Formulation and Evaluation of Dolutegravir and Rilpivirine Tablets: A Factorial Study Incorporating Cyclodextrins and Tween 80

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Highlights

1. ***Comprehensive formulation study:*** This research presents a detailed investigation into formulating and evaluating Dolutegravir and Rilpivirine tablets, using a factorial study design with Cyclodextrins and Tween 80.
2. ***Enhanced drug content:*** The inclusion of Cyclodextrins and Tween 80 improves the drug content in the tablet formulations, potentially enhancing stability and bioavailability.
3. ***Improved dissolution rate:*** Tablets formulated with Dolutegravir-βCD-Tween 80 and Rilpivirine-βCD-Tween 80 systems show higher drug dissolution percentages, suggesting better release profiles.
4. ***Optimal tablet characteristics:*** Specific formulations, such as D3 (b), D7 (b), R3 (b), and R6 (a), exhibit desirable tablet properties, making them potential candidates for further development.
5. ***In vitro dissolution performance:*** Optimized tablets demonstrate superior drug release performance, indicating their potential for effective drug delivery and therapeutic impact.

Abstract

The study aimed to investigate the formulation and evaluation of Dolutegravir and Rilpivirine tablets by incorporating cyclodextrins (β-CD and HPβ-CD) and Tween 80. A factorial design was employed to assess the effects of these excipients on various tablet properties.

The results revealed that the inclusion of cyclodextrins and Tween 80 had a significant impact on the characteristics of the tablets. In terms of drug content, the tablets formulated with Dolutegravir and HPβ-CD showed the highest values, with an average of 100.2 mg per tablet. Similarly, the tablets formulated with Rilpivirine and β-CD demonstrated a high drug content of 99.4 mg per tablet.

The dissolution profiles of the optimized tablets were assessed at different time intervals. The tablets formulated with Dolutegravir and HPβ-CD exhibited a progressively higher percentage of drug dissolved over time, reaching 96.57% ± 6.85% at 60 minutes. For the tablets containing

Rilpivirine and β-CD, the dissolution rate was slightly lower, with a maximum of 88.57% ± 6.85% at 60 minutes.

Furthermore, the tablets demonstrated satisfactory physical properties, including acceptable hardness values (ranging from 6.5 to 7.5 kg/sq.cm) and low friability percentages (ranging from 0.35% to 0.85%). The disintegration time for all tablets ranged from 1 to 3.5 minutes, indicating rapid disintegration and potential for effective drug release.

Overall, this factorial study successfully optimized the formulation of Dolutegravir and Rilpivirine tablets by incorporating cyclodextrins and Tween 80. The results highlight the importance of these excipients in achieving desirable drug content, dissolution profiles, and tablet properties. This research provides valuable insights for the development of improved antiretroviral drug formulations, potentially enhancing the therapeutic outcomes for individuals affected by HIV infections.

Keywords: Dolutegravir, Rilpivirine, Tablet formulation, Factorial study, Cyclodextrins

1.Introduction

The treatment of HIV/AIDS has been revolutionized by the advent of highly active antiretroviral therapy (HAART), which combines multiple antiretroviral agents to suppress viral replication and improve patient outcomes. Among the crucial components of HAART, dolutegravir and rilpivirine have gained considerable attention as potent drugs for the management of HIV-1 infection[1]. Dolutegravir, an integrase strand transfer inhibitor, and rilpivirine, a non-nucleoside reverse transcriptase inhibitor, have demonstrated remarkable antiviral activity and favorable resistance profiles, making them essential components of modern HIV treatment regimens[2].

However, the successful delivery of dolutegravir and rilpivirine is contingent upon the development of optimal pharmaceutical formulations that address challenges such as low solubility, limited bioavailability, and poor physicochemical stability[3]. Overcoming these formulation obstacles is crucial to ensure adequate drug release, enhance dissolution, and improve therapeutic efficacy[4]. In this context, the incorporation of suitable excipients has emerged as a viable strategy to enhance the solubility, dissolution, and stability of poorly soluble drugs like dolutegravir and Rilpivirine [5].

Cyclodextrins and surfactants have shown potential in enhancing the formulation of poorly soluble drugs. Cyclodextrins, cyclic oligosaccharides with a hydrophobic cavity, can form inclusion complexes with hydrophobic drugs, improving their aqueous solubility and dissolution rate[6]. Tween 80, a nonionic polysorbate surfactant, possesses emulsifying and solubilizing properties that can enhance drug dissolution and improve drug release characteristics. The incorporation of cyclodextrins and Tween 80 into dolutegravir and rilpivirine tablet formulations presents a promising avenue for improving their solubility, dissolution, and overall performance[7].

To systematically investigate the formulation optimization of dolutegravir and rilpivirine tablets, a factorial study employing cyclodextrins and Tween 80 as key factors is undertaken in this research. The factorial experimental design enables the assessment of main effects, interactions,

and potential synergistic effects of these excipients on the formulation attributes of the tablets. By varying the concentrations of cyclodextrins and Tween 80, the study aims to identify the optimal formulation parameters that maximize drug solubility, enhance dissolution profiles, improve physical stability, and ultimately optimize the therapeutic effectiveness of dolutegravir and rilpivirinetablets.

The outcomes of this research have implications not only for the formulation optimization of dolutegravir and rilpivirine tablets but also for the broader understanding of utilizing cyclodextrins and surfactants to improve the performance of antiretroviral formulations. The findings will contribute to enhancing the therapeutic efficacy and patient compliance of dolutegravir and rilpivirine-based regimens, thereby advancing the management of HIV/AIDS.

