RESEARCH ARTICLE

Complexation and Solubility Enhancement of BCS Class II Drug using Cyclodextrins

Rajesh Asija, Avinash K Gupta*

Department of Pharmaceutics, Maharishi Arvind Institute of Pharmacy, Jaipur (Rajasthan) India, Affiliated to Rajasthan University of Health Sciences (RUHS)

Received: 16th Oct, 2024; Revised: 19th Nov, 2024; Accepted: 4th Dec, 2024; Available Online: 25th Dec, 2024

ABSTRACT

Complexation can improve the solubility of drug substances by forming a complex between the drug substance and a complexing agent. Complexing agents are typically small molecules that have the ability to form stable complexes with the drug substance through non-covalent interactions such as hydrogen bonding, Van der Waals forces, or electrostatic interactions. The formation of a complex between the drug substance and the complexing agent can increase the solubility of the drug substance by improving its dispersibility in the solvent. This can occur through several mechanisms, such as increasing the polarity of the solvent system, reducing the crystal lattice energy of the drug substance, or decreasing the intermolecular forces between drug molecules. Common complexing agents used in pharmaceutical formulations include cyclodextrins, polymeric compounds such as polyvinylpyrrolidone (PVP), and amino acids such as arginine and lysine. In the present study solubilization and release properties of Celecoxib was tried to enhance by complexation with the βCD & HPβCD.

Keywords: Celecoxib, Complexation, Cyclodextrin

How to cite this article: Rajesh Asija, Avinash K Gupta. Complexation and Solubility Enhancement of BCS Class II Drug using Cyclodextrins. International Journal of Pharmaceutical Quality Assurance. 2024;15(4):2589-92. doi: 10.25258/ijpqa.15.4.60

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Drug solubility refers to the ability of a drug to dissolve in a solvent, usually water. It is an important factor in drug development, as the solubility of a drug affects its bioavailability, efficacy, and toxicity. A drug with poor solubility may not be absorbed efficiently in the body, resulting in a lower therapeutic effect.[1]

Drug solubility is influenced by several factors, including the physicochemical properties of the drug, the solvent properties, and the formulation. Some of the physicochemical properties that affect drug solubility include the molecular weight, polarity, and crystallinity of the drug. For example, drugs with high molecular weight and high crystallinity tend to have low solubility.[2]

Solvent properties also play a significant role in drug solubility. The polarity of the solvent, its pH, and its ionic strength can all affect the solubility of a drug. For example, polar solvents such as water are generally better at dissolving polar drugs, while non-polar solvents like oil are better at dissolving non-polar drugs.[3]

Finally, the formulation of the drug can also affect its solubility. For example, adding surfactants or other excipients to a drug formulation can increase its solubility by improving its wetting properties or reducing its interfacial tension.[4]

Overall, understanding and optimizing drug solubility is an important aspect of drug development, as it can significantly affect the efficacy and safety of a drug.

Cyclodextrins are cyclic oligosaccharides that are composed of several glucose molecules bound together in a ring-like structure. They are typically produced from starch through enzymatic conversion and have a truncated cone-like shape with a hydrophobic cavity in the center and hydrophilic outer surfaces. Cyclodextrins have the ability to form inclusion complexes with other molecules, such as drugs, due to their unique structure. The drug molecule is able to enter the hydrophobic cavity of the cyclodextrin, resulting in increased solubility and stability of the drug. This can lead to improved bioavailability and efficacy of the drug.[5]

There are several types of cyclodextrins, including alpha-cyclodextrin, beta-cyclodextrin and gamma-cyclodextrin. The type of cyclodextrin used depends on the physicochemical properties of the drug and the desired formulation. For example, beta-cyclodextrin is often used due to its relatively high solubility and ability to form inclusion complexes with a wide range of molecules.[6]

Cyclodextrins are commonly used in pharmaceuticals, cosmetics, and food industries. They are generally considered safe and have been approved for use by regulatory agencies such as the US Food and Drug Administration (FDA). However, it is important to note that cyclodextrins can potentially interact with other molecules in the body, so careful consideration should be given to the choice of cyclodextrin and its dosage when used in pharmaceutical formulations.[7]

**Author for Correspondence: avinashgjpr@gmail.com*

Table 1: Manufacturing Formula Prepared with Cyclodextrins

	Composition				
Component	E39 (Qty/tab.)	E40 (Qty/tab.)	E41 (Qty/tab.)	E42 (Qty/tab.)	E43 (Qty/tab.)
Celecoxib	100.00 mg	100.00 mg	100.00 mg	100.00 mg	100.00 mg
βCD	0.00	100.00 mg	200.00 mg	0.00	0.00
HPβCD	0.00	0.00	0.00	100.00 mg	200.00 mg
Gum Arabic	5.00 mg	5.00 mg	5.00 mg	5.00 mg	5.00 mg
PPL XL-10	20.00 mg	20.00 mg	20.00 mg	20.00 mg	20.00 mg
Talcum	2.00 mg	2.00 mg	2.00 mg	2.00 mg	2.00 mg
Compritol	3.00 mg	3.00 mg	3.00 mg	3.00 mg	3.00 mg
Vivapurup to	550.00 mg	550.00 mg	550.00 mg	550.00 mg	550.00 mg

