tablets with improved dissolution rate." *Heliyon.* **2019**; *5(12)*: e02911.
10. Modi A, and Zalavadia B. "Formulation and evaluation of Ezetimibe loaded chewable tablets in the treatment of hyperlipidemia." *European Journal of Pharmaceutical and Medical Research.* **2025**; *12(5)*: 479–492.
11. Gokulakrishnan S, Anitha K, Bharathi S, Jothika J, Keerthana T, Bilal NM, Sashtika DS, Shree K, Vignesh K, and Ilango KB. "A comprehensive review of formulation methods of chewable tablet – a novel approach." *International Journal of Pharmaceutical Sciences and Research.* **2025**; *16(10)*: 2692–2699.
12. Divyanshu D, Martolia J, and Saxena A. "Formulation and evaluation of chewable tablets containing Dexibuprofen as an antipyretic drug." *Educational Administration: Theory and Practice.* **2024**; *30(6)*:3253–3261.
13. Dighe VS, Chopade BL, and Salve MT. "Formulation and evaluation of extended release matrix tablets of Piribedil". *International Journal of Progressive Research in Engineering, Management and Science.* **2025**; *5(4)*:3392–3396.
14. Demirel M, Yazan Y, Müller RH, Kilic F, and Bozan B. "Formulation and *in vitro*–in vivo evaluation of piribedil solid lipid micro- and nanoparticles*." Journal of Microencapsulation.* **2001**; *18(3)*: 359–371.
15. Bhargavi C, and Raghuveer P. "Enhancing nose-to-brain delivery of piribedil: development of a nanosuspension dispersed in nasal in-situ gelling system." *Journal of Drug Delivery Science and Technology.* **2024**; 92:102164
16. Amr H, Sherien EK, Ahmed K and Ahmed AE, "Preparation, Characterization, and In-vitro/vivo

Evaluation of Indion-based Chewable Tablets of Paracetamol and Ibuprofen for Pediatric Use." *Journal of American Science*. **2011**; *7(12)*: 831-844.

17. Amarjeet Y, Navneet G and Jat RK, "Evaluation and Formulation of Ofloxacin Suspension using Ion Exchange Resins." *Pharmacophore*. **2014**; *5(3)*, 371-377.

18. Wipada S, Prasert A, Tanasait N, Theerasak R and Praneet O, "Formulation and evaluation of meloxicam oral disintegrating tablet with dissolution enhanced by combination of cyclodextrin and ion exchange resins." *Drug Development and Industrial Pharmacy*. **2014**; *41(6)*: 1-11.

19. Mutha, S, Kshirsagar, C, Shelke, V and Sawant S, "Formulation, development and evaluation of chewable tablet of Dicyclomine hydrochloride." *International Journal of Health Sciences*. **2022**; *6(S7)*: 1224 1236.

20. Prasad SG, Das P, Kiran CVS and Vasia. "Formulation and evaluation of chewable tablets of montelukast." *Indian Journal of Research in Pharmacy and Biotechnology.* **2013**; *1(1)*: 29–34.

21. Suruse PB, Band KS, Ingole AR, and Baheti JR. "Formulation and evaluation of chewable tablets of anti-asthmatic drug." *Research Journal of Pharmacy and Technology.* **2022**; *15(1)*: 137–142.

22. Raval K, Devamurari P, and Agravat M. "Formulation and evaluation of orodispersible tablets of Piribedil." *International Journal of Current Science*. **2025**; *15(3)*:874–892.

23. Suruse P. B., Band K. S., Ingole A. R., and Baheti J. R. "Formulation and Evaluation of Chewable Tablets of Anti-Asthmatic Drug." *Research Journal of Pharmacy and Technology*. **2022**; *15(1)*:137-2.

24. Damle MC, Bhalekar MR, Rao S, and Godse M. "Formulation and evaluation of chewable tablets of pomegranate peel extract." *Journal of Drug Delivery and Therapeutics*. **2019**; *9(4)*: 318–321. doi:10.22270/jddt.v9i4.3049

25. Patel RV, Ansari GY, and Bhangale JO, "Development and Characterization of Solid Dispersion of Rasagilline Mesylate for Improvement of Dissolution Rate Using Hydrophilic Carriers." *International Journal of Current Science Research and Review*. **2023**; *6(6)*: 3223-3239.

26. Patil J, Vishwajith V, and Gopal V. "Formulation development and evaluation of chewable tablets containing non-sedating antihistamine." *Journal of Pharmaceutical and Scientific Innovation*. **2012**; *1(3)*: 112–117.