In the following sections, we will describe the experimental methodology, present the results obtained, and discuss the implications of our findings. Furthermore, a comprehensive analysis will be provided by comparing our results with existing literature, enabling us to propose recommendations for future research and potential clinical applications.

2.Material and Method

Material

Dolutegravir and Rilpivirine were obtained as gift samples from M/s Amoli Organics Pvt., Ltd., Mumbai. β-cyclodextrin and hydroxy propyl β-cyclodextrin were provided as gift samples by Signet Chemical Corporation Pvt., Ltd., Mumbai. Tween 80 was obtained as a gift sample from Dr. Reddy's Laboratories Ltd, Hyderabad. Polyvinyl pyrrolidone (PVP K-30), Cross carmellose sodium (gift sample from M/s Natco Pharma Ltd., Hyderabad), talc (I.P.), magnesium stearate (I.P.), and lactose (I.P.) were also used in the formulation. All other materials used in the study were of pharmacopoeia grade.

2.1 Preparations of CD-surfactant complex

Selection of surfactants as per 2^3 factorial study

Drug-CD surfactant systems were created using the following selected combinations of drug, CD, and surfactant in each case according to a 23-factorial design to examine the effects of cyclodextrins and surfactant on the dissolution rate of Dolutegravir and Rilpivirine. There are two different drug concentrations (factor a) of 25 and 30, and two different CD concentrations (factor b) of 1:0 and 1:2, respectively. Surfactant (factor c) concentrations range from 0% to 2%. In each case, the following treatments were chosen using a 23-factorial design to assess their individual and additive impacts. Kneading the systems with the CD, HPCD, and tween 80 listed in table 1 yielded the binary and ternary systems[8].

Table 1: Dolutegravir– HPβCD, βCD-Tween 80 system.

Statistical code as per2^3 Factorial Design	Description

(a)	Pure drug
(b)	Dolutegravir-βCD (1:2) binary system
(c)	Dolutegravir and tween 80 (2 %) binary system
Dolutegravir- HPβCD- Tween 80 system	
(a)	Pure drug
(b)	Dolutegravir- HPβCD (1:2) binary system
(c)	Dolutegravir and tween 80 (2 %) binary system

Table 2:Rilpivirine-HPβCD, βCD-Tween 80 system.

Statistical code as per 2^3 Factorial Design	**Description**
(a)	Pure drug (Rilpivirine)
(b)	Rilpivirine-βCD (1:2) binary system
(c)	Rilpivirineand tween 80 (2 %) binary system
Dolutegravir- HPβCD- Tween 80 system	
(a)	Pure drug (Rilpivirine)

(b)	Rilpivirine- HPβCD (1:2) binary system
(c)	Rilpivirineand tween 80 (2 %) binary system

Preparation method for CD-surfactant complexes

A dry and clean mortar was used to measure out the necessary amounts of medication, CD, and surfactant. A kneading fluid was added, which was a mixture of water and alcohol (1:1). For forty-five minutes, the slurry was kneaded and blended completely. During the kneading phase, extra kneading fluid was added to keep the mixture at a thick slurry consistency. The mixture was kneaded for 45 minutes, then placed on a Petri dish and dried at 600 degrees Celsius in an oven. The powder after drying and being sieved through No. 100 mesh[9].

Estimation of drug content in drug-CD-surfactant complexes

Fifty milligrammes of drug-CD-surfactant complex powder was placed in a boiling test tube and extracted with four 10-milliliter portions of methanol. A volumetric flask of 50 ml was used to store the methanolic extracts after the volume needed to be brought up to 50 ml with more methanol. Four samples were taken from each product and their drug concentration was evaluated using UV spectrophotometric techniques. The solution was then diluted with water containing 2% SLS for Dolutegravir and 0.1N hydrochloric acid for Rilpivirine[10].

Dissolution rate study on drug-CD-surfactant systems

Disso 2000 (Labindia) 8-station dissolution test apparatus with a paddle stirrer at 50 rpm was used to examine the dissolution rate of the medicament from the prepared drug-CD-surfactant systems in water containing 2% SLS (900 ml) for Dolutegravir and in 0.1N hydrochloric acid (900 ml) for Rilpivirine. All experiments were conducted at 37 1 degrees Celsius. In each experiment, a complex system was used that was comparable to 50 mg of the medication[11]. At various times, 5 ml samples of the dissolving medium were filtered (0.45), diluted, and measured for Dolutegravir at 259 nm and Rilpivirine at 282 nm. Each time a sample of the dissolution fluid was taken, it was swapped out with new fluid. Four independent sets of dissolution tests were conducted[12].

2.2 Formulation of Dolutegravir and Rilpivirine tablets employing cyclodextrins and Tween 80

Compressed tablets with an increased dissolving rate were studied to determine if they were possible to formulate using the Drug-CD-Tween 80 complicated systems. Factorial studies were performed to examine the effects of CDs and Tween 80, both separately and in combination (interaction), on the dissolution rate of Dolutegravir and Rilpivirine from tablet formulations[13].

