

Journal of Advanced Zoology

ISSN: 0253-7214 Volume **43** Issue **1 Year 2022** Page **919-928**

Formulation and Evaluation of Cabotegravir and Etravirine Tablets: A Factorial Study Incorporating Cyclodextrins and Tween 80

Mrs. Shital Vijay Sirsat^{1*}, Dr. Govind Soni²

^{1*}Oriental University Indore MP India, 9619457450, Email: vijshi2006@gmail.com ²Faculty of Pharmacy Oriental University Indore Madhya Pradesh India

> *Corresponding Author: Mrs. Shital Vijay Sirsat *Email: vijshi2006@gmail.com

Abstract

The study aimed to investigate the formulation and evaluation of Cabotegravir and Etravirine tablets by incorporating cyclodextrins (β-CD and HPβ-CD) and Tween 80. 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 Cabotegravir +HPβ-CD and β-CD formulation exhibited slightly higher drug content percentages (97.42±1.03 to 96.12±1.01). Similarly, the tablets formulated with Etravirine HPβ-CD and β-CD exhibited slightly higher drug content percentages (99.78±2.12 to 99.23±1.25). The Cabotegravir +HPβ-CD and β-CD formulation exhibited slightly higher dissolution percentages, ranging from 54.46±0.43 and 53.03±1.26. In the case of the Etravirine HPβ-CD and β-CD formulation, the dissolution percentages ranged from 94.52±3.41 to 93.23±1.21. Overall, this factorial study successfully optimized the formulation of Cabotegravir and Etravirine 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.

CC License CC-BY-NC-SA 4.0

Keywords: Cabotegravir, Etravirine, Tablet formulation, HP β -CD and β -CD.

Introduction:

Highly active antiretroviral therapy (HAART) has transformed the treatment of HIV/AIDS by combining various antiretroviral medicines to reduce viral replication and enhance patient outcomes. Cabotegravir and Etravirine are two essential HAART components that have drawn a lot of attention for their effectiveness in treating HIV-1 infection. Due to their exceptional antiviral effectiveness and advantageous resistance profiles, the integrase strand transfer inhibitor cabotegravir and the non-nucleoside reverse transcriptase inhibitor etravirine are now staples of contemporary HIV treatment regimens. However, the creation of ideal pharmaceutical formulations that address issues including low solubility, restricted bioavailability, and poor physicochemical stability is necessary for the effective distribution of Cabotegravir and Etravirine. He imperative to overcome these formulation barriers in order to guarantee sufficient drug release, promote dissolution, and raise therapeutic efficacy. Under these circumstances, adding appropriate excipients has

become a practical tactic to improve the solubility, dissolution, and stability of medications that are poorly soluble, such as Cabotegravir and Etravirine.⁽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 Cabotegravir and Etravirine tablet formulations presents a promising avenue for improving their solubility, dissolution, and overall performance. (7)

To systematically investigate the formulation optimization of Cabotegravir and Etravirine tablets, a factorial study employing cyclodextrins and Tween 80 as key factors is undertaken in this research. The interactions, and potential synergistic effects of these excipients on the formulation attributes of the tablets. (8) 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 Cabotegravir and Etravirine.

The outcomes of this research have implications not only for the formulation optimization of Cabotegravir and Etravirine 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 Cabotegravir and Etravirine -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.

Material and Method

Material

Cabotegravir and Etravirine 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.

Method

Preparation of 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 45 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°C in an oven. The powder after drying and being sieved through No. 100 mesh. (9) The ration of CD-surfactant complexes show in table no 01.

Table 1: Ratio of CD-surfactant complexes.

F1	Cabotegravir -βCD (1:2)
F2	Cabotegravir - HPβCD (1:2)
F3	Cabotegravir: βCD: Tween 80 (1:2:0.02)
F4	Cabotegravir: HPβCD: Tween 80 (1:2:0.02)
F5	Etravirine- βCD (1:2)
F6	Etravirine - HPβCD (1:2)
F7	Etravirine: βCD: Tween 80 (1:2:0.02)
F8	Etravirine: HPβCD: Tween 80 (1:2:0.02)

