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FORMULATION AND CHARACTERIZATION OF SPRAY-DRIED CLARITHROMYCIN MICROPARTICLES WITH IMPROVED DISSOLUTION AND POTENTIAL FOR ORAL BIOAVAILABILITY

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ABSTRACT

Background: Clarithromycin, a macrolide antibiotic, exhibits limited aqueous solubility, which restricts its dissolution and bioavailability. Enhancing its solubility through novel formulation strategies is essential to improve therapeutic efficacy. Spray drying with hydrophilic carriers is an effective approach for drug particle engineering to improve dissolution. **Methodology:** Clarithromycin microparticles were prepared by the spray drying technique using hydroxypropyl-β-cyclodextrin (HP-β-CD) and Kollicoat IR® as hydrophilic polymers. The formulations were prepared in different drug-to-polymer ratios. Physicochemical characterization was performed using differential scanning calorimetry (DSC) and powder X-ray diffractometry (XRD) to study the crystalline-to-amorphous transition. Scanning electron microscopy (SEM) was used to assess particle morphology. Dissolution studies were carried out and compared with the pure drug, physical mixtures, and marketed clarithromycin tablets. **Results and Discussion:** DSC and XRD analyses confirmed the transformation of clarithromycin from a crystalline to an amorphous state within the spray-dried microparticles. SEM images revealed uniform spherical particles with porous surfaces. The optimized spray-dried formulation (CH 1:1) achieved 85.42 ± 0.47% drug release within 10 min and 96.28 ± 1.13% at 60 min, compared to 57.54 ± 1.54% and 81.54 ± 1.87%, respectively, for the marketed tablet. This corresponds to an approximately 1.5-fold enhancement in early dissolution. **Conclusion:** Spray drying with HP-β-CD and Kollicoat IR® successfully enhanced the solubility and dissolution of clarithromycin. The approach demonstrates potential to develop effective immediate-release tablets, with markedly improved in-vitro dissolution compared with the marketed product, indicating potential for enhanced oral bioavailability.

INTRODUCTION

Clarithromycin exhibits pH-dependent stability and solubility, with reported susceptibility to degradation under strongly acidic conditions, which may influence its oral dissolution behavior [1-2]. Depending on its concentration and the microorganism's sensitivity, clarithromycin may function as either a bacteriostatic

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or bactericidal agent. Its antimicrobial mechanism involves binding to the 50S subunit of bacterial ribosomes, thereby disrupting protein synthesis. This antibiotic is effective against numerous aerobic and anaerobic bacteria, including both gram-positive and gram-negative species, such as Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, and other clinically relevant organisms, such as Mycobacterium avium complex and Helicobacter pylori. Although clarithromycin exhibits susceptibility to degradation under strongly acidic conditions, formulation strategies such as polymeric encapsulation can help minimize this effect while improving dissolution performance [3].

Kollicoat IR® is a specialized graft copolymer made by combining polyvinyl alcohol with polyethylene glycol [4]. In immediate-release tablet formulations, it serves as a coating polymer. The polyvinyl alcohol segment imparts excellent film-forming properties, while the polyethylene glycol segment acts as an inherent plasticizer. Its hydrophilic nature allows rapid dissolution in aqueous media and effectively reduces surface tension [5]. Cyclodextrins are known to form inclusion complexes with numerous organic molecules in both liquid and solid phases. They are widely utilized to enhance solubility, stability, and bioavailability of various drugs, particularly polar compounds [6].

Complexation with cyclodextrins often modifies the physicochemical properties of the guest molecules. Spray-drying is a single-step process that converts a liquid feed into a dry powder, suitable for large-scale microencapsulation and continuous particle production, and applicable to a diverse range of materials [7-8]. This technique can encapsulate drugs within water-soluble or water-insoluble polymers, whether synthetic, semi-synthetic, or natural.

Spray-drying is a versatile method for formulating dosage forms using polymers that may be heat-stable or heat-labile, hydrophilic or hydrophobic, and soluble or insoluble in water. This technique plays a crucial role in developing pharmaceutical carriers for drugs with poor aqueous solubility, a major hurdle in drug delivery research [9].

Polymeric systems produced by spray-drying can be customized for different delivery routes, including oral solid preparations, targeted systems, and sustained-release parenteral formulations. Enhancing the solubility of poorly soluble drugs can be achieved by incorporating suitable hydrophilic excipients. Notable advantages of spray-drying include excellent reproducibility, dependable operation, tunable particle size, and effective control over drug release behavior [10]. The present investigation was designed to enhance the aqueous solubility and dissolution performance of clarithromycin by developing spray-dried microparticles using hydrophilic carriers. Hydroxypropyl-β-cyclodextrin and Kollicoat IR® were selected based on their established solubilizing potential and compatibility with immediate-release formulations. The spray-drying approach was employed to induce solid-state modification and generate porous spherical particles, thereby promoting rapid wetting and drug release. The prepared formulations were systematically evaluated for physicochemical properties, particle morphology, solid-state characteristics, and in-vitro dissolution behavior, compared with the pure drug, physical mixtures & marketed tablet [11–13].

The present research focused on improving the solubility and dissolution rate of clarithromycin by developing spray-dried microparticles using hydrophilic carriers, namely HP-β-cyclodextrin and Kollicoat IR®. The prepared systems were evaluated for solid-state characteristics, morphology, and dissolution behavior, compared with the pure drug, physical mixtures, and marketed tablets. This work aims to establish spray drying as a practical formulation strategy for improving the dissolution behavior of clarithromycin and to evaluate its suitability for immediate-release oral delivery.

MATERIAL AND METHOD

Materials

Clarithromycin was received as a courtesy sample from Murli Krishna Pharma Pvt. Ltd., Ranjangaon, Maharashtra. Hydroxypropyl-β-Cyclodextrin was provided by Gangwal Chemicals Pvt. Ltd., Mumbai, India. Kollicoat IR® was obtained as a complimentary material from BASF India Ltd., Mumbai, India. All other reagents used during the investigation were of analytical grade.

Formulation of a spray-dried binary system

Clarithromycin was combined with either Kollicoat IR® or HP-β-Cyclodextrin at molar ratios of 2:1, 1:1, 1:2, and 1:3 and dissolved in a hydroalcoholic medium consisting of ethanol and water (2:1 v/v), adjusted to pH 9.5. The feed solution was adjusted to pH 9.5 to enhance clarithromycin solubility in the hydroalcoholic medium and to minimize potential acid-

catalyzed degradation during processing, thereby ensuring homogeneous drug distribution prior to spray drying. The mixture was stirred continuously for 4 hours to ensure complete dissolution. The resulting solution was then subjected to spray drying using a Technosearch Instrument (Mumbai, India) while maintaining magnetic agitation. Spray-drying conditions were optimized with an inlet temperature of 110 °C, an outlet temperature of 60–65 °C, a feed rate of 3 mL/min, an airflow of 40-50 m^3/h, and an atomizing air pressure of 1.0–1.1 bar [14].

