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Inclusion Complex of Iloperidone with sulfobutyl ether beta-cyclodextrin: Characterization and dissolution studies

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Abstract: Iloperidone (ILO) is a second-generation antipsychotic drug, is the first-line treatment, and approved by USFDA in May 2009. Iloperidone belongs to Biopharmaceutical Classification Systems (BCS) class II; thus, it is poorly water-soluble, highly permeable, and has pH-dependent solubility. Cyclodextrins and its derivatives have a wide range of applications in different formulations due to their complexation ability, which improves the solubility, stability, safety, and bioavailability of a drug. We have tried the complexation of iloperidone with sulfobutyl ether-β-cyclodextrin (SEβCD) to improve its solubility and dissolution. Complexation was done by the kneading method. Characterization of SEβCD complexes with Iloperidone was done by FTIR, DSC, saturation solubility, etc. Multimedia dissolution of the complex was carried out and compared with the plain drug. Significant improvement in drug release was found from SEβCD complexes in all media when compared with drug alone.

Keywords: β-cyclodextrin; binary complex; antipsychotic drug; dissolution studies

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Results and Discussion

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Phase solubility studies

- ILO solubility linearly improved with an increase in the concentration of SEβCD.
- ILO showed an AL-type of a graph, demonstrating the first-order dependency of interaction with SEβCD.
- The linear AL-type of the solubility curve suggests a 1:1 ratio for the complexation of ILO and SEβCD [1].

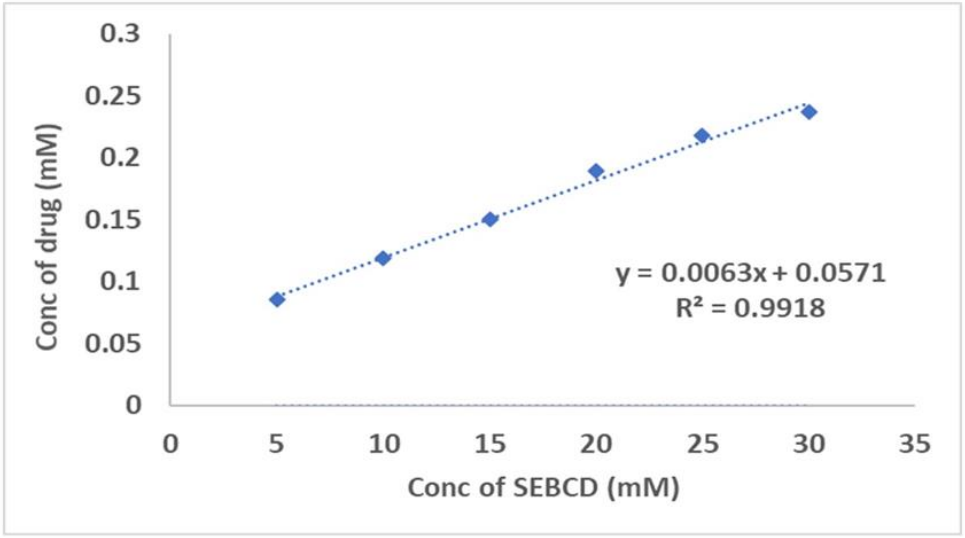

Figure 1. Solubility curve of ILO: SEβCD in water (Mean±SD)

Table 1. Phase solubility studies of inclusion complex

Parameters	Observation
Slope	0.0063
R^2	0.9918
y-intercept (S_0)	0.051
K_c (M^{-1})	124.31
CE	0.0063

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Saturation solubility and drug content

- The improved solubility of ILO in multimedia compared with plain ILO resulted from the inclusion complex of ILO and SEβCD.
- The percent drug content was found to be 99.23± 0.49, which complies with specifications.