Estimation of drug content in drug-CD-surfactant complexes

50 mg of drug-CD-surfactant complex powder was taken into a 50 ml volumetric flask and dissolved in 40 ml of methanol. The solution was made up to the volume with methanol. The solution was then diluted with water

containing 2% SLS for Cabotegravir and 0.1N hydrochloric acid for Etravirine and assayed for drug content using the UV spectrophotometric techniques. (10)

Formulation of Cabotegravir and Etravirine 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. The studies were performed to examine the effects of CDs and Tween 80, both separately and in combination (interaction), on the dissolution rate of Cabotegravir and Etravirine from tablet formulation.⁽¹¹⁾

Table 2: A ratio of Cabotegravir and Etravirine on tablet formulation

Formulation	Formulation	Cabotegravir	Formulation	Etravirine
Number	code	8	code	
code				
1	C1	Tablets of Cabotegravir alone	E1	Tablets of Etravirine alone
A	C2	Tablets of Cabotegravir - βCD (1:	E2	Tablets of Etravirine -βCD (1:
		2) inclusion complex		2) inclusion complex
В	C3	Tablets of Cabotegravir - Tween	E3	Tablets of Etravirine - Tween
		80 (5%) blend		80 (5%) blend
AB	C4	Tablets of Cabotegravir - βCD-	E4	Tablets of Etravirine - βCD-
		Tween 80 (1: 2: 0.05) ternary		Tween 80 (1: 2: 0.05) ternary
		complexes		complexes
Drug Tablets w	vith HPβCD and	Tween 80.		
1	C5	Tablets of Cabotegravir	E5	Tablets of Etravirine alone
		alone		
A	C6	Tablets of Cabotegravir	E6	ablets of Etravirine - HPβCD
		- HPβCD (1: 2) inclusion complex		(1: 2) inclusion complex
В	C7	Tablets of Cabotegravir -Tween	E7	Tablets of Etravirine - Tween
		80 (5%) blend		80 (5%) blend
AB	C8	Tablets of Cabotegravir	E8	Tablets of Etravirine -
		- HPβCD- Tween 80 (1:		HPβCD- Tween 80
		2: 0.05) ternary complexes		(1: 2: 0.05) ternary complexes

The specified formulations were followed in the preparation of the 100 mg tablets of cabotegravir and etravirine using wet granulation. 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. 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°C. The aggregates in the dried granules were broken up by sieving them using a No. 16 mesh screen. Hended 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.

Table 3: Formulation of Cabotegravir Tablets Employing βCD and HPβCD.

Ingredient	Formul	ae of Cal	ootegravi	r Tablets	Formul	ae of Cal	botegravi	r Tablets
	(βCD)				(НРВСД)			
	C1 (1)	C2 (A)	C3 (B)	C4 (AB)	C5 (1)	C6 (A)	C7 (B)	C8 (AB)
Cabotegravir	100	100	100	100	100	100	100	100
β-CD		200		200		200		200
Tween 80			5	5			5	5
Cross Carmellose	14	14	14	14	14	14	14	14
Sodium								
PVP	8	8	8	8	8	8	8	8
Talc	6	6	6	6	6	6	6	6
Magnesium	7	7	7	7	7	7	7	7
stearate								
Lactose	215	15	210	10	215	15	210	10
Total weight	300	300	300	300	300	300	300	300
(mg)								

Table 4: Formulation of Etravirine Tablets Employing βCD, HPβCD

Ingredient		lae of Etr				lae of Etr		ablets
	(BCD)				(НРВСД)			
	E1 (1)	E2 (A)	E3 (B)	E4 (AB)	E5 (1)	E6 (A)	E7 (B)	E8 (AB)
Etravirine	100	100	100	100	100	100	100	100
β-CD		200		200		200		200
Tween 80			5	5			5	5
Cross Carmellose	14	14	14	14	14	14	14	14
Sodium								
PVP	8	8	8	8	8	8	8	8
Talc	6	6	6	6	6	6	6	6
Magnesium	7	7	7	7	7	7	7	7
stearate								
Lactose	215	15	210	10	215	15	210	10
Total weight	300	300	300	300	300	300	300	300
(mg)								

Evaluation of tablet

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.⁽¹⁶⁾

Thickness

The tablet thickness was calculated using Vernier calipers. It is expressed as mm. (17)

Friability

Roche friabilator was used for testing the friability of prepared tablets. It subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm for 4 min or 100 revolutions. Pre-weighed sample (Wi) of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dedusted using a softmuslin cloth and reweighed (Wf). The friability (F) is given by the formula. (18)