Table 2: Effect of β-Cyclodextrin quantity on Solubilization

Concⁿ of β CD	Concⁿ of Celecoxib
0mM	2.13mM
1mM	4.22mM
2mM	3.93mM
3mM	4.95mM
6mM	6.64mM

Table 3: Effect of HP β-Cyclodextrin quantity on Solubilization

Concⁿ of HPβCD	Concⁿ of Celecoxib
0mM	2.13mM
1mM	3.11mM
2mM	3.06mM
3mM	4.08mM
6mM	5.06mM

MATERIALS AND METHODS

Celecoxib was received as gift sample from M/s Ind-Swift limited and other excipients received from different vendors as gift sample.

Solubility Estimation

An excess amount of drug was dissolved in the solvent and kept on stirring for overnight. On following day, sample quantity was withdrawn and after dilution with the 0.1N HCl solution absorbance was taken in spectrophotometer at the λ of 254 nm.

Manufacturing of Tablets

According to table 1.0 composition, Celecoxib, SMC, and PPLXL-10 were combined and passed through mesh number 20. Binder agent was prepared using purified water. This binder solution was used for granulation of dry mix powder. Wet mass was dried at 60°C for 35 minutes. Dried granules were further sized using suitable sieve. Dried granules were lubricated using lubricants and compressed into the tablet form.

Table 4: Physical Parameters of Tablets

Composition	Assay	Tablet Strength	Friability	DT
E 39	100.51 mg	5.0- 6.0 Kp	0.48%	3.90 min
E 40	99.95 mg	4.0- 5.5 Kp	0.65%	2.15 min
E 41	99.68 mg	4.0- 6.0 Kp	0.23%	2.43 min
E 42	100.05 mg	4.5- 6.0 Kp	0.41%	15.10 min
E 43	99.45 mg	4.0-5.5 Kp	0.81%	20.10 min

Physicochemical Parameters of Tablets

Tablets were crushed into the form of fine powder. This powder form was dissolved in the solvent and further diluted with the dissolution media. This solution was analyzed using UV visible spectroscopy at the wavelength of 254 nm. Tablet Hardness, Friability and Disintegration time was analyzed by using respective equipment. Drug