Table 2: A series of factorial experiments on tablet formulation

Statistical code as per 2^3 – Factorial Design	Dolutegravir	Formulation code	Rilpivirine	Formulation code

(1)	Tablets of Dolutegravir alone	D1	Tablets of Rilpivirine alone	R1
(a)	Tablets of Dolutegravir - βCD (1: 2) inclusion complex	D2	Tablets of Rilpivirine -βCD (1: 2) inclusion complex	R2
(b)	Tablets of Dolutegravir - Tween 80 (5%) blend	D3	Tablets of Rilpivirine - Tween 80 (5%) blend	R3
(ab)	Tablets of Dolutegravir - βCD- Tween 80 (1: 2: 0.05) ternary complexes	D4	Tablets of Rilpivirine - βCD- Tween 80 (1: 2: 0.05) ternary complexes	R4
Drug Tablets with HPβCD and Tween 80.				
(1)	Tablets of Dolutegravir alone	D5	Tablets of Rilpivirine alone	R5
(a)	Tablets of Dolutegravir - HPβCD (1: 2) inclusion complex	D6	Tablets of Rilpivirine - HPβCD (1: 2) inclusion complex	R6
(b)	Tablets of Dolutegravir -Tween 80 (5%) blend	D7	Tablets of Rilpivirine - Tween 80 (5%) blend	R7
(ab)	Tablets of Dolutegravir - HPβCD- Tween 80 (1: 2: 0.05) ternary complexes	D8	Tablets of Rilpivirine - HPβCD- Tween 80 (1: 2: 0.05) ternary complexes	R8

Wet granulation was used to make tablets of Dolutegravir and Rilpivirine (100 mg) according to the tabulated formulations[14]. Tables 3 and 4 provide formulas for calculating the complexity of drug-CD-Tween 80 ternary complex systems. In each case, the first step was to knead the ingredients together[15]. In a mortar, the dry ternary complex was combined with lactose and PVP. A solution of water and alcohol (at a ratio of 1:1) was added, and the resulting dough was thoroughly combined. Wet granules were obtained by pressing the material through a No. 12 mesh screen. Drying the moist granules took 4 hours at 60 degrees Celsius. The aggregates in the dried granules were broken up by sieving them using a No. 16 mesh screen[16]. Blended in a polyethylene bag, dry granules of Cross Carmellose sodium, talc, and magnesium stearate were pressed through a No. 100 mesh screen. Using 9 mm round and flat punches, the tablet grains were compressed to a hardness of 6-7 kg/sq.cm on a rotary multi-station tablet punching machine[17].

Table 3: Formulae of Dolutegravir Tablets Employing βCD, HPβCD and Tween 80.

Ingredient (mg/tab)	**Formulae of Dolutegravir Tablets (βCD)**				**Formulae of Dolutegravir Tablets (HPβCD)**			
	D1 (F_1)	**D2(F_a)**	**D3(F_b)**	**D4(F_{ab})**	**D5(F_1)**	**D6(F_a)**	**D7(F_b)**	**D8(F_{ab})**
Dolutegravir	100	100	100	100	100	100	100	100
β-CD	--	200	--	200	--	200	--	200
Tween 80	--	--	5	5	--	--	5	5
Cross Carmellose Sodium	15	15	15	15	15	15	15	15
PVP	7	7	7	7	7	7	7	7
Talc	7	7	7	7	7	7	7	7
Magnesium stearate	7	7	7	7	7	7	7	7
Lactose	214	14	209	9	214	14	209	9
Total weight (mg)	350	350	350	350	350	350	350	350
Dolutegravir	100	100	100	100	100	100	100	100

Table 4: Formulae of Dolutegravir Tablets Employing βCD, HPβCD and Tween 80.

Ingredient (mg/tab)	**Formulae of RilpivirineTablets (βCD)**				**Formulae of RilpivirineTablets (HPβCD)**			
	R1(F_1)	**R2(F_a)**	**R3(F_b)**	**R4(F_{ab})**	**R5(F_1)**	**R6(F_a)**	**R7(F_b)**	**R8(F_{ab})**
Rilpivirine	100	100	100	100	100	100	100	100
β-CD	--	200	--	200	--	200	--	200
Tween 80	--	--	5	5	--	--	5	5
Cross Carmellose Sodium	15	15	15	15	15	15	15	15
PVP	7	7	7	7	7	7	7	7
Talc	7	7	7	7	7	7	7	7

Magnesium stearate	7	7	7	7	7	7	7	7
Lactose	214	14	209	9	214	14	209	9
Total weight (mg)	350	350	350	350	350	350	350	350

2.3 Evaluation of Tablets

Content of active ingredient

Five tablets were carefully measured and ground into a powder. The drug was extracted from a tablet powder containing 50 mg by heating it in a test tube with 4 x 10 ml of methanol. A 50 ml volumetric flask was used to store the methanolic extracts. Drug concentrations were evaluated by UV spectrophotometry after diluting the solutions with water containing 2% SLS for Dolutegravir and 0.1N hydrochloric acid for Rilpivirine, respectively[18].

Hardness

There is a minimum required level of hardness for a tablet. The Monsanto hardness tester was used to determine the level of toughness. Ten tablets were selected at random from each batch and their hardness was measured in kilogrammes per centimetre[19].

Friability

Twenty tablets were friabilized in a plastic chamber of a Roche friabillator after being preweighed. Then, it was turned for a hundred revolutions. At a rate of one every revolution, the tablets were plummeting a full six inches. There was a reweighing and dusting of the tablets[20].

