
Solubility Enhancement of BCS Class II Drug by Complexation using Cyclodextrins**Avinash K Gupta*, Rajesh Asija****Department of Pharmaceutics, Maharishi Arvind Institute of Pharmacy, Jaipur
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Abstract

Complexation is the method by which solubility of drug substances can be improved by forming a complex between the drug substance and a complexing agent. Complex formation between the drug molecule and complexing agent increases the solubility of the drug by its improved dispersibility in the solvent. Complexing agents have the ability to form stable complexes with the drug substance through non-covalent interactions such as Van der Waals forces, hydrogen bonding, or electrostatic interactions. Several mechanisms are usually involved for such interaction, such as enhancing the polarity of the solvent system, reduction in the crystal lattice energy of the drug substance or decreasing the intermolecular forces among drug molecules. Complexing agents used in pharmaceutical formulations commonly include cyclodextrins, amino acids such as lysine & arginine and polymeric compounds such as polyvinylpyrrolidone (PVP). In the present study solubility and release properties of Celecoxib were tried to enhance by complexation with the β CD & HP β CD.

Keywords: Celecoxib, Complexation, Cyclodextrin

1.0 Introduction

Solubility of drug refers to the ability of a drug to be dissolved in a solvent, usually water. It is one of the most important factors in drug development, as the solubility of a drug largely affects its bioavailability, efficacy and toxicity. Drugs with poor solubility may not be absorbed efficiently in the body, resulting in a lower therapeutic effect¹.

There are several factors which influence drug solubility including the physicochemical properties of the drug, the solvent properties, and the formulation. Drug solubility is broadly affected by some of the physicochemical properties which include particle size, molecular weight, polarity, crystallinity of the drug etc. For example, drugs with high molecular weight

and high crystallinity tend to have low solubility².

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 drugs³.

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 tension⁴.

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 drug⁵.

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 molecules⁶.

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 formulations⁷.

2.0 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.

2.1 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.

2.2 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.

2.3 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 equipments. Drug 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.

Table 1.0 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
β CD	0.00	100.00 mg	200.00 mg	0.00	0.00
HP β CD	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

3.0 RESULTS

3.1 Effect of Drug Complex on Solubility

Table 2.0 Effect of β -Cyclodextrin quantity on Solubilization

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

Table 3.0 Effect of HP β -Cyclodextrin quantity on Solubilization

Conc ⁿ of HP β CD	Conc ⁿ of Celecoxib
0mM	2.13mM
1mM	3.11mM
2mM	3.06mM
3mM	4.08mM
6mM	5.06mM