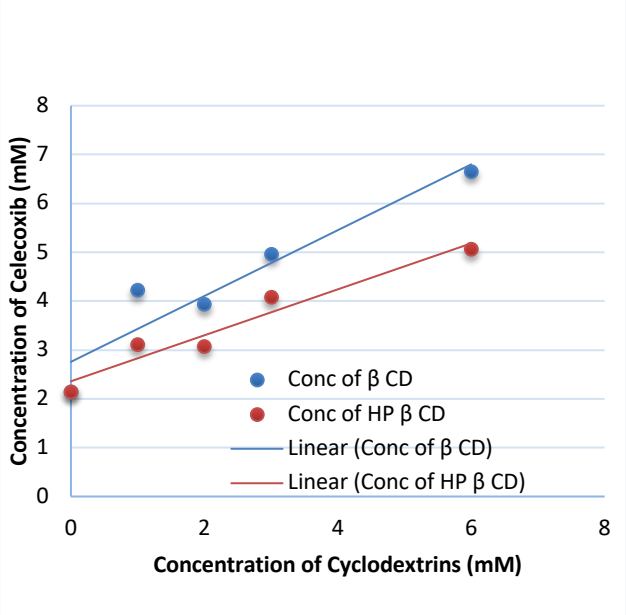

Figure 1: Impact of Cyclodextrin on the Solubility

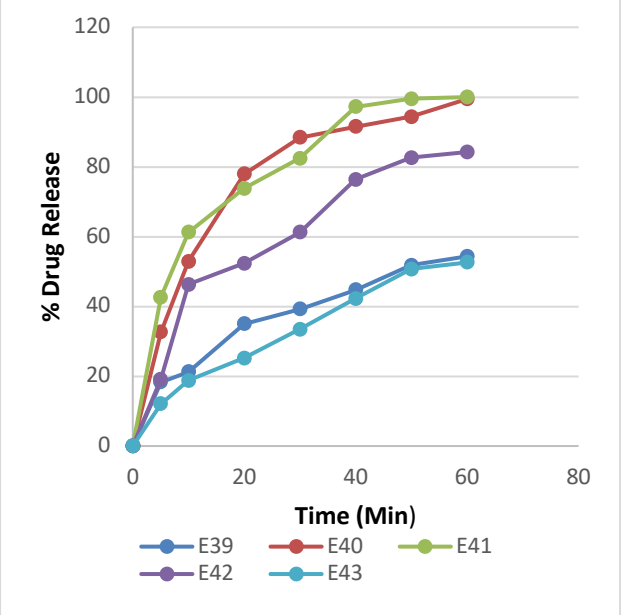

Figure 2: Percentage Drug Release of Tablets

Table 5: Drug Release of Tablets

Time (min)	% Drug Release (X ± SD)				
	E39	E40	E41	E42	E43
5	18.32 % ± 1.23	32.68 % ± 1.27	42.68 % ± 1.14	19.18 % ± 1.25	12.09 % ± 1.53
10	21.23 % ± 1.18	52.88 % ± 1.37	61.28 % ± 1.39	46.28 % ± 1.43	18.82 % ± 1.72
20	35.05 % ± 1.45	77.95 % ± 1.95	73.81 % ± 1.21	52.32 % ± 1.11	25.22 % ± 1.16
30	39.21 % ± 1.28	88.41 % ± 1.45	82.43 % ± 1.43	61.28 % ± 1.31	33.45 % ± 1.93
40	44.71 % ± 1.41	91.55 % ± 1.56	97.18 % ± 1.92	76.38 % ± 1.75	42.28 % ± 1.13
50	51.81 % ± 1.95	92.36 % ± 1.18	98.05 % ± 1.55	82.65 % ± 1.76	50.72 % ± 1.45
60	54.36 % ± 1.28	98.24 % ± 1.48	98.89 % ± 0.95	84.25 % ± 1.32	52.61 % ± 1.28

Table 6: Values of (r) according to different Kinetics

Formulation	Zero Order R^2	First Order R^2
E39	0.900	0.955
E40	0.781	0.925
E41	0.776	0.914
E42	0.868	0.971
E43	0.962	0.984

dissolution was analyzed using Dissolution test apparatus using 0.1N HCl as dissolution media. Sample collected at different time periods were treated with sufficient dilution media and analyzed using UV-Visible spectroscopy at the wavelength of 254 nm.