MICROPARTICLES CHARACTERIZATION

Particle Size Distribution

The size distribution of the spray-dried particles was evaluated by a zeta sizer (Malvern Instruments Limited) [15].

Entrapment Efficiency

Clarithromycin was combined with either Kollicoat IR® or HP-β-Cyclodextrin in molar ratios of 2:1, 1:1, 1:2, and 1:3. The mixture was then dissolved in a hydroalcoholic solvent system composed of ethanol and water (2:1 v/v) maintained at pH 9.5. This solution was continuously stirred for 4 hours to ensure complete drug solubilization. The encapsulation efficiency of clarithromycin in the resulting spray-dried material was evaluated as the percentage of drug incorporated within the microparticles compared to the theoretical drug loading. For assessment, a pre-weighed quantity of the dried sample, equivalent to 10 mg of clarithromycin, was reconstituted in ethanol and diluted to a defined volume with phosphate buffer.

The clarithromycin concentration was quantified spectrophotometrically at 213 nm after suitable dilution. At higher polymer ratios, reduced entrapment efficiency may result from increased feed viscosity and incomplete drug solubilization, leading to partial drug precipitation during atomization. Additionally, rapid solvent evaporation at elevated polymer concentrations may promote surface localization of the drug, thereby lowering apparent encapsulation efficiency [16].

Morphological Analysis

The surface morphology and structural characteristics of the spray-dried particles were studied through scanning electron microscopy (SEM). During analysis, the samples were properly mounted and visualized, and micrographs were captured using a field emission SEM (FESEM, Nova Nano SEM NPEP303). As BET surface area measurements were not performed, porosity assessment is based solely on SEM visualization [17].

Differential Scanning Calorimetry (DSC)

The thermal properties of both the unprocessed drug and the spray-dried microparticles were assessed using a Shimadzu DSC-60 instrument (Shimadzu, Kyoto, Japan). The analysis was performed with a sample mass between 3 & 5 mg at a heating rate of 10 °C per min., over a temperature range. range of 25 °C to 300 °C. Each sample was enclosed in aluminum pans, and the equipment was calibrated using indium as the reference material [18].

Powder X-Ray Diffractometry (XRD)

Wide-angle X-ray diffraction was employed to examine the crystalline nature and phase composition of the spray-dried microparticles. Measurements were conducted in the 2θ configuration over the 10°–60° range, with a data-collection interval of 1 s per step [19].

Tablet Formulation

An accurately weighed portion of the spray-dried powder, formulated at a 1:1 drug-to-polymer ratio using either Kollicoat IR® or HP-β-CD, was used for direct compression. Tablets were produced using a rotary tablet press equipped with a 10 mm circular punch. For each batch, the compression pressure was manually regulated based on the powder's flow & compaction properties. Individual tablets were formed manually by operating the press, without continuous tablet production. The finished tablets were kept at ambient temp., protected from light, until further evaluation [20].

Dissolution Study – In Vitro Release from Microparticles

Drug release evaluation was performed using the USP Dissolution Apparatus II (paddle system) operating at 50 rpm (Electrolab Pvt. Ltd., TDT-08L). Each dissolution vessel contained 750 mL of 0.1 N hydrochloric acid, maintained at 37 ± 0.5°C, with a total test duration of 1 hour. For analysis, one tablet from each formulation—SD 1:1 drug-to-polymer (Kollicoat IR® or HP-β-CD) and the marketed product Klarinova™-250—was assessed in triplicate. The absorbance at 212 nm was captured automatically, and cumulative drug release values were determined at successive time intervals [21-22].

Statistical Analysis

Data are presented as mean ± SD (n = 3). Statistical comparisons among multiple groups were performed using one-way analysis of variance (ANOVA), followed by Tukey's post-hoc test to identify significant pairwise differences. A p-value < 0.05 was considered statistically significant.

RESULTS & DISCUSSION

Production Yield

The yield obtained from all formulated samples ranged from 64.24% to 78.75% for both Kollicoat IR® and HP-β-CD-based systems. The composition of the solvent blend showed no major impact on the overall yield; however, modifications in polymer concentration and the feed mixture spraying rate notably affected the percentage yield of the produced microparticles.

Drug Entrapment Efficiency

The spray-dried microparticles exhibited an entrapment efficiency between 68% and 90%, as shown in Table 1. Results revealed that raising the drug-to-polymer proportion improved entrapment efficiency until a 1:1 ratio was reached, after which additional polymer reduced efficiency. Furthermore, increasing the spray rate tended to lower entrapment efficiency, which may be attributed to the formation of smaller particles possessing greater surface area. Material loss during spray drying was primarily attributed to wall deposition in the drying chamber and cyclone inefficiency, both common challenges in laboratory-scale spray dryers. Although yields ranged from 64–79%, process optimization (e.g., higher solids loading, improved cyclone design, and surface-treated chambers) could substantially improve recovery during scale-up, supporting the feasibility of industrial translation.

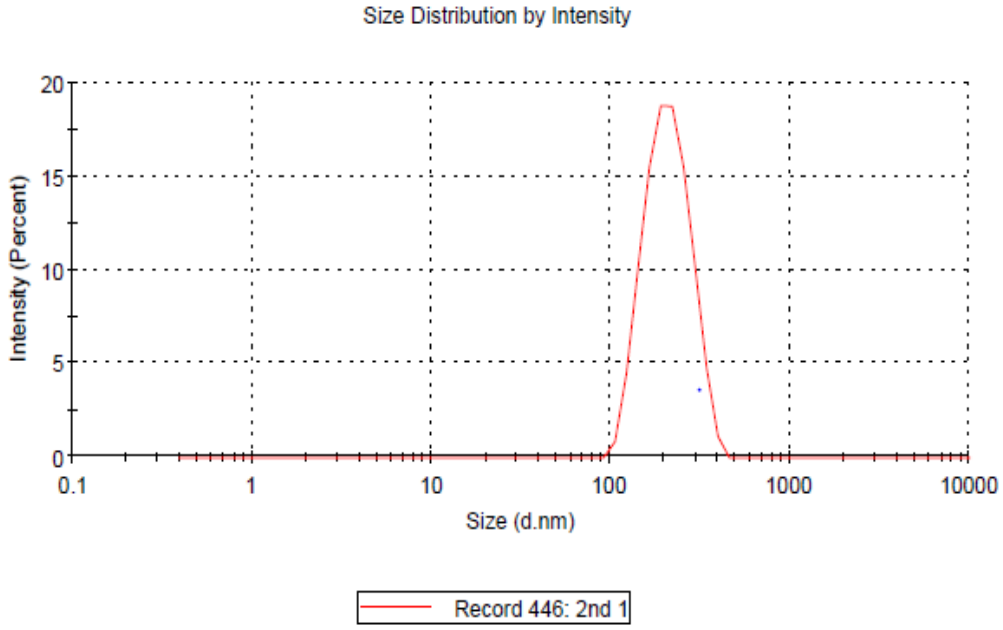

Figure 1: Particle size distribution by intensity of clarithromycin-loaded microparticles formulated with HP-β-cyclodextrin