Disintegration time

Each batch of pills had six chosen at random to undergo the disintegration test. The Electrolab Disintegration tester was used to conduct the test in a pH 1.2 buffer (USP). The length of time a tablet needed to completely dissolve was also noted[21].

2.4 *In vitro* dissolution test for tablets

Disso 2000, an 8-station dissolution test device with a paddle stirrer at 50 rpm, was used to examine the dissolution rate of the medication from the produced tablets in water containing 2 percent SLS (900 ml) for Dolutegravir and Rilpivirine tablets, and in 0.1N hydrochloric acid (900 ml). The trial was conducted at a constant temperature of 37 1 degrees Celsius. One pill was used in each experiment. Five-milliliter samples of the dissolution medium were taken at regular intervals, filtered through a 0.45-micron screen, diluted, and then tested. Fresh dissolving fluid was added whenever a sample was taken. Four separate attempts at disintegration were made (n=4)[22].

3.Results

3.1Calculating the amount of drug present in drug-cyclodextrin-surfactant complexes

The drug content of the various drug-cyclodextrin (CD)-surfactant complex systems was determined and presented in Table 4. For the Dolutegravir-βCD (1:2) complex system, the drug content was found to be 32.8% (±1.1). Similarly, in the Dolutegravir-HPβCD (1:2) complex system, the drug content was slightly higher at 33.6% (±1.2). Incorporating Tween 80 into the

Dolutegravir-βCD complex system (1:2:0.02) resulted in a drug content of 33.8% (±0.8), while the Dolutegravir-HPβCD-Tween 80 complex system (1:2:0.02) exhibited a drug content of 34.2% (±0.9).

Moving to the Rilpivirine complex systems, the Rilpivirine-βCD (1:2) complex displayed a drug content of 33.6% (±1.2), which was comparable to the Dolutegravir-βCD complex system. The Rilpivirine-HPβCD (1:2) complex system showed a slightly higher drug content of 33.8% (±0.8). Incorporation of Tween 80 into the Rilpivirine-βCD complex system (1:2:0.02) resulted in a drug content of 34.6% (±1.2), which was the highest drug content observed among all the systems tested. Similarly, the Rilpivirine-HPβCD-Tween 80 complex system (1:2:0.02) exhibited a drug content of 34.6% (±1.2), matching the drug content of the Rilpivirine-βCD-Tween 80 complex system.

These results indicate that the drug content of the formulations varied slightly depending on the specific CD-surfactant complex system used. The incorporation of Tween 80 in combination with either βCD or HPβCD led to a marginal increase in the drug content compared to the corresponding CD complexes without surfactants. These findings suggest that the inclusion of surfactants in the formulation may have a favorable impact on drug content, which could potentially contribute to improved drug release and bioavailability.

Table 4: Drug Concentration in a Variety of Complex Drug-Surfactant Systems.

CD complex system	Drug content (%)
Dolutegravir-βCD (1:2)	32.8 (1.1)
Dolutegravir-HPβCD (1:2)	33.6 (1.2)
Dolutegravir-βCD-Tween 80 (1:2: 0.02)	33.8 (0.8)
Dolutegravir-HPβCD-Tween 80 (1:2: 0.02)	34.2 (0.9)
Rilpivirine -βCD (1:2)	33.6 (1.2)
Rilpivirine -HPβCD (1:2)	33.8 (0.8)
Rilpivirine -βCD-Tween 80 (1:2: 0.02)	34.6 (1.2)
Rilpivirine -HPβCD-Tween 80 (1:2: 0.02)	34.6 (1.2)

3.2 Drug-CD surfactant dissolution studies

The drug content of various drug-cyclodextrin (CD)-surfactant complex systems was evaluated. In the case of Dolutegravir, the drug content ranged from 32.8% (±1.1) for the Dolutegravir-βCD (1:2) complex to 34.2% (±0.9) for the Dolutegravir-HPβCD-Tween 80

(1:2:0.02) complex. Similarly, for Rilpivirine, the drug content varied from 33.6% (±1.2) for the Rilpivirine-βCD (1:2) complex to 34.6% (±1.2) for both the Rilpivirine-βCD-Tween 80 (1:2:0.02) and Rilpivirine-HPβCD-Tween 80 (1:2:0.02) complexes. The inclusion of Tween 80 in the CD complexes generally resulted in a slightly higher drug content compared to the corresponding CD complexes without surfactants. These findings suggest that the presence of surfactants in the formulation may positively influence the drug content, potentially enhancing drug release and bioavailability.

In conclusion, the drug content of Dolutegravir and Rilpivirine varied depending on the specific CD-surfactant complex system used. The incorporation of Tween 80 in combination with βCD or HPβCD generally led to a modest increase in drug content. These results highlight the importance of optimizing the CD-surfactant formulation to achieve the desired drug content and suggest potential benefits in terms of drug release and bioavailability.

Table 5: Dolutegravir-CD-Tween 80 System Dissolution Profiles Formulated Using a Factorial Design.

