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OVERVIEW ON: CYCLODEXTRN INCLUSION COMPLEX

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Abstract

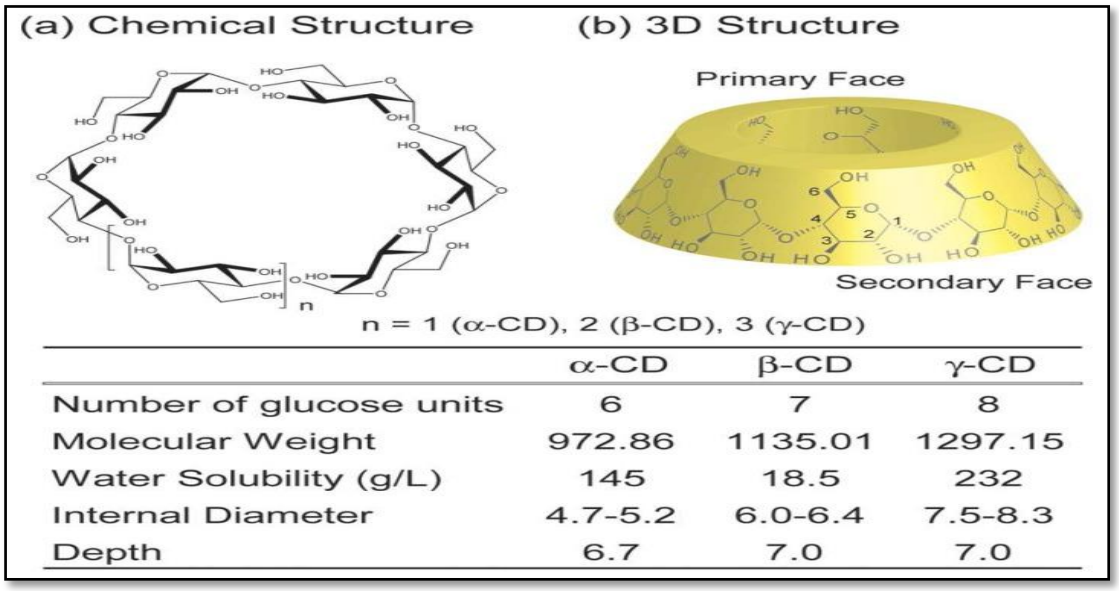
Today, 35 - 90% of all new chemical entities (NCE) suffer from poor water solubility; hence the improvement of the solubility of poorly water-soluble drugs is one of challenging aspects of modern drug development. Pre-formulation studies are the preliminary studies carried out to evaluate the drug substance to obtain the necessary information for the formulation of bio-pharmaceutically appropriate drug dosage form. Solubility of drugs in water is the first step in initial pre-formulation stages of product development program.

Cyclodextrins can improve water solubility by forming non-covalent, water-soluble inclusion complexes.

Keywords- Cyclodextrin, Dissolution, Solubility.

Introduction[6,7]

Cyclodextrins are cyclic oligosaccharides containing at least 6 D-(+) glucopyranose units attached by α-(1, 4) Glucoside bonds. Cyclodextrins have many pharmaceutical applications which make them a valuable tool for improving the physicochemical properties of drugs and removing undesirable effects related to the drug molecule. Cyclodextrins have the competencies to encapsulate the visitor molecule into its hollow space and enhance the solubility, stability, and launch profile of the drugs. Different types of cyclodextrins such as α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, and their derivatives are used for pharmaceutical purpose. Cyclodextrin interact with lipophilic molecules and form a non- covalent inclusion complex that lowers the chemical potency of the molecule in solution and thus improve the solubility of the molecule. Pharmaceutical modification of drug molecule by inclusion complex with cyclodextrins has been extensively developed to improve solubility, dissolution rate, chemical stability, absorption and bioavailability of hydrophobic drugs and reduces side effects and toxicity of drugs.



	α-CD	β-CD	γ-CD
Number of glucose units	6	7	8
Molecular Weight	972.86	1135.01	1297.15
Water Solubility (g/L)	145	18.5	232
Internal Diameter	4.7-5.2	6.0-6.4	7.5-8.3
Depth	6.7	7.0	7.0

Fig no. 1: Comparison Between Types of Cyclodextrin.

Preparation of solid inclusion complexes between cyclodextrins and various drugs includes kneading, co-evaporation, co-grinding, spray-drying and freeze-drying. The use of supercritical carbon dioxide has been recently proposed for the preparation of various drug cyclodextrin inclusion complexes for enhanced solubility and dissolution rate. Cyclodextrins are able to form host–guest complexes with a very wide range of solid, liquid and gaseous compounds. In these complexes, a guest molecule is held within the cavity of the cyclodextrin host molecule. The hydrophobic cavity of cyclodextrin molecules provides an environment into which appropriately sized moieties can enter to form inclusion complexes. The driving force of complex formation is the release of enthalpy-rich water molecules from the cavity. Water molecules are displaced by more lipophilic guest molecules present in the solution,