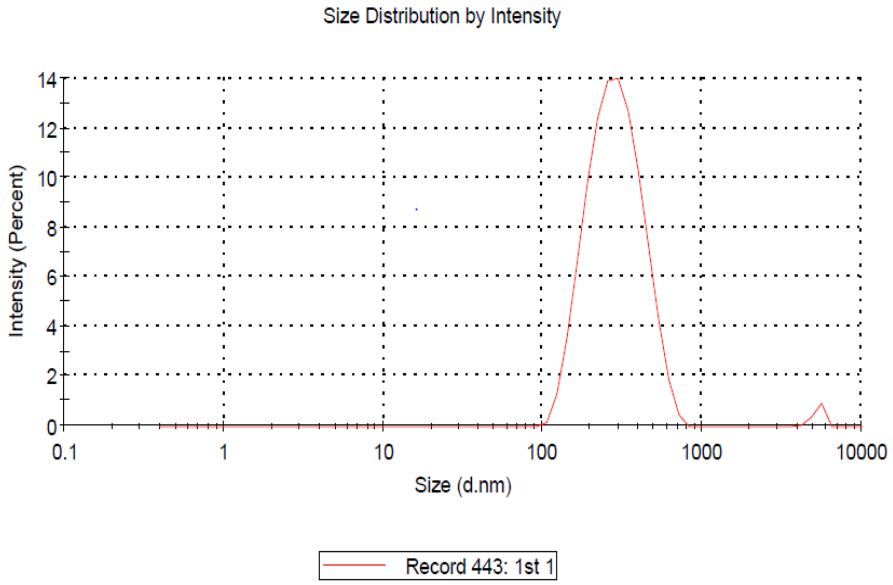

Figure 2: Particle size distribution by intensity of clarithromycin-loaded microparticles formulated with Kollicoat IR®

Scanning Electron Microscopy (SEM)

The surface morphology of the optimized HP-β-CD-based formulation was examined using scanning electron microscopy. Microparticles produced via spray drying exhibited a consistent spherical shape and a porous outer surface. Their diameters ranged approx. between 0.20 & 0.29 µm.

In the micrographs, Figures 3(A) and 4(A) display the general arrangement of microspheres at 50,000× magnification, while Figures 3(B) & 4(B) highlight individual particles at 100,000× magnification, confirming their spherical form. Figures 3(C) & 4(C) depict the pronounced porosity of the particle surfaces at 200,000× magnification, alongside particle size details.

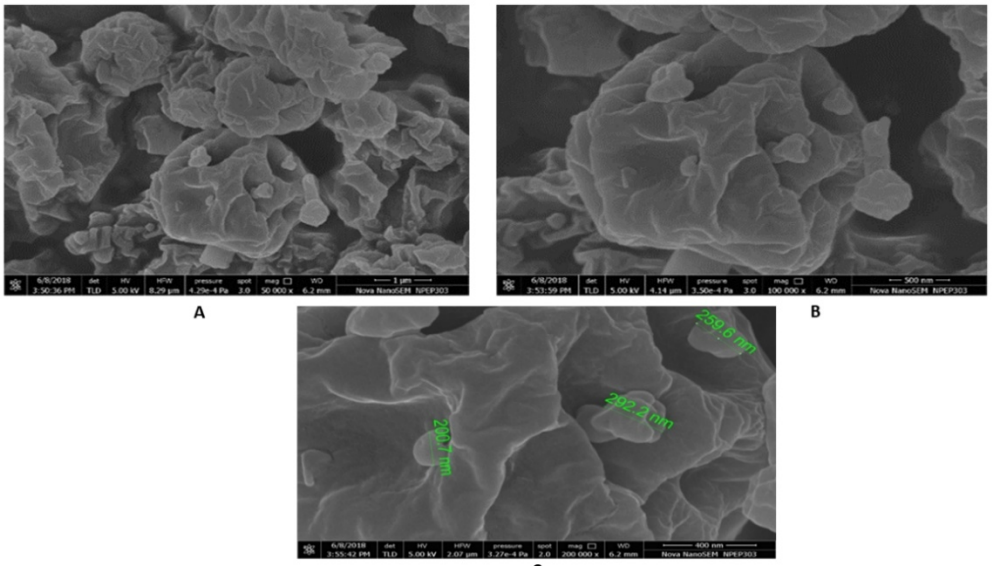

Figure 3: Scanning electron microscopy (SEM) images of the optimized clarithromycin-loaded microparticles formulated using HP-β-cyclodextrin and prepared by spray drying. (A) Low-magnification micrograph (50,000×) showing the overall morphology and arrangement of microparticles. (B) Higher-magnification image (100,000×) illustrating the spherical shape and surface characteristics of individual microparticles. (C) High-resolution micrograph (200,000×) revealing the porous surface architecture and particle size distribution, with particle diameters ranging approximately from 0.20 to 0.29 µm

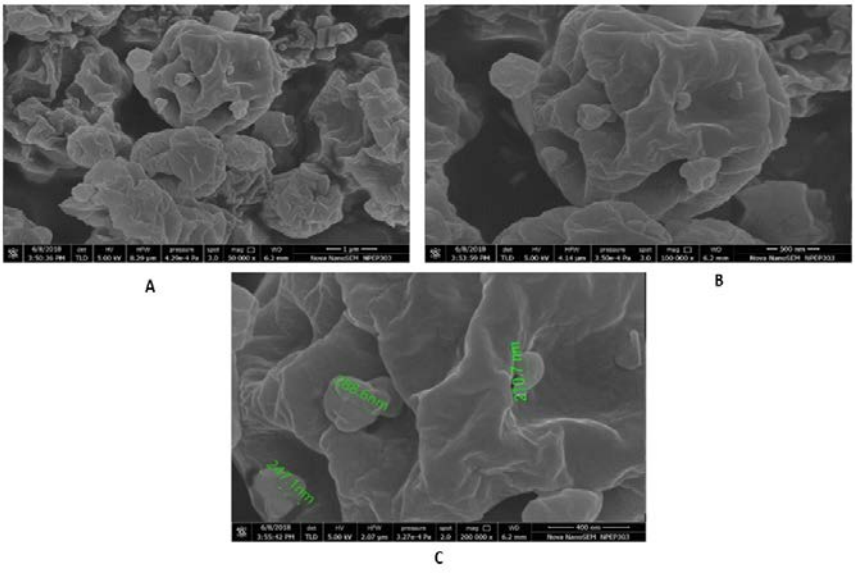

Figure 4: Scanning electron microscopy (SEM) images of the optimized clarithromycin-loaded microparticles formulated using Kollicoat IR® and prepared by spray drying. (A) Low-magnification micrograph (50,000×) illustrating the overall morphology and distribution of microparticles. (B) Higher-magnification image (100,000×) showing individual microparticles with well-defined spherical geometry and surface features. (C) High-magnification micrograph (200,000×) revealing the surface texture and particle size details, with particle diameters ranging approximately from 0.21 to 0.29 µm