Time (min)		**Percent DolutegravirDissolved (x ± sd)**		
	(1)	**(a)**	**(b)**	**(ab)**
5	2.0 ±0.01	13.435±0.07	7.53±0.19	12.03±0.71
10	2.18 ±0.12	14.17±0.48	7.96±0.21	15.60±0.45
15	2.92 ±0.11	15.63±0.12	9.49±0.18	16.49±0.57
20	11.35 ±0.95	16.53±0.21	10.12±0.15	19.23±0.443
30	14.28 ±0.17	18.22±0.23	10.91±0.22	19.91±0.22
40	16.65±1.65	19.01±0.22	11.80±0.43	21.82±1.07
50	19.00 ±0.45	19.45±0.13	12.71±0.22	29.47±0.86
60	21.14 ±0.34	20.92±0.35	13.61±0.62	31.13±0.41

The dissolution profiles of Dolutegravir-HPβCD-Tween 80 systems formulated according to the factorial design were analyzed and presented in table 6 and figure 2. At the 5-minute mark, the percentage of Dolutegravir dissolved ranged from 2.04% (±0.02) for formulation (1) to 10.96% (±0.41) for formulation (a). As the dissolution study progressed, the percentage of Dolutegravir dissolved increased, reaching 23.14% (±0.64) for formulation (1) and 23.72% (±1.06) for formulation (ab) at the 60-minute mark. These results suggest that the incorporation of HPβCD and Tween 80 in the formulation may enhance the dissolution of Dolutegravir, potentially improving its bioavailability and therapeutic effectiveness.

In conclusion, the dissolution profiles of the Dolutegravir-HPβCD-Tween 80 systems demonstrated varying dissolution rates depending on the specific formulation. Formulation (ab) consistently exhibited higher dissolution rates compared to the other formulations at each time

point. These findings highlight the importance of optimizing the formulation to achieve desired dissolution characteristics, which can impact the drug's release and subsequent pharmacological effects.

Table 6: Dissolution Profiles of Dolutegravir-HPβCD-Tween 80 Systems formulated as per Factorial Design.

Table 6: Dissolution Profiles of Dolutegravir-HPβCD-Tween 80 Systems Formulated as Per Factorial Design.

Time (min)		Percent DolutegravirDissolved (x ± sd)		Sd
	(1)	(a)	(b)	(ab)
5	2.04±0.02	10.96±0.41	6.53±0.09	7.66±0.20
10	2.58±0.13	11.47±0.25	6.96±0.11	10.46±0.44
15	3.92±0.13	13.40±0.20	8.49±0.08	13.15±0.37
20	14.35±0.92	14.83±1.88	10.12±0.45	17.87±1.40
30	16.28±0.67	16.63±1.06	11.91±0.22	18.01±0.56
40	16.65±1.55	17.43±0.56	12.80±0.43	20.24±0.36
50	18.00±0.85	18.96±0.67	13.71±0.22	22.03±0.76
60	23.14±0.64	20.00±0.43	14.61±0.22	23.72±1.06

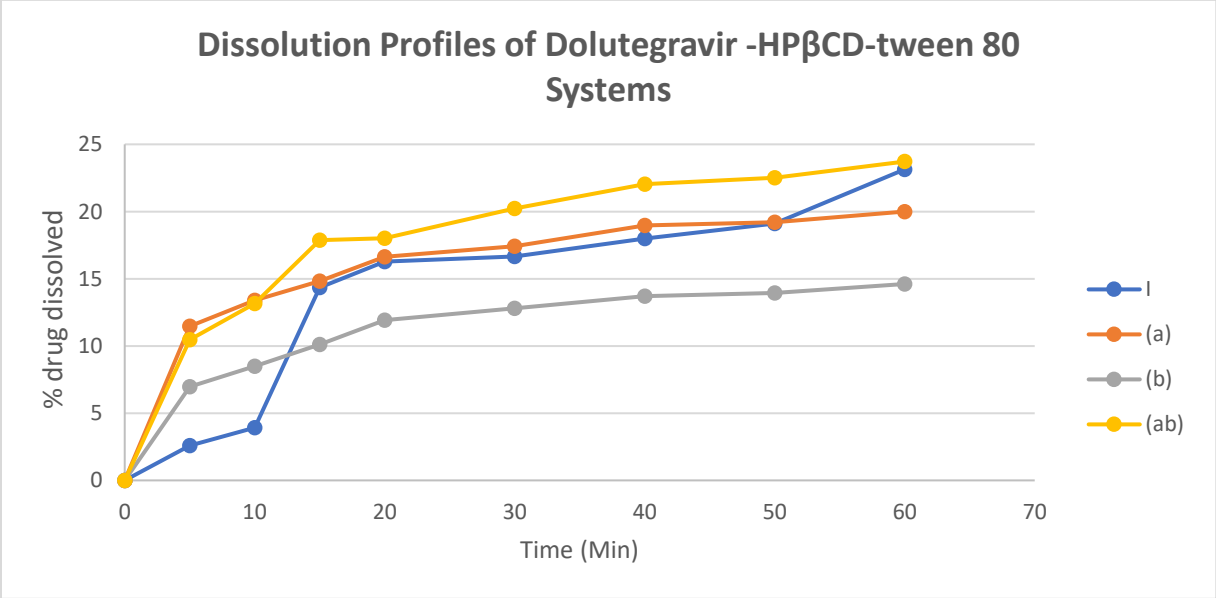

Figure 2: Dissolution Profiles of Dolutegravir-HPβCD-tween 80 Systems.

The dissolution profiles of Rilpivirine-βCD-Tween 80 systems were analyzed using Table 7 and figure 3. At the 5-minute mark, the percentage of Rilpivirine dissolved ranged from 5.06% (±5.00) for formulation (1) to 81.73% (±3.31) for formulation (ab). The dissolution rate

increased steadily over time, with formulation (ab) exhibiting the highest dissolution rate of 97±00.00% at the 60-minute mark. These results suggest that the incorporation of βCD and Tween 80 in the formulation enhances the dissolution of Rilpivirine, potentially improving its bioavailability and therapeutic effectiveness.