 $F = Wi-Wf \times 100$

Wi

Weight variation test

The weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weights to the average. The percentage weight deviation was calculated and then compared with IP Limits, variation within the IP limits; it passes the weight variation test.⁽¹⁹⁾

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.⁽²⁰⁾

Drug Content

Five tablets were weighed and powdered using a glass mortar and pestle. An accurately weighed 100 mg of powder was taken into 50 ml volumetric flask, dissolved in methanol and the solution was filtered through what man filter paper no.41. Drug concentrations were evaluated by UV spectrophotometry after diluting the solutions with water containing 2% SLS for Cabotegravir and 0.1N hydrochloric acid for Etravirine respectively.⁽²¹⁾

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 Cabotegravir and Etravirine tablets, and in 0.1N hydrochloric acid (900 ml). The trial was conducted at a constant temperature of 37.1°C. One tablet was used in each experiment. 5 ml samples of the dissolution medium were taken at regular intervals, filtered through a 0.45-micron screen and diluted then tested. Fresh

dissolving fluid was added whenever a sample was taken. Four separate attempts at disintegration were made (n=4).

Results and Discussion

Drug Content in Cyclodextrin-surfactant complexes

The drug content of the various drug-cyclodextrin (CD)-surfactant complex systems was determined and presented in Table 5. For the Cabotegravir - β CD (1:2) complex system, the drug content was found to be 34.7% (±1.1). Similarly, in the Cabotegravir -HP β CD (1:2) Complex system, the drug content was slightly higher at 35.6% (±1.2). Incorporating Tween 80 into the Cabotegravir - β CD complex system (1:2:0.02) resulted in a drug content of 34.9% (±0.7), while the Cabotegravir-HP β CD-Tween 80 complex system (1:2:0.02) exhibited a drug content of 35.8% (±1.2).

Moving to the Etravirine complex systems, the Etravirine - β CD (1:2) complex displayed a drug content of 35.8% (±1.2), which was comparable to the Cabotegravir - β CD complex system. The Etravirine -HP β CD (1:2) complex system showed a slightly higher drug content of 36.9% (±0.8).

Incorporation of Tween 80 into the Etravirine - β CD complex system (1:2:0.02) resulted in a drug content of 36.1% (±1.2), which was the highest drug content observed among all the systems tested. Similarly, the Etravirine -HP β CD-Tween 80 complex system (1:2:0.02) exhibited a drug content of 37.6% (±1.2), matching the drug content of the Etravirine - β CD-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 β CD or HP β CD 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 No 5: Drug Content of CD-surfactant

	CD-surfactant complexes	Drug content (%)
F 1	Cabotegravir -βCD (1:2)	34.7
F2	Cabotegravir - HPβCD (1:2)	35.6
F3	Cabotegravir: βCD: Tween 80 (1:2:0.02)	34.9
F4	Cabotegravir: HPβCD: Tween 80 (1:2:0.02)	35.8
F5	Etravirine- βCD (1:2)	35.8
F6	Etravirine - HPβCD (1:2)	36.9
F7	Etravirine: βCD: Tween 80 (1:2:0.02)	36.1
F8	Etravirine: HPβCD: Tween 80 (1:2:0.02)	37.6

The evaluation of Cabotegravir tablets, formulated with β CD, HP β CD and Tween 80, was conducted based on the data presented in Table 6. During weight variation test none of the tablet was found to deviate by permissible percentage as per Indian Pharmacopoeia 1996 (5%) from the mean value of the 10 tablets. Thus it was found that all formulations complied the weight variation test. Hardness of the tablets was found to be range of 6.1 ± 0.16 to 7.3 ± 0.23 kg/cm². which was found to be well within the required hardness for the tablets. Thickness was found to be in the range of 4.0 ± 0.46 to 5.3 ± 0.23 nm. Percentage friability was found to be inhering of 0.42 ± 0.10 to 0.59 ± 0.23 which was well within the acceptable limit (less than 1 %) which confirms the required toughness available with the tablets and also confirms the tablets ability to with stand shocks during handling, transportation or shipping. The disintegration of tablets was found to be in the range of 1 to 3 min. The drug content of ranged from 97.42 ± 1.03 to 87.74 ± 0.26 % with formulation exhibiting the highest drug content in the C7. All evaluation parameter results show in table no 06.