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) is a widely used thermal characterization method in pharmaceutical research, providing valuable information on thermal behavior, phase transitions, and physicochemical characteristics of drug substances and formulations. The DSC thermogram of clarithromycin and its spray-dried microparticles is presented in Figure 5. The pure drug exhibited a distinct endothermic signal at approximately 226.30 °C, characteristic of its melting transition, confirming its crystalline, anhydrous nature. In contrast, the physical mixtures prepared with Kollicoat IR® and HP-β-CD (Figures 6 and 7) exhibited lower endothermic peak intensities, likely due to the dilution effect of the polymeric carriers. These combinations also demonstrated a noticeable decrease in the exothermic event. The spray-dried microparticles exhibited a minor endothermic transition, indicating partial preservation of clarithromycin's crystalline form. Importantly, no degradation-associated thermal events were detected up to 300 °C (Figures 6 and 7), suggesting that the formulation retained good thermal stability after the spray-drying process.

X-ray Diffraction (XRD)

The solid-state characteristics of clarithromycin and its spray-dried microparticles were investigated using X-ray diffraction (XRD) analysis. The diffractogram of pure clarithromycin exhibited intense and sharp diffraction peaks at approximately 2θ values of 17°, 22°, 25°, 37°, 40°, and 42°, confirming its crystalline nature (Figure 8). In contrast, the spray-dried microparticles formulated with HP-β-cyclodextrin and Kollicoat IR® showed a marked reduction or complete disappearance of these characteristic crystalline peaks (Figures 9 and 10), indicating a transition of clarithromycin from a crystalline to an amorphous state induced by the spray-drying process. Although XRD patterns indicated a substantial reduction of crystalline peaks, the presence of a minor endothermic event in DSC suggests residual crystallinity. Therefore, the spray-dried microparticles can be described as predominantly amorphous rather than completely amorphous.

In-vitro drug release study

The in-vitro drug release behavior of clarithromycin-loaded microparticles was evaluated using the USP dissolution apparatus type II. The cumulative percentage drug release profiles are summarized in Table 2 and illustrated in Figures 11 and 12. It was observed that formulations containing a higher polymer-to-drug ratio (above 1:1) exhibited a comparatively slower drug release. This reduction in release rate can be attributed to the formation of a denser polymeric matrix, which increases the diffusion path length and reduces drug mobility within the microspheres. Among all formulations, the 1:1 polymer-to-drug ratio demonstrated the highest drug release, indicating an optimal balance between matrix integrity and drug diffusion. The marketed product (Klarinova-250) is a film-coated tablet, which plausibly accounts for its longer disintegration time (19.27 min) and delayed dissolution, introducing an inherent lag phase compared with the porous spray-dried formulations.

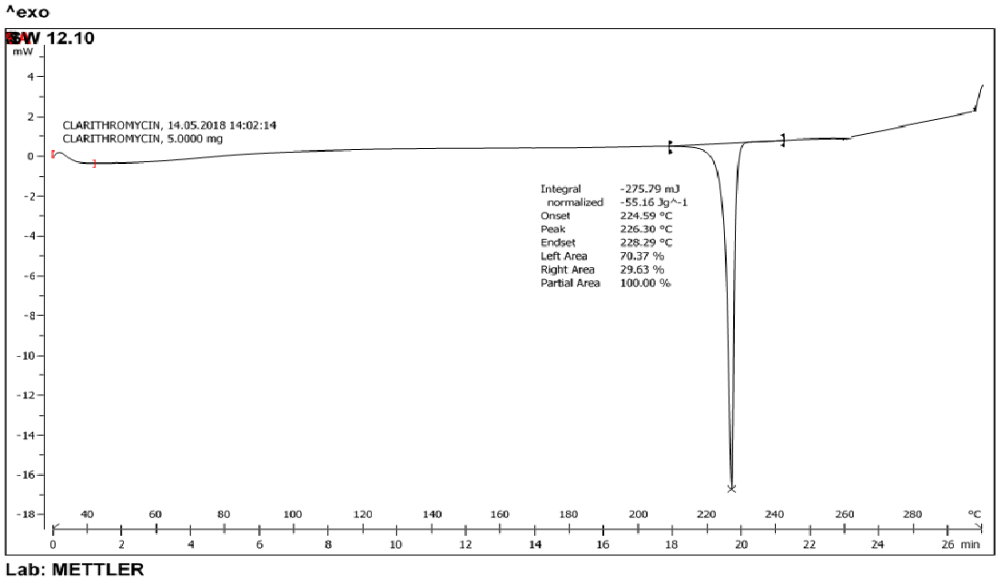

Figure 5: Differential scanning calorimetry (DSC) thermogram of pure clarithromycin showing a sharp endothermic melting peak at approximately 226.3 °C