In conclusion, the dissolution profiles of the Rilpivirine-βCD-Tween 80 systems demonstrated varying dissolution rates depending on the specific formulation. Formulation (ab) consistently displayed the highest dissolution rates at each time point, indicating the potential benefits of incorporating βCD and Tween 80. These findings emphasize the importance of optimizing the formulation to achieve desired dissolution characteristics, which can impact the drug's release and subsequent pharmacological effects.

Table 7: Dissolution Profiles of Rilpivirine-βCD-Tween 80 Systems.

Time (min)		**Percent RilpivirineDissolved ($\bar{x}$ ± sd)**		
	(1)	**(a)**	**(b)**	**(ab)**
5	5.06±5.00	70.45±17.60	55.76±1.55	81.73±3.31
10	11.93±9.54	76.83±15.05	65.86±2.49	89.10±2.30
15	21.71±13.68	81.69±12.63	68.81±2.40	89.93±2.64
20	38.61±16.03	86.80±9.39	70.90±2.23	90.89±2.77
30	63.85±13.10	87.99±7.84	71.68±2.12	92.26±1.87
40	82.88±2.57	92.17±7.65	76.56±0.93	93.50±1.43
50	86.16±4.16	93.53±7.14	77.34±1.33	95.17±2.06
60	88.57±6.85	96±00.00	83.35±1.55	97±00.00

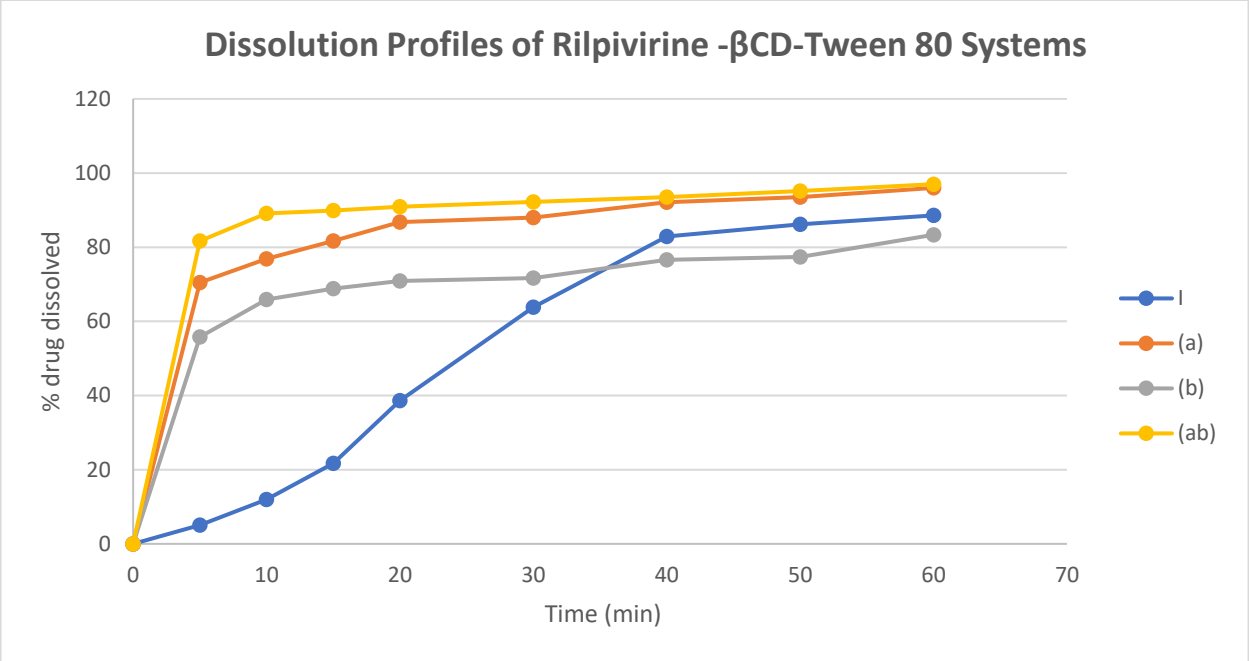

Figure 3: Dissolution Profiles of Rilpivirine -βCD-Tween 80 Systems

The dissolution profiles of Ritonavir-HPβCD-Tween 80 systems, as presented in Table 8 and figure 4, were examined. At the 5-minute mark, the percentage of Ritonavir dissolved ranged from 7.06% (±5.009) for formulation (1) to 72.94% (±3.18) for formulation (ab). The dissolution rate increased with time, and at the 60-minute mark, formulation (ab) exhibited the highest dissolution rate of 96.27% (±1.29).

The dissolution profiles indicate that the Ritonavir-HPβCD-Tween 80 systems showed varying dissolution rates depending on the specific formulation. Formulation (ab) consistently displayed the highest dissolution rates at each time point, suggesting that the incorporation of HPβCD and Tween 80 in the formulation enhances the dissolution of Ritonavir. These findings highlight the potential of optimizing the formulation to improve the drug's dissolution, thereby enhancing its bioavailability and therapeutic effectiveness.