RESULTS

Effect of Drug Complex on Solubility

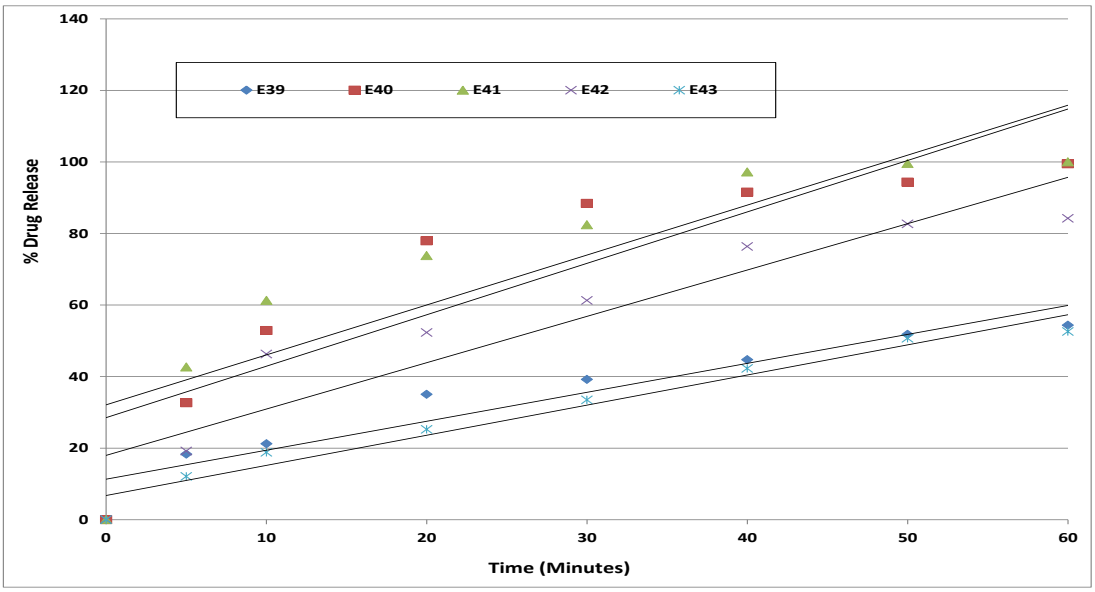

Figure 3: Zero order drug release kinetics of Tablets

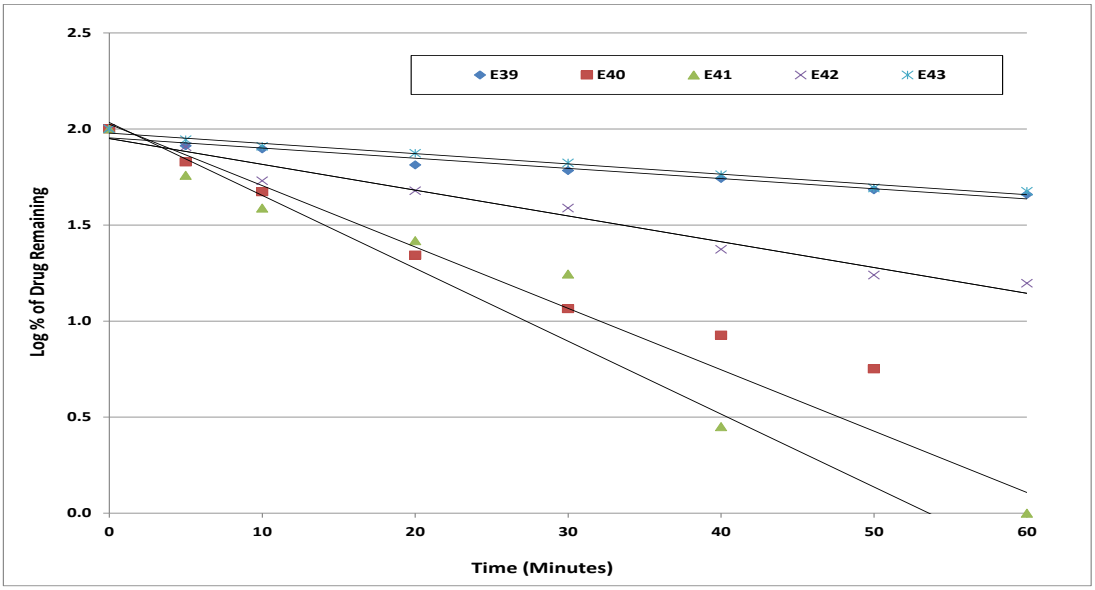

Figure 4: First order drug release kinetics of Tablets

As per the comparative solubility profile of the Cyclodextrin and the HP β-Cyclodextrin it can be observed that the drug solubility is increased to a great extend when it get complexed with the Cyclodextrin.

Evaluation of Tablets

For different formulations (Table 4) observed tablet hardness was satisfactory i.e. 4.0 kp to 6.0 kp. Additionally, the tablets friability was also within the Pharmacopoeial acceptance criteria. Disintegration time of the all formulations was satisfactory except the formulation E42 & E43. In those formulations DT was observed to be more than 15 min. Assay of the drug for all formulations were also well within the acceptance criteria.

Among all formulation drug dissolution profile (Table 5.0; Fig. 2.0) for the formulation E40 & E41 was satisfactory. In rest of the formulations, incomplete drug release was observed.

Release kinetics and there R2 values are mentioned in Fig. 3 & 4 and Table 6.0. As per the Results Drug release for all formulations are following first order kinetics.

CONCLUSION

Formulations manufactured with the complex of Drug and HP β-Cyclodextrin were unsatisfactory as the drug release was incomplete after the final time point of 60 minutes. Therefore, the β-Cyclodextrin helps in the enhancement of the solubility of the drug.

REFERENCES

1. Jain NK. Advances in Controlled and Novel Drug Delivery,15th edition, CBS Publishers and Distributors. 2017; 290.
2. Pooja A, Arora SV. Orodispersible tablets: A comprehensive review. Int J Res Dev Pharm Life Sci. 2017; 2(2):270-84.
3. Gupta AK., Charanjeet S., YashwantK. Formulation Optimization and Evaluation of Orally Disintegrating Tablets of Moxifloxacin. International Journal of Drug Delivery Technology. 2022;12(4):1658-1662.
4. Shah M, Shah V, Ghosh A, Zhang Z, Minko T. Molecular Inclusion Complexes of β-Cyclodextrin Derivatives Enhance Aqueous Solubility and Cellular Internalization of Paclitaxel: Preformulation and In vitro Assessments. J PharmPharmacol (Los Angel). 2015; 2(2):8.
5. Koshta A, Malviya N. Formulation and Evaluation of Floating-pulsating Drug Delivery System containing Fixed-dose Combination for Chronotherapy of Hypertension. International Journal of Drug Delivery Technology. 2022;12(4):1725-1732.
6. Saigal N, Baboota S, Ahuja A, Ali J. Site specific chronotherapeutic drug delivery systems: A patent review. Recent patents on drug delivery and formulation. 2009 Jan 1;3(1):64-70.
7. Remington's pharmaceutical Sciences, 22nd edition. 2021.