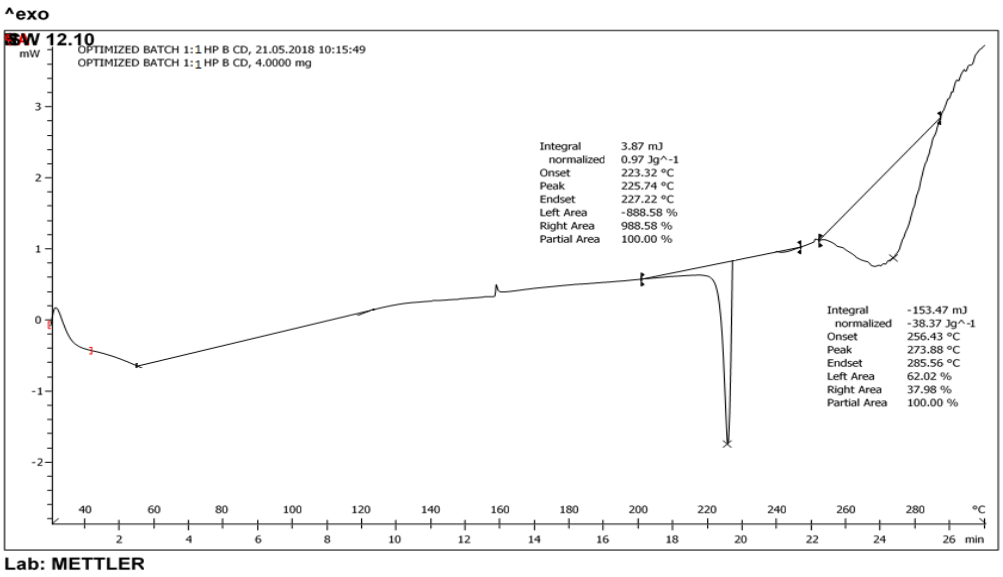

Figure 6: Differential scanning calorimetry (DSC) thermogram of the physical mixture of clarithromycin with HP-β-cyclodextrin

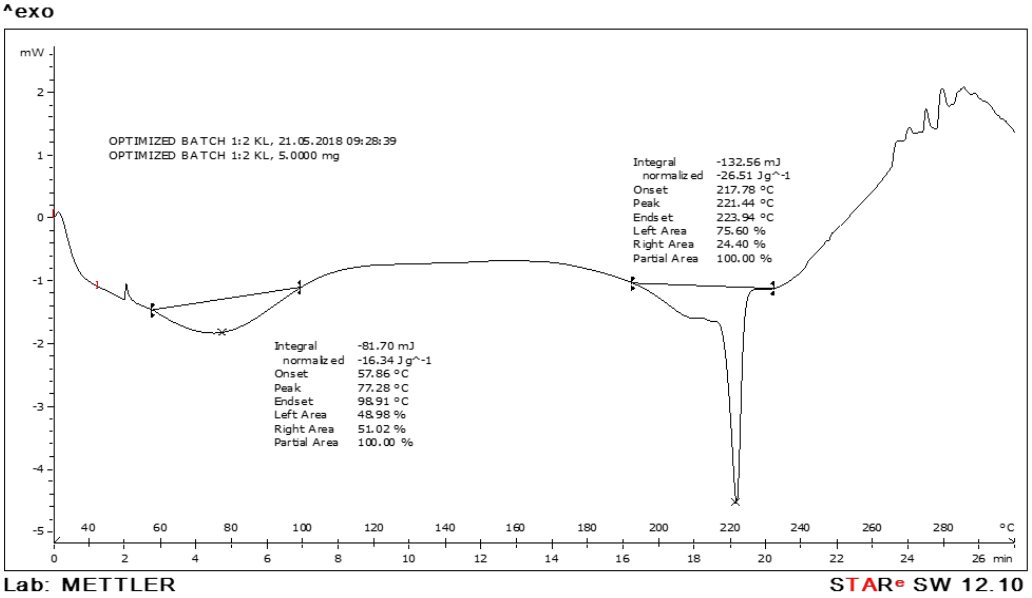

Figure 7: Differential scanning calorimetry (DSC) thermogram of the physical mixture of clarithromycin with Kollicoat IR®

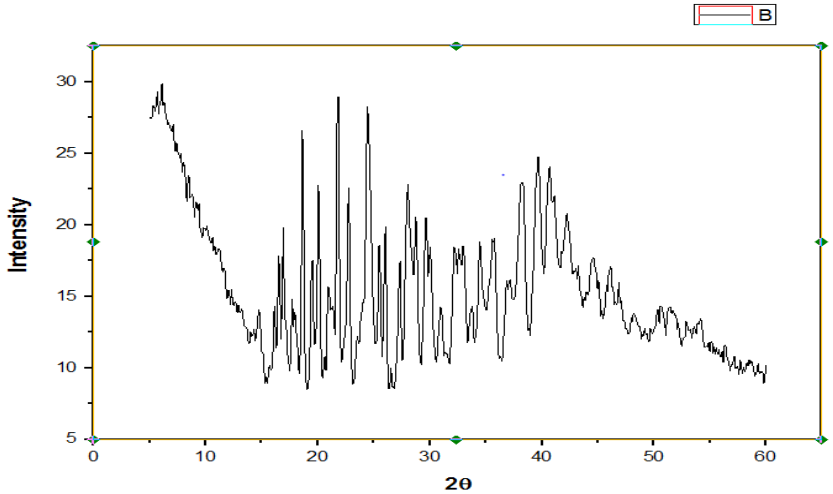

Figure 8: X-ray diffraction (XRD) pattern of pure clarithromycin

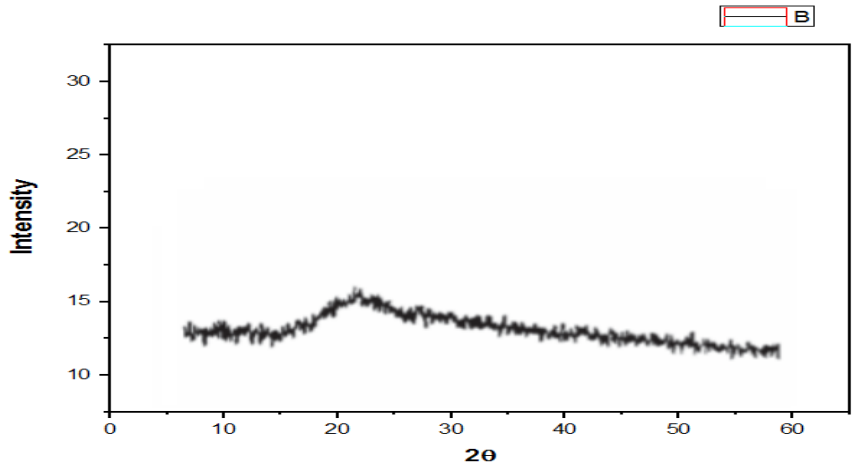

Figure 9: X-ray diffraction (XRD) pattern of spray-dried clarithromycin-loaded microparticles formulated with HP-β-cyclodextrin