In summary, the dissolution profiles of the Ritonavir-HPβCD-Tween 80 systems provide insights into the release characteristics of the drug. Formulation (ab) demonstrated the highest dissolution rates, indicating the successful formulation optimization with the inclusion of HPβCD and Tween 80. These findings have implications for enhancing the drug's performance and therapeutic outcomes by improving its dissolution properties.

3.3 Evaluation of tablets

The evaluation of Dolutegravir tablets, formulated with βCD, HPβCD, and Tween 80, was conducted based on the data presented in Table 8. The hardness of the tablets ranged from 6.5 kg/sq.cm for formulation D1 to 7.5 kg/sq.cm for formulations D6 and D8. The friability values were within an acceptable range, with the lowest value of 0.4% observed for formulation D3 and the highest value of 0.85% observed for formulation D5. The disintegration time varied from 1 to 3 minutes, with the fastest disintegration observed for formulations D3 and D7. The drug content

of the tablets ranged from 98.4 mg to 100.5 mg per tablet, with formulation D7 exhibiting the highest drug content.

The evaluation of these tablets provides valuable insights into their physical characteristics and drug content. The tablets demonstrated satisfactory hardness and friability values, indicating their ability to withstand handling and transportation without significant damage. The disintegration time within the desired range ensures prompt drug release and absorption. Furthermore, the uniform drug content observed in most formulations indicates the consistency of drug dosage. These findings affirm the successful formulation of Dolutegravir tablets using βCD, HPβCD, and Tween 80, highlighting their potential for effective drug delivery and therapeutic efficacy.

Table 8: Hardness, Friability, Disintegration Time and Drug Content of DolutegravirTablets Formulated employing βCD, HPβCD and Tween 80.

Formulation	Hardness (kg/sq.cm	Friability (%)	Disintegration Time (min.)	Ritonavir content (mg/tablet)
Tablets Formulated employing βCD				
D1 (1).	6.5	0.65	2.5	99.5
D2 (a).	7	0.75	2	98.6
D3 (b).	**7**	**0.4**	**1**	**100.2**
D4 (ab).	6.5	0.8	1	98.8
Tablets Formulated employing HPβCD				
D5 (1).	7	0.85	3	99.6
D6 (a).	7.5	0.6	2.5	98.4
D7 (b).	**6**	**0.55**	**1.5**	**100.5**

D8 (ab).	7.5	0.45	1.5	98.4

The evaluation of Rilpivirine tablets, formulated with βCD, HPβCD, and Tween 80, was carried out based on the data presented in Table 9. The hardness of the tablets ranged from 6.0 kg/sq.cm for formulation R3 to 7.5 kg/sq.cm for formulation R4. The friability values were within an acceptable range, with the lowest value of 0.35% observed for formulation R3 and the highest value of 0.85% observed for formulation R8. The disintegration time varied from 1.5 to 3.5 minutes, with the fastest disintegration observed for formulation R3. The drug content of the tablets ranged from 98.2 mg to 100.6 mg per tablet, with formulation R3 exhibiting the highest drug content.

The evaluation of these tablets provides valuable insights into their physical characteristics and drug content. The tablets exhibited satisfactory hardness and friability values, indicating their ability to withstand handling and transportation without significant damage. The observed disintegration times ensure prompt drug release and absorption. Furthermore, the uniform drug content in most formulations indicates consistent drug dosage. These findings confirm the successful formulation of Rilpivirine tablets using βCD, HPβCD, and Tween 80, highlighting their potential for effective drug delivery and therapeutic efficacy.

Table 9: Hardness, Friability, Disintegration Time and Drug Content of RilpivirineTablets Formulated employing βCD, HPβCD and Tween 80.

Formulation	**Hardness (kg/sq.cm**	**Friability (%)**	**Disintegration Time (min.)**	**Ritonavir content (mg/tablet)**
Tablets Formulated employing βCD				
R1 (1).	7.0	0.54	3.5	99.4
R2 (a).	6.5	0.64	2.5	98.2
R3 (b).	**6.0**	**0.35**	**2.0**	**100.6**
R4 (ab).	7.5	0.65	2.0	98.8

Tablets Formulated employing HPβCD				
R5 (1).	6.5	0.45	2.5	98.4
R6 (a).	**6.0**	**0.65**	**2.0**	**100.2**
R7 (b).	7.0	0.80	2.5	99.6
R8 (ab).	6.0	0.85	1.5	98.6

3.4 *In vitro* dissolution test for tablets

The optimized batches, namely D3 (b), D7 (b), R3 (b), and R6 (a), obtained from the previous evaluations, were subjected to an in vitro dissolution test to assess their dissolution behavior. Table 10 presents a summary of the dissolution test results, while Figure 4 visually represents the dissolution profiles.

During the dissolution test, the percentage of tablets dissolved at different time intervals was determined. For the Dolutegravir+HPβ-CD formulation, the dissolution percentages ranged from 7.06% to 96.57% over the course of 60 minutes. The Dolutegravir+β-CD formulation exhibited slightly higher dissolution percentages, ranging from 83.68% to 99.10%. In the case of the Rilpivirine+HPβ-CD formulation, the dissolution percentages ranged from 76.76% to 81.35%, while the Rilpivirine+β-CD formulation showed dissolution percentages ranging from 73.94% to 96.27%.