Table 6: Evaluation of Tablet for Etravirine

Table 0. Evaluation of Tablet for Etravitine										
Formulation No	Weight variation		Thickness	Disintegration Time (min.)	%Friability	%Drug content				
	(mg)*									
C1	Passes	7.3±0.23	4.1±0.47	2.5	0.59 ± 0.23	91.61±1.02				
C2	Passes	6.2±0.23	4.0 ± 0.47	2	0.52 ± 0.20	89.23±0.68				
C3	Passes	7±0.47	4.2±0.48	1	0.42±0.10	96.12±1.01				
C4	Passes	7.5±0.41	4.0±0.46	2.5	0.49 ± 0.25	92.01±0.51				

Available online at: https://jazindia.com

C5	Passes	6.4±0.23	4.1±0.23	3	0.54 ± 0.47	88.23±1.11
C6	Passes	6.1±0.16	4.0 ± 0.47	2.5	0.50 ± 0.40	93.12±1.23
C7	Passes	7.3±0.12	5.3±0.23	1.5	0.51 ± 0.23	97.42±1.03
C8	Passes	7.2±0.21	5.2±0.23	1.8	0.45 ± 0.23	87.74±0.26

The evaluation of Etravirine tablets, formulated with β CD, HP β CD, and Tween 80, was carried out based on the data presented in Table 07 . 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 Etravirine tablets using β CD, HP β CD, and Tween 80, highlighting their potential for effective drug delivery and therapeutic efficacy.

Table no 07: Evaluation of Tablet for Cabotegravir

Formulation	Weight	Hardness	Thickness	Disintegration	%Friability	%Drug
Code	variation	(kg/cm ²)		Time (min.)		content
	(mg)*					
E 1	Passes	6.3±0.14	5.1±0.71	3.5	0.61±0.21	89.42±1.04
E2	Passes	6±0.46	5.0±0.47	2	0.32±0.19	99.23±1.25
E3	Passes	7.4±0.58	5.2±0.43	2.5	0.47 ± 0.11	93.12±2.35
E4	Passes	6.5±1.2	5.0±0.40	4	0.51±0.24	89.78±1.51
E5	Passes	7.1±1.1	5.1±0.23	3	0.54 ± 0.37	91.43±0.9
E6	Passes	6.1±0.25	5.0±0.34	2.5	0.49 ± 0.27	94.75±2.45
E7	Passes	7.3±0.17	5.3±0.52	2	0.37±0.22	99.78±2.12
E8	Passes	6.2±0.81	5.2±0.64	4.5	0.41±0.26	92.74±0.71

In-Vitro dissolution studies

During the dissolution test, the percentage of tablets dissolved at different time intervals was determined. For the Cabotegravir β -CD formulation, the dissolution percentages ranged from 46.03 ± 0.94 to 53.03 ± 1.26 percent over the course of 60 minutes. The Cabotegravir +HP β -CD formulation exhibited slightly higher dissolution percentages, ranging from 45.2 ± 0.89 to 54.46 ± 0.43 percent. In the case of the Etravirine + β -CD formulation, the dissolution percentages ranged from 84.52 ± 0.9 to 93.23 ± 1.21 percent while the Etravirine +HP β -CD formulation showed dissolution percentages ranging from 85.68 ± 2.3 to 94.52 ± 3.41 percent. 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 HP β -CD generally exhibited better dissolution characteristics compared to the formulations containing β -CD. These results suggest that the optimized batches, particularly C3 (B), C7 (B), E2 (A), and E7 (B), 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 No 08: In vitro drug release profile of formulations of tablet Cabotegravir

Time	Percent Dru	g release of C	Cabotegravir ((βCD)	Percent Drug release of Cabotegravir (HPβCD)			
(min)	$(x \pm sd)$				$(x \pm sd)$			
	C1	C2	C3	C4	C5	C6	C7	C8
0	0	0	0	0	0	0	0	0
5	8.72±1.94	8.73±0.74	3.91±0.87	7.77±1.05	4.91±2.06	6.39±1.85	8.92±2.92	4.68±0.27
10	16.71±2.19	17.84±1.20	10.35±0.80	24.39±3.10	12.77±1.32	19.98±1.52	21.76±3.52	19.08±0.99
15	25.15±0.91	22.50±1.45	16.71±0.89	29.43±1.82	21.75±2.14	22.61±0.77	26.75±0.98	21.05±1.35
20	31.70±0.76	29.22±1.39	26.52±1.10	32.91±2.23	27.86±1.91	24.56±0.49	32.64±2.14	23.23±1.30