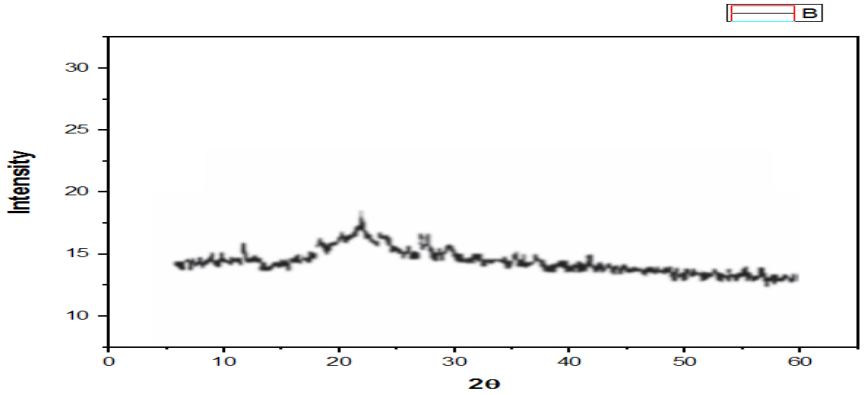

Figure 10: X-ray diffraction (XRD) pattern of spray-dried clarithromycin-loaded microparticles formulated with Kollicoat IR®

Table 2: In-vitro cumulative percentage drug release profile of clarithromycin from microparticles formulated with HP-β-cyclodextrin (CH series) and Kollicoat IR® (CK series) at different polymer-to-drug ratios (mean ± SD, n = 3)

Time (min)	CH 2:1	CH 1:1	CH 1:2	CH 1:3	CK 2:1	CK 1:1	CK 1:2	CK 1:3
0	0	**0**	0	0	0	**0**	0	0
05	51.12±1.03	**82.20±0.3**	54.0±1.17	48.24±0.78	57.6±0.11	**79.92±0.57**	62.64±1.04	47.52±0.5
10	52.84±0.69	**85.42±0.47**	57.18±0.68	52.82±1.0	60.8±0.48	**82.52±1.09**	65.86±0.64	52.82±0.61
15	55.01±1.1	**89.03±1.05**	63.67±1.05	58.59±0.65	64.42±0.55	**86.13±0.88**	68.04±0.89	55.01±1.22
20	60.06±0.76	**90.49±0.78**	67.31±1.04	60.08±0.13	67.32±0.57	**89.03±1.02**	70.93±0.94	57.9±0.65
30	62.97±1.39	**91.22±1.08**	73.09±0.75	62.25±1.25	69.49±1.15	**91.93±0.92**	71.67±1.06	62.24±0.41
40	65.87±0.49	**93.38±1.39**	75.28±0.57	65.86±0.45	73.1±1.15	**92.66±0.56**	74.55±0.57	64.42±1.56
50	68.04±0.54	**94.83±0.34**	77.45±0.69	69.48±0.77	73.84±0.73	**94.11±0.89**	76.33±0.87	68.03±0.55
60	68.78±0.72	**96.28±1.13**	76.02±0.50	71.66±0.96	74.57±0.69	**93.42±0.83**	77.46±0.09	68.77±0.62

Formulation and development of immediate-release tablet

The pre-compression parameters of spray-dried clarithromycin microparticles and their blends with excipients are summarized in Table 3. The bulk density values of the microparticles and their excipient blends ranged between 0.30 & 0.40 g/cm³, which falls within the acceptable limits for solid oral dosage form development. The tapped density values were slightly higher, reflecting adequate particle packing upon mechanical tapping. Hausner's ratio values for spray-dried microparticles ranged from 1.20 to 1.21, indicating fair to poor flow properties, whereas the blends containing excipients exhibited improved flow behavior with Hausner's ratio values between 1.14 and 1.16, which are classified as good flow characteristics. Similarly, Carr's Index values for spray-dried microparticles were relatively high (16.66–17.39%), suggesting inferior flowability. However, upon blending with excipients, Carr's Index values

decreased to 12.82–14.28%, confirming a significant enhancement in powder flow properties. The angle of repose values ranged from 28.74° to 34.12°, indicating good to excellent flow behavior for all formulations.

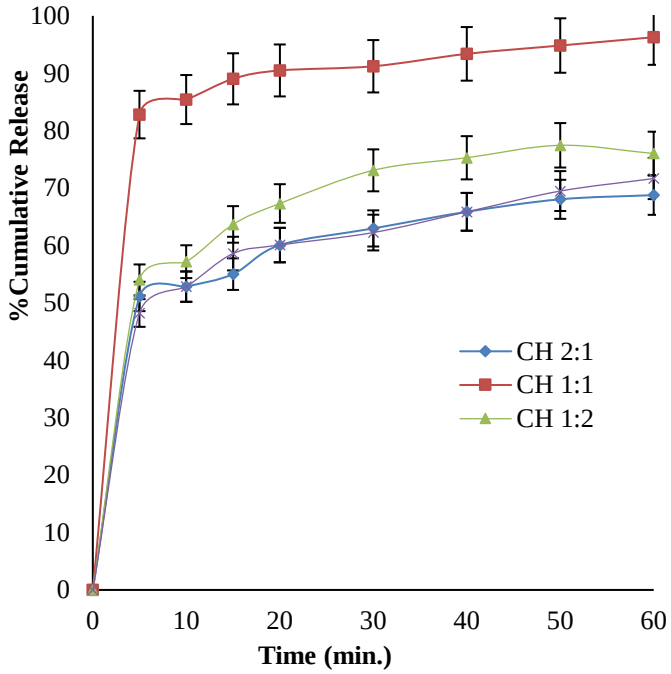

Figure 11: In-vitro cumulative drug release profiles of clarithromycin-loaded microparticles formulated with HP-β-cyclodextrin (CH 2:1, CH 1:1, CH 1:2, and CH 1:3)

Notably, the excipient-containing blends exhibited lower angles of repose than pure spray-dried microparticles, further supporting improved flow characteristics. Since all measured angles were below 35°, the powders were considered suitable for direct compression during immediate-release tablet formulation (Table 3).

Tablet appearance

Visual inspection of tablets from each batch revealed flat, circular shapes with smooth surfaces, free from cracks, and white in color.

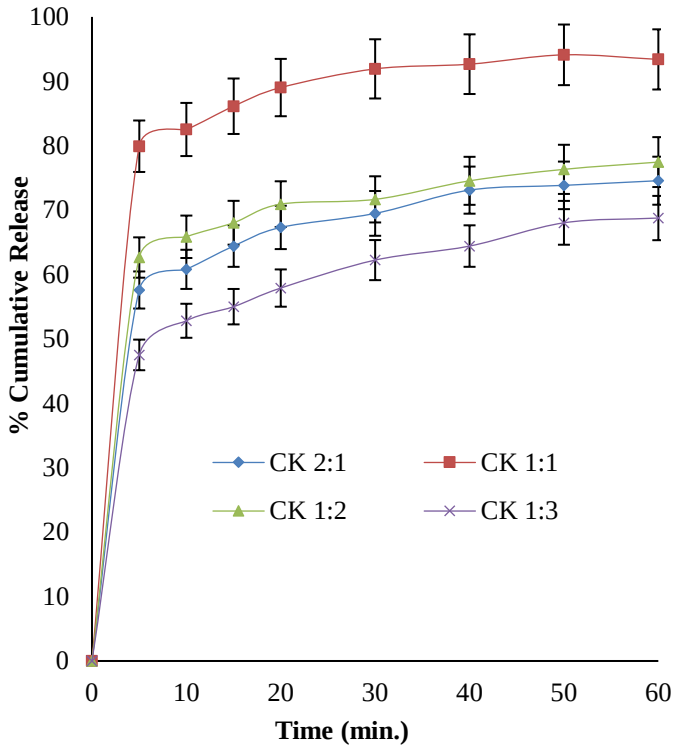

Figure 12: In-vitro cumulative drug release profiles of clarithromycin-loaded microparticles formulated with Kollicoat IR® (CK 2:1, CK 1:1, CK 1:2, and CK 1:3)