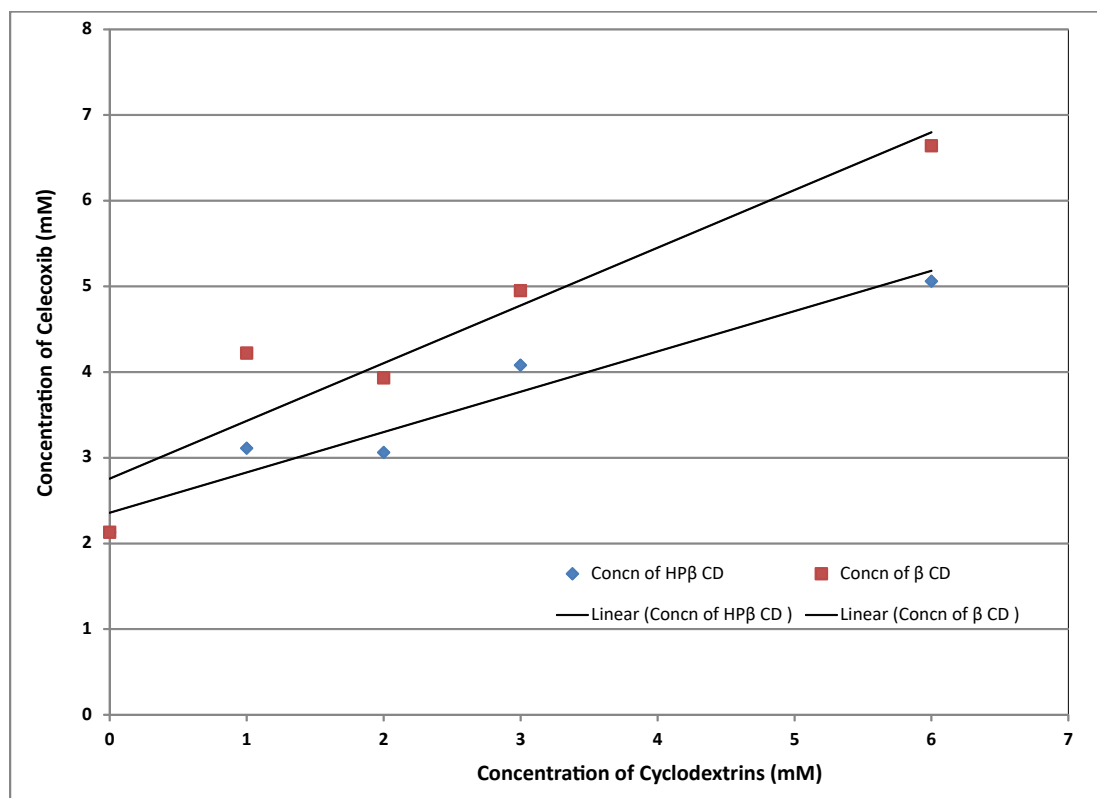


Fig. 1.0: Impact of Cyclodextrin on the Solubility

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 extent when it get complexed with the Cyclodextrin.

3.2 Evaluation of Tablets

Table 4.0 Physical Parameters of Tablets

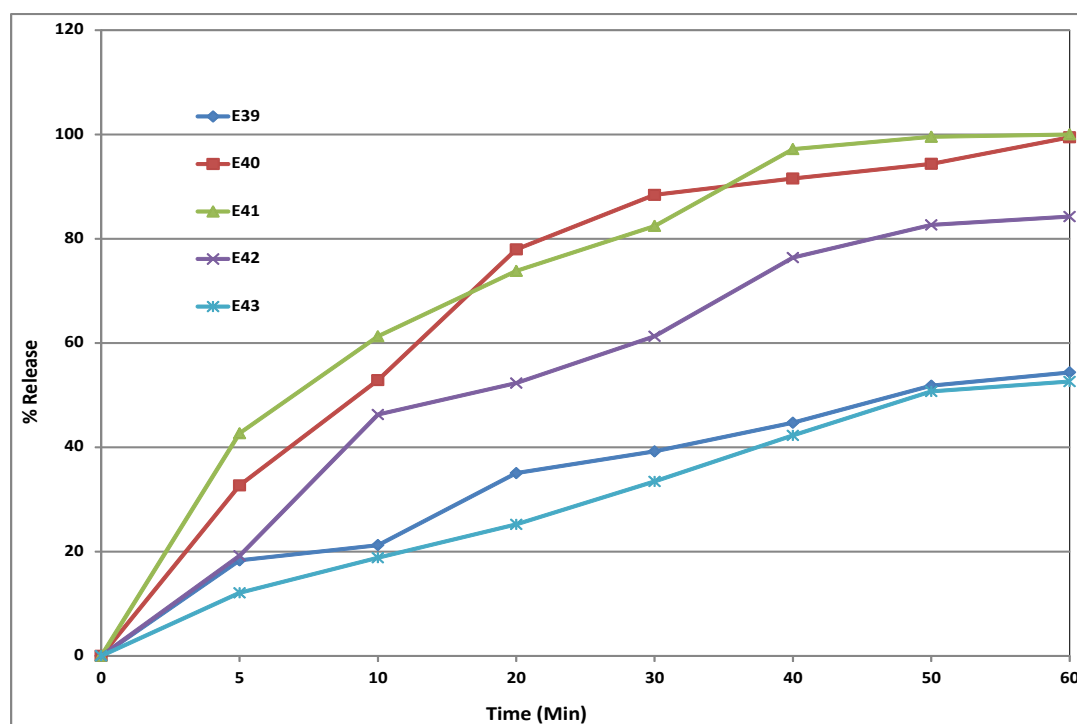
Composition	Assay	Tablet Strength	Friability	DT
E39	100.51 mg	5.0 – 6.0Kp	0.48%	3.9 min
E40	99.95 mg	4 – 5.5Kp	0.65%	2.15 min
E41	99.68 mg	4 – 6.0Kp	0.23%	2.43 min
E42	100.05 mg	4.5 – 6.0Kp	0.41%	15.1 min
E43	99.45 mg	4 – 5.5Kp	0.81%	20.1 min

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.