30	37.80±1.43	31.99±0.70	32.35±1.01	38.38±1.87	32.37±1.99	28.63±0.51	38.41±2.60	27.64±0.95
40	41.52±1.15	36.12±1.59	39.74±0.98	46.03±2.45	36.55±2.26	32.20±0.77	42.07±0.59	34.37±1.82
50	47.18±1.32	41.72±0.97	46.24±1.36	47.19±1.72	40.04±0.94	40.03±1.01	47.18±2.84	40.62±2.69
60	52.89±0.53	46.03±0.94	53.03±1.26	51.02±1.52	45.2±0.89	47.80±1.46	54.46±0.43	49.5±0.77

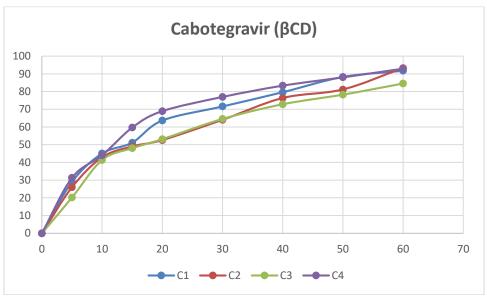


Figure 1: In – Vitro Dissolution Profile of Cabotegravir (βCD)

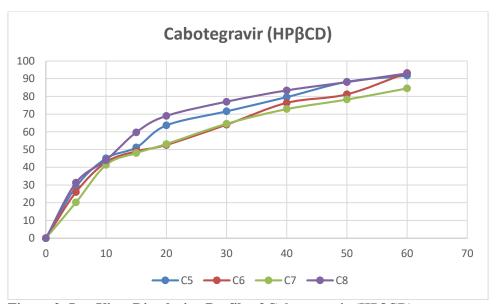


Figure 2: In – Vitro Dissolution Profile of Cabotegravir (HPβCD)

Table no 09: In vitro drug release profile of formulations of tablet Etravirine

Time	Percent Drug	release of Etrav	virine (βCD)		Percent Drug	release of Etra	avirine (HPβCl	D)
(min)	$(x \pm sd)$				$(x \pm sd)$			
	E1	E2	E3	E4	E5	E6	E7	E8
0	0	0	0	0	0	0	0	0
5	29.01±1.08	26.01±1.27	20.21±1.8	31.33±2.1	29.84±0.9	23.21±2.41	21.01±1.89	28.02±3.24
10	45.03±1.24	42.85±1.32	41.36±1.56	44.00±1.9	38.00±1.71	32.25±2.1	33.00±3.21	39.57±1.83
15	51.15±2.9	49.00±0.71	48.02±0.6	59.68±1.6	55.89±1.14	41.78±1.9	46.01±2.44	48.00±2.44
20	63.64±1.1	52.58±2.14	53.12±1.63	68.95±1.56	67.81±1.32	54.63±3.1	51.36±0.99	59.01±1.78
30	71.58±1.23	64.01±1.02	64.54±0.89	76.98±2.2	73.23±1.63	62.89±2.81	69.52±1.47	69.65±2.10
40	79.6±2.32	76.32±1.06	72.84±1.7	83.35±2.03	81.21±0.8	70.26±1.98	77.91±2.11	76.01±1.63
50	88.23±1.8	81.15±2.1	78.25±1.4	88.03±1.89	86.53±1.96	78.08±1.56	88.42±1.63	84.47±3.65
60	91.75±0.91	93.23±1.21	84.52±0.9	92.94±1.78	91.03±2.11	85.68±2.3	94.52±3.41	91.68±2.93

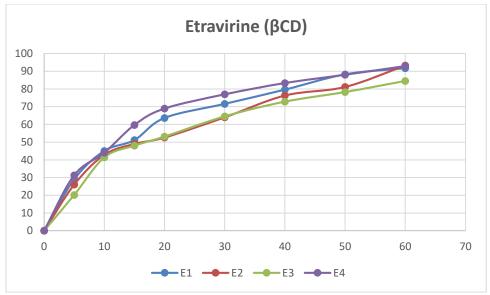


Figure 3: In – Vitro Dissolution Profile of Etravirine (βCD)