Table 3: Pre-compression parameters of spray-dried clarithromycin microparticles and their blends with excipients for immediate-release tablet formulation

Parameters	MHP	Result	MHP with Excipient	Result	MKL	Result	MKL with Excipient	Result
Bulk Density (g/cm^3)	0.38	-	0.34	-	0.40	-	0.30	-
Tapped Density($g/cm^{3)}$	0.46	-	0.39	-	0.48	-	0.35	-
Hausnner's Ratio	1.21	Fair	1.14	Good	1.20	Fair	1.16	Good
Carr's Index (%)	17.39	Fair	12.82	Good	16.66	Fair	14.28	Good
Angle of Repose (˚)	34.12	Good	29.36	Excellent	33.82	Good	28.74	Excellent

Weight variation

The weight variation data for all formulations are presented in Table 4. Tablets containing drug microparticles with Kollicoat IR® weighed between 553 and 555 mg, while those prepared with the microparticles-excipient blend weighed between 653 and 657 mg. Similarly, tablets containing drug microparticles with HP-β-CD weighed between 558 and 562 mg, and those with the corresponding excipient blend weighed between 658 and 661 mg. All tablet weights were consistent across batches.

Tablet hardness and thickness

The acceptable hardness range for tablets is 4–10 kg/cm³. Tablets prepared from microparticles maintained hardness values between 4 and 6 kg/cm³. Low standard deviation values indicated uniform hardness across batches, signifying good mechanical strength. Tablet thickness for each formulation was measured using a micrometer on three randomly selected tablets, and mean values are presented in Table 4.

Tablet friability

The post-compression evaluation parameters of the developed immediate-release tablet formulations are presented in Table 4. All formulations exhibited satisfactory mechanical strength, as evidenced by friability values within the pharmacopeial acceptable limit of ≤ 1%. The friability values ranged from 0.42 ± 0.081% to 0.64 ± 0.094%, indicating good resistance to abrasion and mechanical stress during handling, packaging, and transportation. Formulations containing excipients showed slightly higher friability values compared to formulations without excipients; however, all values remained well below the specified limit, confirming adequate tablet robustness. The observed friability results correlate with the measured tablet hardness values (5.37–5.71 kg/cm²), suggesting an optimal balance between tablet strength and compressibility. Overall, the low friability values confirm the suitability of the developed formulations for routine manufacturing and handling processes (Table 4).

Table 4: Post-compression evaluation parameters of immediate-release tablets prepared from spray-dried microparticles and their excipient blends (*All values are mean ±SD, n=3***)**

Post Compression Parameters	MHP	MHP with Excipient	MKL	MKL With Excipient
Thickness (mm)	6.1±0.24	6.9±0.18	6.2±0.28	6.8±0.39
Hardness (kg/cm^3)	5.65±1.15	5.37±0.98	5.71±0.93	5.43±1.04
Weight Variation (mg)	561.40±1.27	661.58±2.08	555.10±1.75	654.35±2.04
Friability (%)	0.42±0.081	0.58±0.074	0.46±0.089	0.52±0.094

Drug content of the tablet

The drug content uniformity of the developed immediate-release tablet formulations was evaluated using a UV–visible spectrophotometric method, and the results are summarized in Table 5. For each formulation, three tablets were analyzed to ensure uniformity and reproducibility. The percentage drug content across all formulations ranged from 94.56 ± 1.87% to 98.27 ± 1.04%, indicating satisfactory drug distribution within the tablets. Formulations MHP and MHP with excipients exhibited higher drug content values (97.24–98.12%), comparable to the marketed tablet (98.27 ± 1.04%). In contrast, MKL-based formulations showed slightly lower drug content; however, all values remained within the pharmacopeial acceptance range of 90–110%. These findings confirm the adequacy of the formulation process and the effectiveness of the mixing and compression steps in achieving uniform drug content across all tablet formulations (Table 5).

Table 5: Drug content uniformity of immediate-release tablet formulations prepared from spray-dried microparticles in comparison with a marketed product (*All values are mean ±SD, n=3***)**

Post compression parameter	MHP	MHP with excipients	MKL	MKL with excipient	Marketed Tablet
Drug content (%)	98.12 ±1.2	97.24 ±1.52	95.36 ±1	94.56 ±1.87	98.27 ±1.04

In-vitro disintegration time

The in-vitro disintegration behavior of the developed immediate-release tablet formulations and the marketed tablet is presented in Table 6. Tablet disintegration is governed by internal structural characteristics such as pore size distribution, liquid penetration rate, and the swelling efficiency of incorporated disintegrating agents, which collectively determine the tablet break-up mechanism in an aqueous medium. All formulated tablets exhibited disintegration times of less than 15 minutes, indicating compliance with pharmacopeial requirements for immediate-release tablets. In contrast, the marketed tablet showed a comparatively longer disintegration time of 19.27 ± 1.04 minutes. Formulations containing excipients disintegrated faster (11.42 ± 1.52 to 11.56 ± 1.57 minutes) than those without excipients, highlighting the enhanced effectiveness of the disintegrant system. The observed disintegration behavior may be attributed to optimized tablet hardness and efficient swelling action of the disintegrating

agents, which promote rapid water uptake and subsequent tablet fragmentation. These findings confirm the suitability of the developed formulations for immediate-release drug delivery applications (Table 6).

Table 6: In-vitro disintegration time of immediate-release tablet formulations prepared from spray-dried microparticles and comparison with marketed tablet (*All values are mean ±SD, n=3*)

Post compression parameter	MHP	MHP with excipients	MKL	MKL with excipient	Marketed Tablet
Disintegration Time (min)	14.30 ±1	11.42 ±1.52	14.36 ±1.3	11.56 ±1.57	19.27 ±1.04

***In-Vitro* dissolution studies**

Each prepared formulation was assessed for in vitro dissolution using a tablet dissolution tester (Model TDT-08, Electrolab, Mumbai, India). The drug release profiles obtained from these studies are presented in Tables 7, 8, and 9, while their graphical illustrations are provided in Figure 13.