Table 5.0 Drug Release of Tablets

Time	% Release ($X \pm SD$)				
	E39	E40	E41	E42	E43
5 min	18.32%± 1.23	32.68%± 1.27	42.68%± 1.14	19.18%± 1.25	12.09%± 1.53
10 min	21.23%± 1.18	52.88%± 1.37	61.28%± 1.39	46.28%± 1.43	18.82%± 1.72
20 min	35.05%± 1.45	77.95%± 1.95	73.81%± 1.21	52.32%± 1.11	25.22%± 1.16
30 min	39.21%± 1.28	88.41%± 1.45	82.43%± 1.43	61.28%± 1.31	33.45%± 1.93
40 min	44.71%± 1.41	91.55%± 1.56	97.18%± 1.92	76.38%± 1.75	42.28%± 1.13
50 min	51.81%± 1.95	94.36%± 1.18	99.55%± 1.55	82.65%±1.76	50.72%± 1.45
60 min	54.36%± 1.28	99.45%± 1.48	100.0%± 0.95	84.25%±1.32	52.61%± 1.28

**Fig. 2.0: Percentage Drug Release of Tablets**

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.

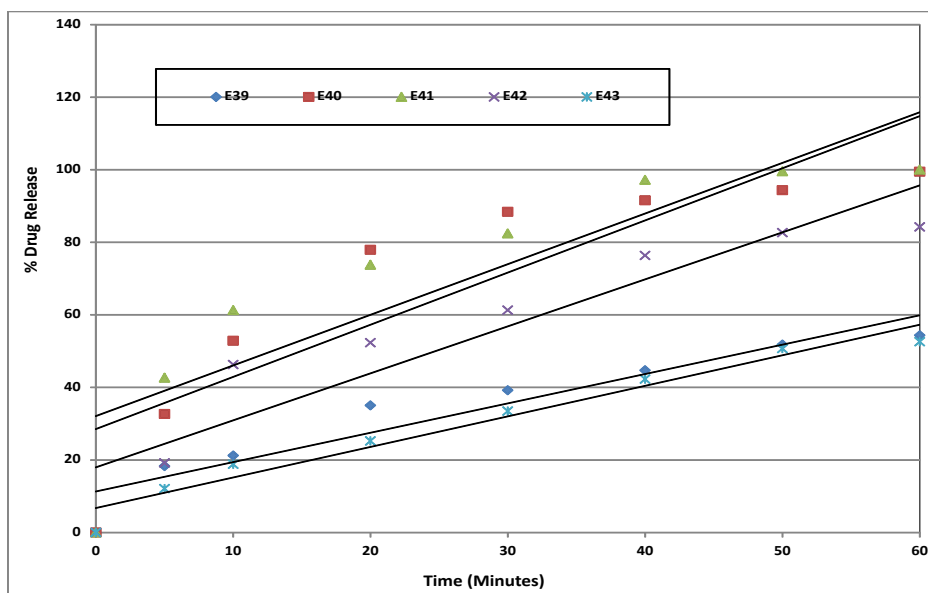


Fig. 3.0: Zero order drug release kinetics of Tablets

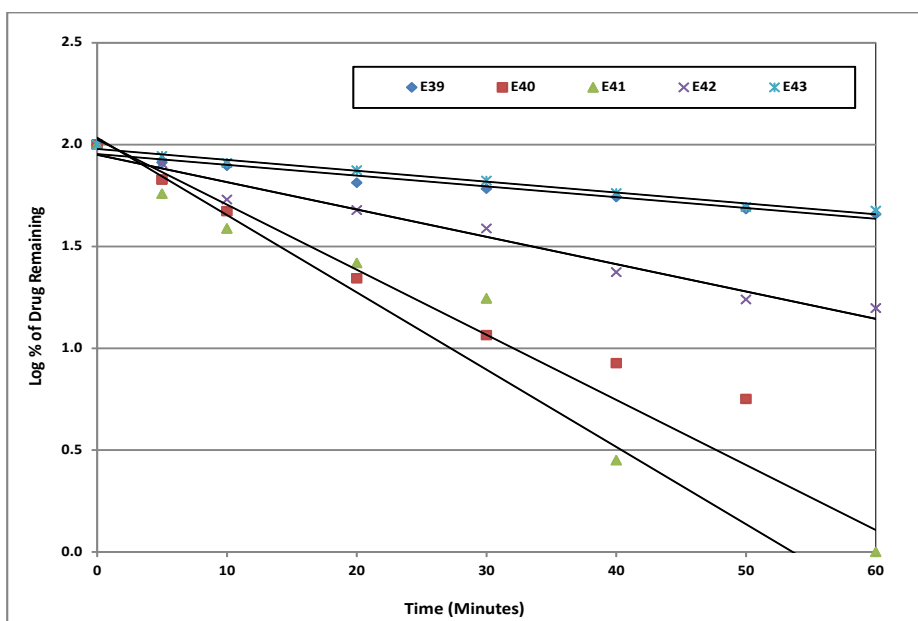


Fig. 4.0: First order drug release kinetics of Tablets

Table 6.0 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

Release kinetics and their 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.

4.0 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.

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