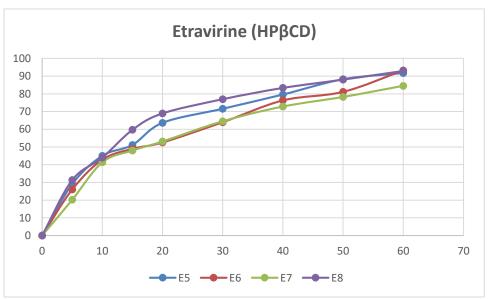


Figure 4: In – Vitro Dissolution Profile of Etravirine (HPβCD)

Conclusion

In summary, the research article titled "Formulation and Evaluation of Cabotegravir and Etravirine Tablet: A Factorial Study Incorporating Cyclodextrins and Tween 80" presents a factorial study that explores the formulation and evaluation of Cabotegravir and Etravirine tablets. The study investigates the effects of incorporating cyclodextrins (β -CD and HP β -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, thickness, 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 Cabotegravir and Etravirine 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.

Conflict of interest.

None

Data Availability Statement:

All the data were presented in the present article.

Acknowledgement:

None

Reference

- 1. Shafer, R. W., & Vuitton, D. A. (1999). Highly active antiretroviral therapy (Haart) for the treatment of infection with human immunodeficiency virus type 1. Biomedicine & Pharmacotherapy, 53(2), 73–86. https://doi.org/10.1016/s0753-3322(99)80063-8
- 2. Smith, R. A., Wu, V. H., Zavala, C. G., Raugi, D. N., Ba, S., Seydi, M., & Gottlieb, G. S. (2018). In VitroAntiviral Activity of Cabotegravir against HIV-2. Antimicrobial Agents and Chemotherapy, 62(10). https://doi.org/10.1128/aac.01299-18
- 3. Trezza, C., Ford, S. L., Spreen, W., Pan, R., & Piscitelli, S. C. (2015). Formulation and pharmacology of long-acting cabotegravir. Current Opinion in HIV and AIDS, 10(4), 239–245. https://doi.org/10.1097/coh.000000000000168
- 4. Rojekar, S., Vora, L. K., Tekko, I. A., Volpe-Zanutto, F., McCarthy, H., Vavia, P. R., & Donnelly, R. F. (2021). Etravirine-loaded dissolving microneedle arrays for long-acting delivery. European Journal of Pharmaceutics and Biopharmaceutics, 165, 41–51. https://doi.org/10.1016/j.ejpb.2021.04.024
- 5. Van Der Merwe, J., Steenekamp, J., Steyn, D., & Hamman, J. H. (2020). The role of functional excipients in solid oral dosage forms to overcome poor drug dissolution and bioavailability. Pharmaceutics, 12(5), 393. https://doi.org/10.3390/pharmaceutics12050393
- 6. Saokham, P., Muankaew, C., Jansook, P., & Loftsson, P. (2018). Solubility of cyclodextrins and Drug/Cyclodextrin complexes. Molecules/Molecules Online/Molecules Annual, 23(5), 1161. https://doi.org/10.3390/molecules23051161
- 7. Prieto, C., & Calvo, L. (2013). Performance of the biocompatible surfactant Tween 80, for the formation of microemulsions suitable for new pharmaceutical processing. Journal of Applied Chemistry, 2013, 1–10. https://doi.org/10.1155/2013/930356
- 8. Loftsson, P. (2021). Cyclodextrins in parenteral formulations. Journal of Pharmaceutical Sciences, 110(2), 654–664. https://doi.org/10.1016/j.xphs.2020.10.026
- 9. Raj R, Arun & Nair, S.S. & Harindran, Jyoti. (2016). Formulation and evaluation of cyclodextrin inclusion complex tablets of carvedilol. 10. 84-94.
- 10. Morina, D., Sessevmez, M., Sinani, G., Mülazımoğlu, L., & Cevher, E. (2020). Oral tablet formulations containing cyclodextrin complexes of poorly water soluble cefdinir to enhance its bioavailability. *Journal of Drug Delivery Science and Technology*, *57*, 101742. https://doi.org/10.1016/j.iddst.2020.101742
- 11. Alghaith, A. F., Mahrous, G. M., Zidan, D. E., Alhakamy, N. A., Alamoudi, A. J., & Radwan, A. E. (2021). Preparation, characterization, dissolution, and permeation of flibanserin 2-HP-β-cyclodextrin inclusion complexes. Saudi Pharmaceutical Journal, 29(9), 963–975. https://doi.org/10.1016/j.jsps.2021.07.019
- 12. Ghorab, M. M., Abdel-Salam, H. M., El-Sayad, M. A., & Mekhel, M. M. (2004). Tablet formulation containing meloxicam and β-cyclodextrin: Mechanical characterization and bioavailability evaluation. AAPS PharmSciTech, 5(4), 63–68. https://doi.org/10.1208/pt050459
- 13. Arza, R. a. K., Gonugunta, C. S. R., & Veerareddy, P. R. (2009). Formulation and evaluation of swellable and floating gastroretentive ciprofloxacin hydrochloride tablets. *AAPS PharmSciTech*, *10*(1), 220–226. https://doi.org/10.1208/s12249-009-9200-y
- 14. Westerhuis, J. A., Coenegracht, P., & Lerk, C. (1997). Multivariate modelling of the tablet manufacturing process with wet granulation for tablet optimization and in-process control. International Journal of Pharmaceutics, 156(1), 109–117. https://doi.org/10.1016/s0378-5173(97)00191-9
- 15. Jadhav, B. K., Khandelwal, K., Ketkar, A. R., & Pisal, S. S. (2004). Formulation and evaluation of mucoadhesive tablets containing eugenol for the treatment of periodontal diseases. Drug Development and Industrial Pharmacy, 30(2), 195–203. https://doi.org/10.1081/ddc-120028715