1. Clarithromycin with HP-β-Cyclodextrin

A clarithromycin immediate-release tablet containing spray-dried clarithromycin and HP-β-cyclodextrin microparticles prepared by the direct compression method was found to release 92.62% and 96.27% of the drug content after 60 minutes. Tablets prepared using an excipient result in a higher amount of drug release because the disintegration time is less in these tablets than in the tablets that are prepared by direct compression of microparticles only.

2. Marketed clarithromycin tablet

Marketed clarithromycin tablets showed lower drug release than tablets prepared using drug microparticles with HP-β-cyclodextrin and Kollicoat IR®. An immediate-release tablet prepared using microparticles of clarithromycin and HP-β-cyclodextrin resulted in higher drug release of 96.27%. The slower release observed for the marketed tablet is likely attributable to formulation-related factors such as film coating, compact matrix structure & longer DT rather than chemical degradation, as the optimized spray-dried formulations demonstrated rapid release under identical acidic conditions.

Table 7: In-vitro drug release profile of immediate-release tablet formulations containing HP-β-cyclodextrin (with and without excipients)

Time (min)	MHP	MHP with excipient
0	0	0
5	52.14±1.93	57.6±1.71
10	63.52±0.82	68±1.32
20	74.47±1.21	76.69±0.98
30	82.15±1.39	87.54±1.09
40	87.23±1.47	89.76±1.47
50	90.15±2.31	93.37±1025
60	92.62±2.18	96.27±2.11

Table 8: In-vitro drug release profile of the marketed immediate-release tablet formulation

Time (min)	Marketed Tablet
0	0
5	53.24±2.04
10	57.54±1.54
20	65.84±1.34
30	72.41±2.14
40	77.64±0.98
50	80.36±1.58
60	81.54±1.87

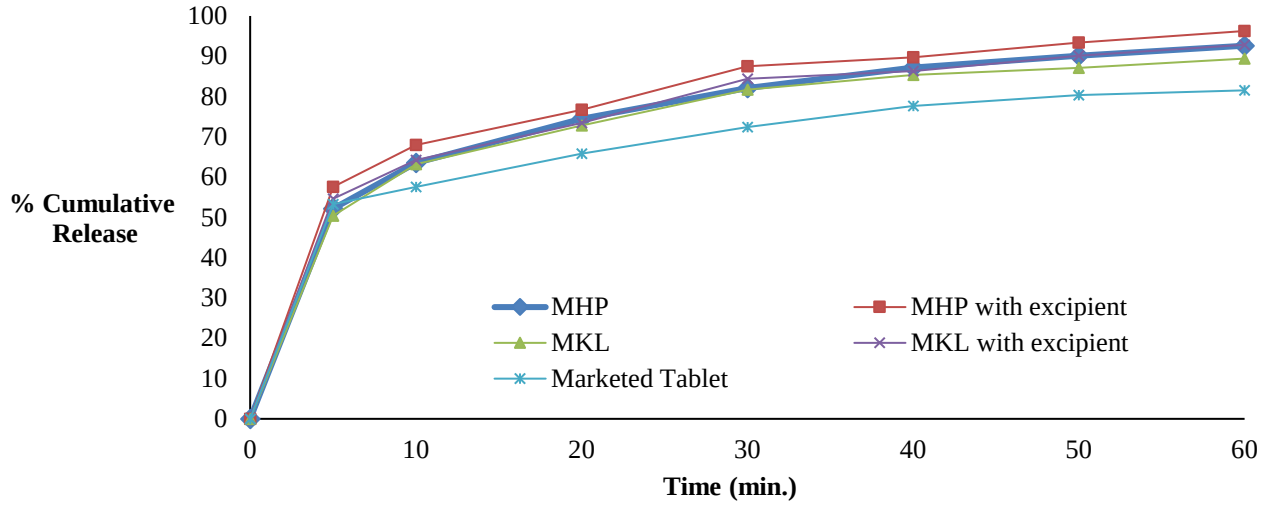

Figure 13: Comparative in-vitro dissolution profiles of developed immediate-release tablet formulations and marketed tablet

3. Clarithromycin with Kollicoat IR®

A clarithromycin immediate-release tablet prepared using microparticles of the drug and Kollicoat IR® polymer showed less drug release than the tablets prepared using HP-β-cyclodextrin polymer. Tablets prepared by microparticles of the drug and Kollicoat IR® using the excipient showed higher drug release than the tablets prepared by using microparticles only.

Table 9: In-vitro drug release profile of immediate-release tablet formulations containing Kollicoat® IR (with and without excipients)

Time (min)	MKL	MKL with excipient
0	0	0
5	50.44±1.09	54.61±0.87
10	63.22±1.21	64.24±2.25
20	72.81±2.01	73.49±1.39
30	81.74±1.67	84.45±1.52
40	85.38±1.14	86.32±1.18
50	87.14±1.08	90.17±1.22
60	89.42±0.54	92.85±1.17

Dissolution profiles were compared using the similarity factor (f_2); f_2 values > 50 indicate similarity between test and reference formulations.

CONCLUSION

Immediate-release clarithromycin tablets were successfully developed by direct compression of spray-dried microparticles, demonstrating a formulation strategy that is both technically efficient and scalable for industrial application. Spray drying with hydrophilic carriers, namely HP-β-cyclodextrin and Kollicoat IR®, produced uniformly spherical microparticles and induced a solid-state transformation of clarithromycin from a crystalline to an amorphous form, as confirmed by X-ray diffraction analysis. This amorphization played a critical role in enhancing aqueous solubility & dissolution performance, leading to faster and more complete drug release compared with the marketed formulation. Among the evaluated carriers, HP-β-cyclodextrin exhibited superior performance, yielding higher cumulative drug release than Kollicoat IR®, particularly when combined with suitable excipients.

The formulated tablets consistently met pharmacopeial requirements for mechanical strength, friability, weight uniformity, drug content, and rapid disintegration, confirming their robustness and suitability for immediate-release oral delivery. Although the study was limited to in-vitro evaluation, the findings provide strong evidence that spray drying is a promising and contemporary formulation approach for addressing solubility- and dissolution-related challenges associated with poorly water-soluble drugs, with clarithromycin serving as a representative model compound.

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FINANCIAL ASSISTANCE

NIL

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Sagar Kamble conceived and designed the study. Ajay Salvi, Yogesh Borhade, and Shivaji Patil performed the experiments and collected the data. Ajay Salvi contributed to data interpretation, manuscript review, and overall guidance. Sagar Kamble drafted the initial manuscript, and all authors reviewed, edited, and approved the final version.

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