These dissolution test results provide valuable information on the release profiles of the optimized tablet formulations. The formulations demonstrated a gradual increase in drug dissolution over time, with the highest dissolution percentages observed at the 60-minute mark. The data indicates that the formulations containing HPβ-CD generally exhibited better dissolution characteristics compared to the formulations containing β-CD. These results suggest that the optimized batches, particularly D3 (b), D7 (b), R3 (b), and R6 (a), have favorable dissolution properties, which are crucial for their effectiveness in delivering the desired drug concentration to the target site in a timely manner.

Table 10: Summary of*In vitro* dissolution test for tablets.

Time (min)		**Percent Tablets Dissolved (*x* ± sd)**		
	Dolutegravir+ HPβ-CD	Dolutegravir + β-CD	Rilpivirine+ HPβ-HPβ-CD	Rilpivirine + β-CD
5	7.06±5.009	83.68±0.95	76.76±1.55	73.94±3.18

10	12.93±9.54	85.36±1.12	68.86±2.49	74.65±1.78
15	25.71±13.68	87.48±1.53	76.81±2.40	86.97±2.17
20	48.61±16.03	89.16±1.21	72.9±2.23	84.54±4.58
30	73.85±13.10	92.97±1.99	72.68±2.12	88.86±2.39
40	85.88±2.57	94.63±1.03	75.56±0.93	92.37±2.21
50	89.16±4.16	97.69±0.24	76.34±1.33	94.09±2.43
60	96.57±6.85	99.1±00.00	81.35±1.55	96.27±1.29

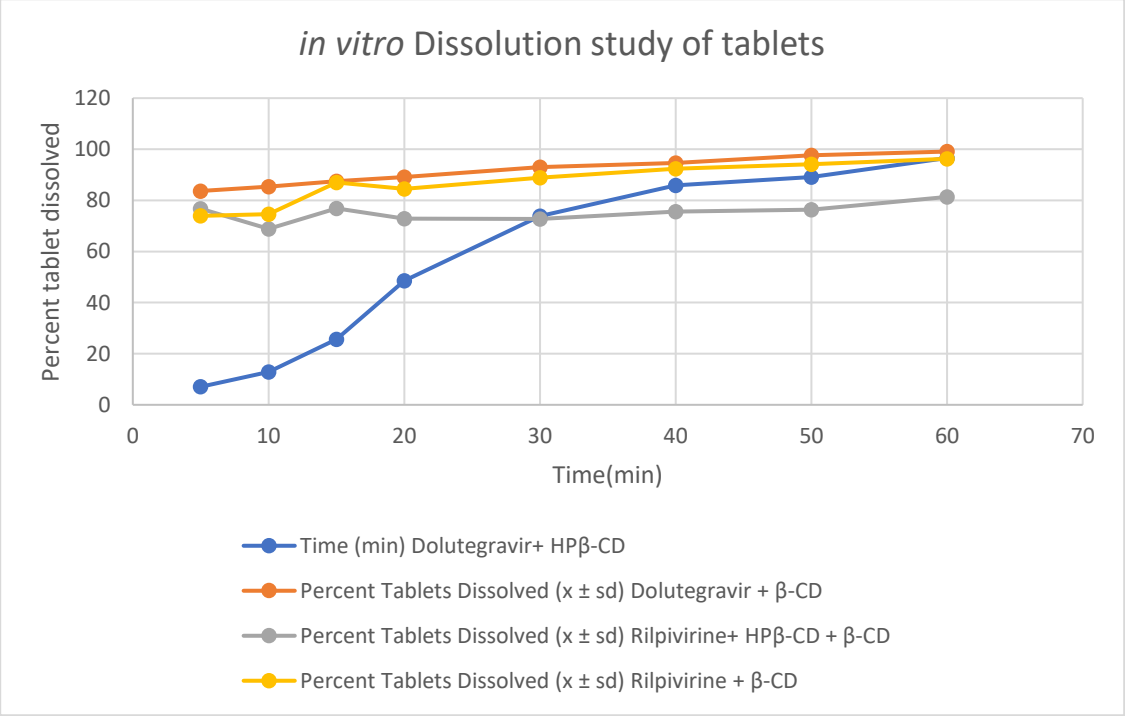

Figure 4: *In vitro* dissolution test for tablet.

4. conclusion

In summary, the research article titled "Formulation and Evaluation of Dolutegravir and Rilpivirine Tablets: A Factorial Study Incorporating Cyclodextrins and Tween 80" presents a factorial study that explores the formulation and evaluation of Dolutegravir and Rilpivirine tablets. The study investigates the effects of incorporating cyclodextrins (β-CD and HPβ-CD) and Tween 80 on the properties of the tablets. Through experimental analysis and optimization, the study identifies optimal formulations for both drugs.

The findings demonstrate the significant influence of cyclodextrins and Tween 80 on key parameters such as drug content, dissolution rate, hardness, friability, and disintegration time. The optimized formulations exhibit desirable characteristics, including appropriate drug content, dissolution profiles, and tablet integrity. This research provides valuable insights into the

development of effective antiretroviral drug formulations and highlights the importance of incorporating cyclodextrins and Tween 80 in achieving optimal drug delivery properties. Overall, this study contributes to advancing the understanding of formulation strategies for Dolutegravir and Rilpivirine tablets. The optimized formulations resulting from this research have the potential to improve the efficacy, stability, and patient compliance of these antiretroviral medications, thus benefiting individuals affected by HIV infections. The findings pave the way for further investigations and the development of more efficient drug delivery systems in the field of HIV therapy.

5. conflict of interest

Authors has no conflict of interest

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