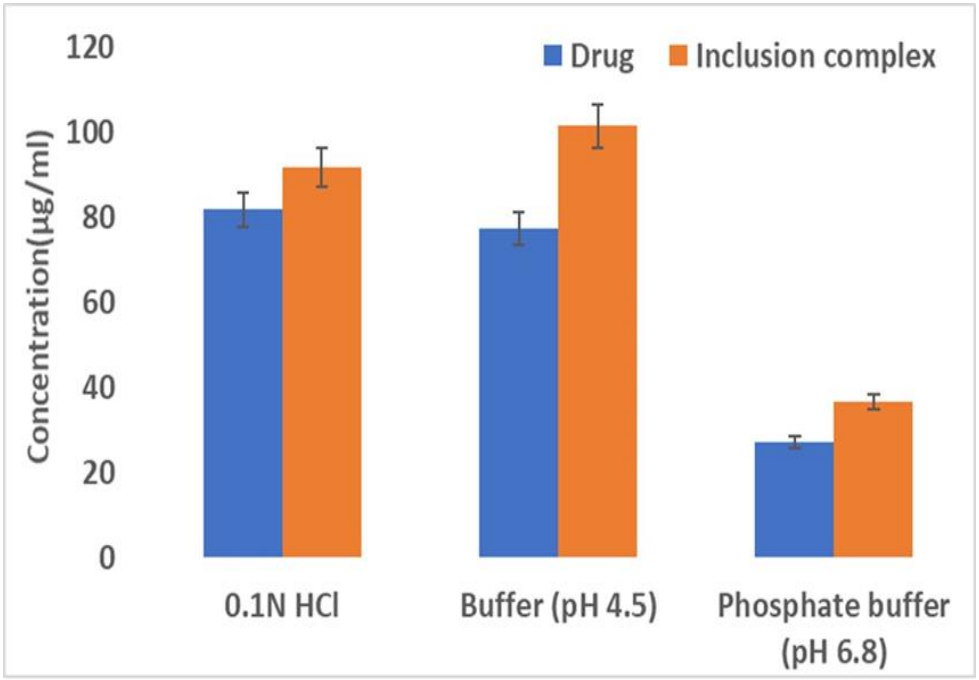

Figure 2. Multimedia saturation solubility of drug and inclusion complex (Mean±SD, n=3)

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ATR-FTIR

- ATR-FTIR is a convenient method to evaluate drug (guest) and SEβCD (host) solid-state interaction [2].
- The IR spectra of the inclusion complex depicted a decrease in intensity, alter, and disappearance of some distinctive IR bands of ILO.
- The interaction of ILO with SEβCD was confirmed by a significant shift of some distinctive bands of ILO.