- 16. Kumar, Davinder & Singh, Jasbir & Antil, Mamta & Kumar, Virender. (2016). INTERNATIONAL JOURNAL OF UNIVERSAL PHARMACY AND BIO SCIENCES IMPACT FACTOR 2.96*** ICV 5.13*** Pharmaceutical Sciences QUALITY CONTROL OF TABLETS: A REVIEW.
- 17. Zhao, H., Yu, Y., Ni, N., Zhao, L., Lin, X., Wang, Y., Du, R., & Shen, L. (2022). A new parameter for characterization of tablet friability based on a systematical study of five excipients. *International Journal of Pharmaceutics*, 611, 121339. https://doi.org/10.1016/j.ijpharm.2021.121339
- 18. Muniyandy, S., Nataraj, K. S., & Ganesh, K. S. (2002). The Effect of Tablet Formulation and Hardness on in Vitro Release of Cephalexin from Eudragit L100 Based Extended Release Tablets. Biological & Pharmaceutical Bulletin, 25(4), 541–545. https://doi.org/10.1248/bpb.25.541
- 19. Prabhakar, Shirse. (2012). Formulation and evaluation of fast dissolving tablets of cyclodextrin inclusion complexed water insoluble drug: Glimipiride. International Journal of Research in Ayurveda and Pharmacy. 3. 465-470.
- 20. Musuc, A. M., Anuţa, V., Atkinson, I., Popa, V. T., Sarbu, I., Mircioiu, C., Abdalrb, G. A., Mitu, M. A., & Ozon, E. A. (2020). Development and characterization of orally disintegrating tablets containing a Captopril-Cyclodextrin complex. *Pharmaceutics*, 12(8), 744. https://doi.org/10.3390/pharmaceutics12080744
- 21. Dua, K., Pabreja, K., Ramana, M. M. V., & Lather, V. (2011). Dissolution behavior of β-cyclodextrin molecular inclusion complexes of aceclofenac. *Journal of Pharmacy and Bioallied Sciences*, *3*(3), 417. https://doi.org/10.4103/0975-7406.84457
- 22. Singh, Rahul & Easwari, T S & Singh, Atul & Singh, Smriti & Panwar, Jonee. (2018). PREPARATION & EVALUATION OF β-CYCLODEXTRINS INCLUSION COMPLEXES OF LORNOXICAM FOR SOLUBILITY ENHANCEMENT. 31-42.