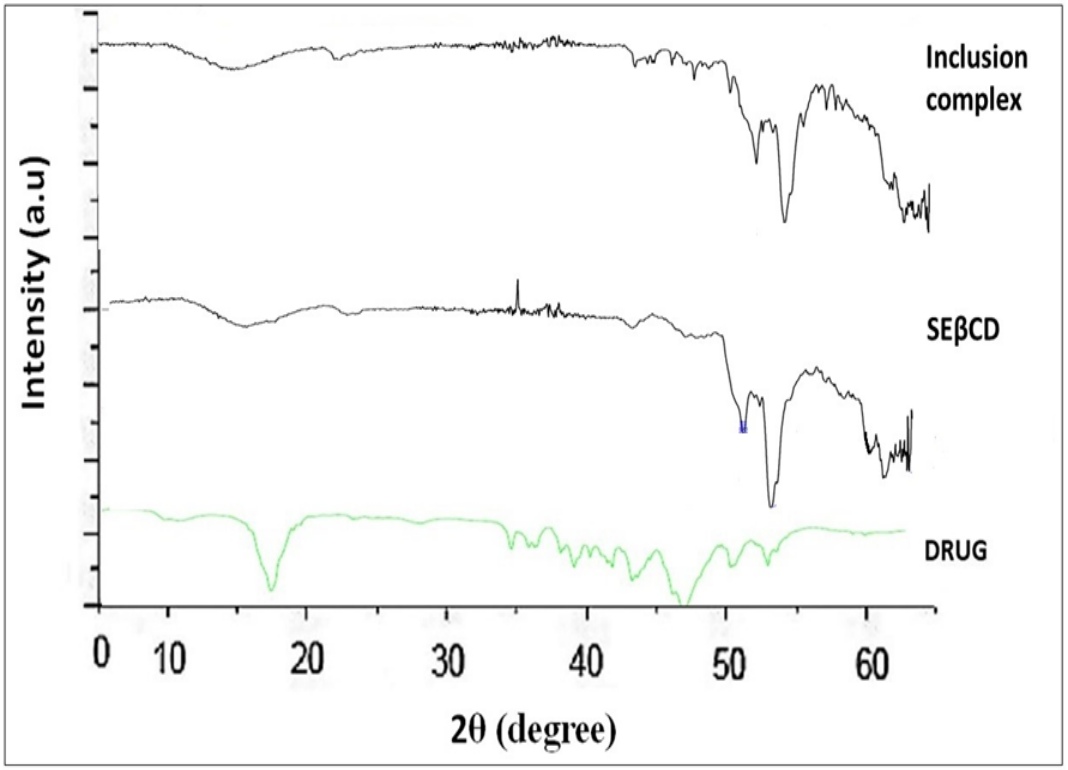

Figure 3. FT-IR spectra of Drug (ILO), SEβCD and inclusion complex

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DSC

- DSC of ILO displayed a sharp and well-defined endothermic peak at 120°C, conforming to the drug (ILO) melt point.
- In the endotherm of SEβCD, a broad peak was detected at 86°C. The endotherm of ILO was utterly disappeared into the stable inclusion complex.
- The amorphization of the drug describes an enhancement in the dissolution profile of ILO [3].

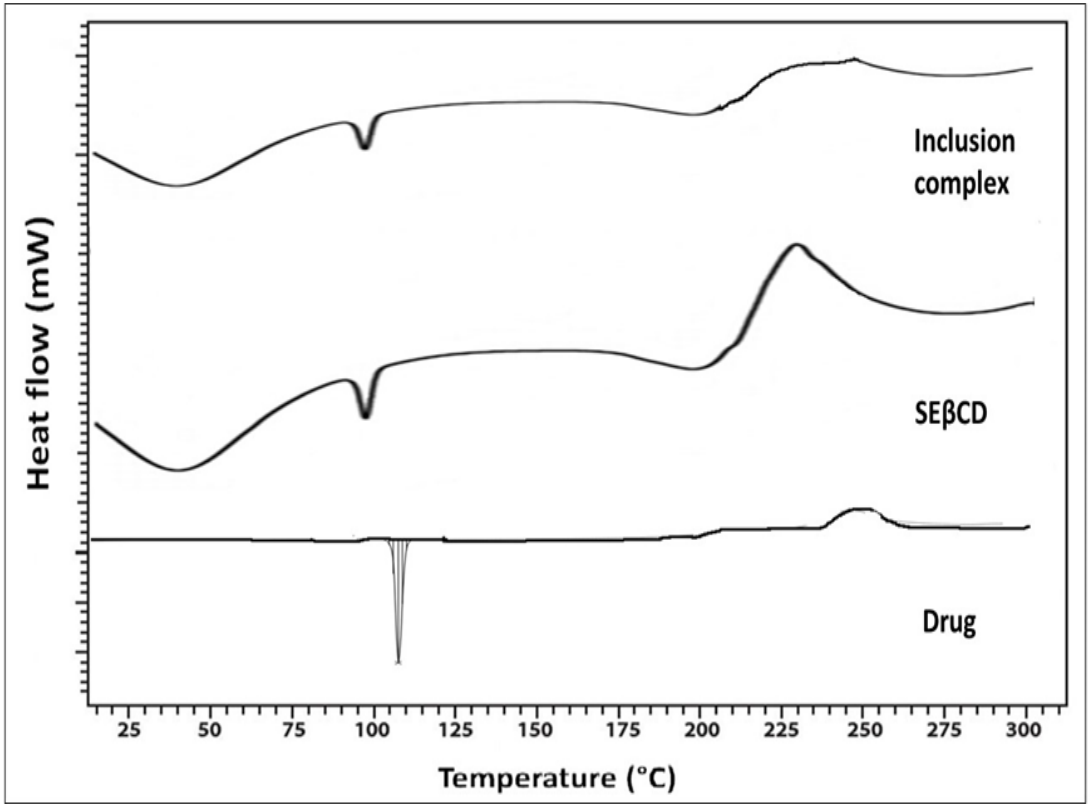

Figure 4. DSC thermogram of Drug (ILO), SEβCD and inclusion complex

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Multimedia dissolution study

- More than 80% of drug release was found in 0.1 N HCl and buffered pH 4.5, which depicts the significant difference between the drug ($p \leq 0.05$).
- In phosphate buffer (pH 6.8), no significant difference was observed between the drug.
- In multimedia, the inclusion complex showed no significant difference when compared with HPβCD based inclusion complex [4].
- The multimedia dissolution data depict that as the buffer's pH decreased from 6.8 to 4.5 and 1.2, the dissolution rate was significantly enhanced.

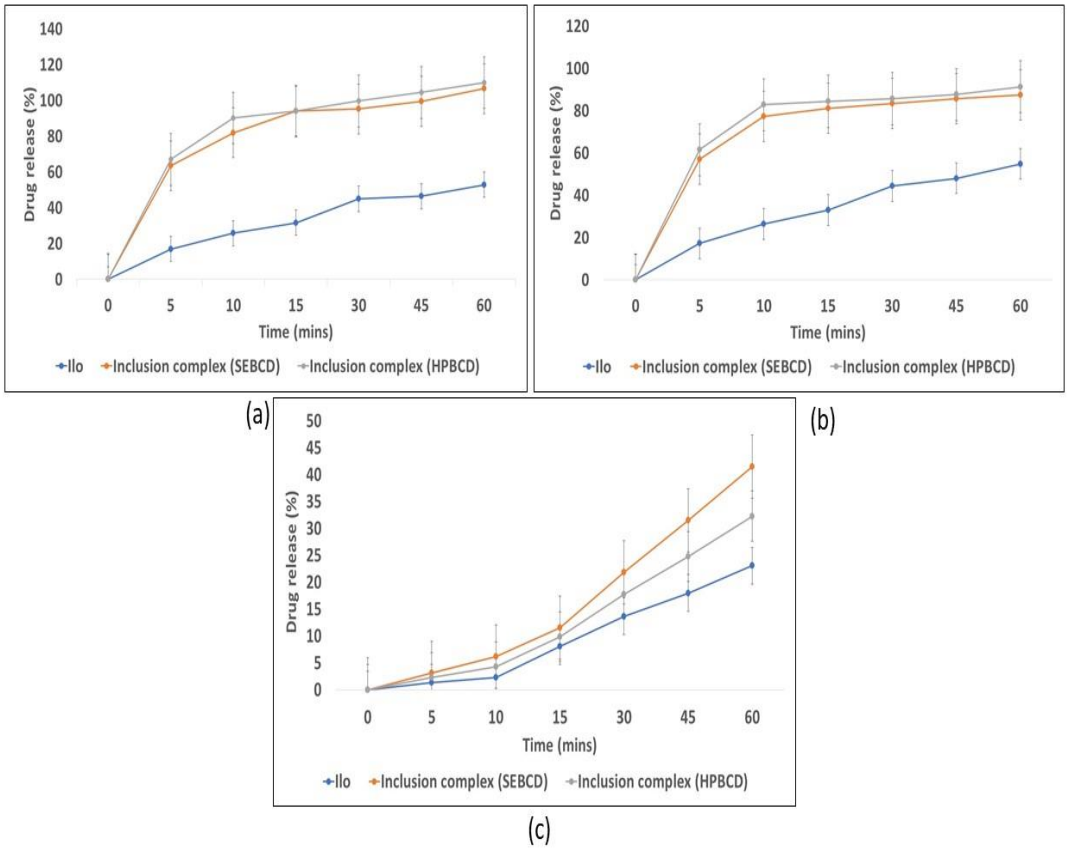

Figure 5. Multimedia dissolution of a drug (ILO) and inclusion complex ($p \leq 0.05$, Mean±SD, n=3)

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Conclusions

- In this research article, we evaluated the inclusion of SEβCD to enhance the solubility of the drug.
- Thermal analysis (DSC) and FT-IR depict the reduction in crystallinity and increase host-guest interaction, suggesting the inclusion of complex formation.
- SEβCD displayed improved complexation efficacy and solubility, more stability, as detected from the FT-IR study.
- The inclusion complex might be attributed to the enhanced dissolution of the drug.
- Thus, it can be concluded that SEβCD based inclusion complexes can lead to an increase in solubility, which may enhance the drug's bioavailability.

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Thank you

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