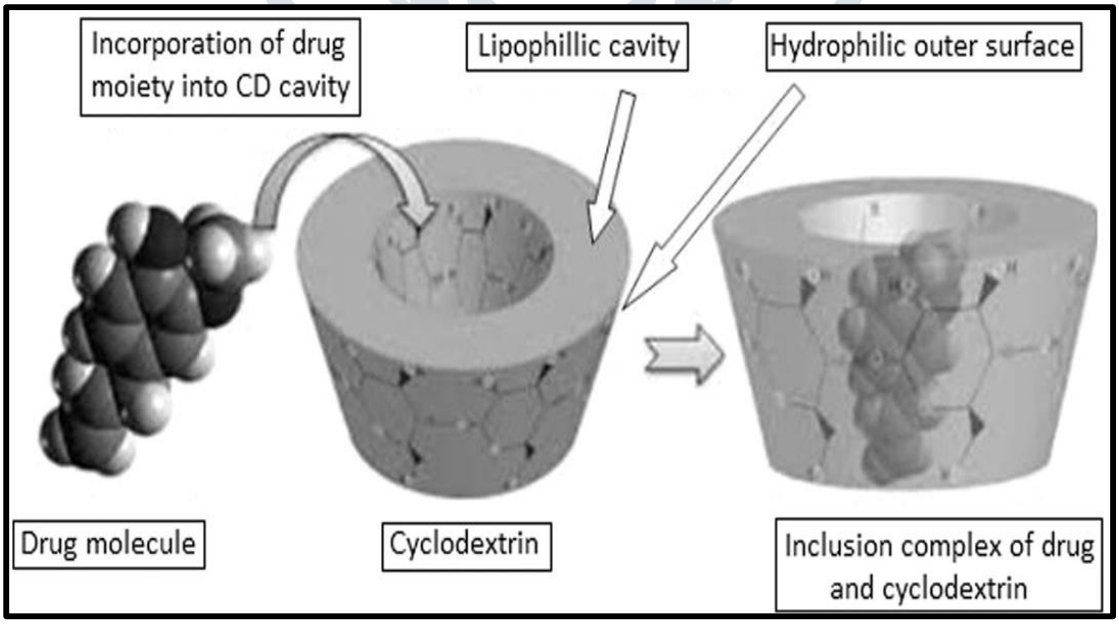


Fig no. 2 : Incorporation of Drug in cyclodextrin Cavity

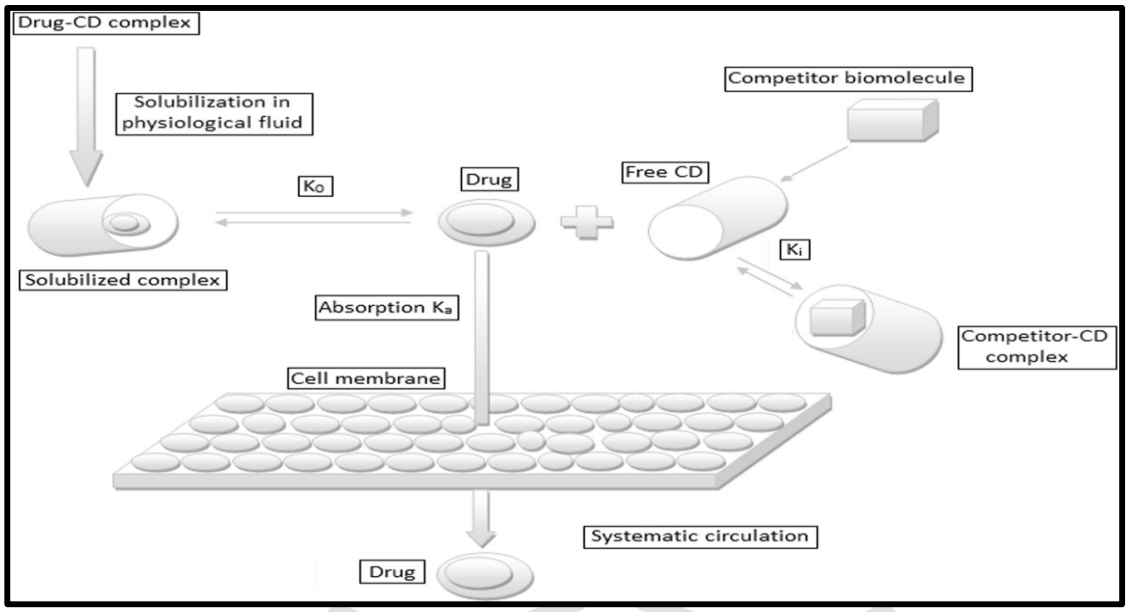


Fig no. 3: Cyclodextrins–drug complexation, release and absorption of drug.

Method of preparation of inclusion complex[8]

1. Physical blending method
2. Kneading method
3. Co-precipitation technique
4. Solvent evaporation method
5. Precipitation method
6. Atomization spray drying method
7. Lyophilization method
8. Microwave irradiation method
9. Supercritical anti- solvent technique

Physical blending method:

A mixture of drug and cyclodextrins are prepared by trituration. Cyclodextrins and drug are mixed together thoroughly by trituration in a mortar and passes through sieve to get the desired particle size in the final product. The preparation of physical mixtures is based on blending of the drug with cyclodextrins in mass granulator usually for 30 minutes.

Kneading method:

The method based on the cyclodextrins mixed with water and make a paste. The drug is then added to the paste and kneaded. The mixture is then dried and passed through appropriate size sieve. In small scale it is achieved by using a mortar and Pestel.

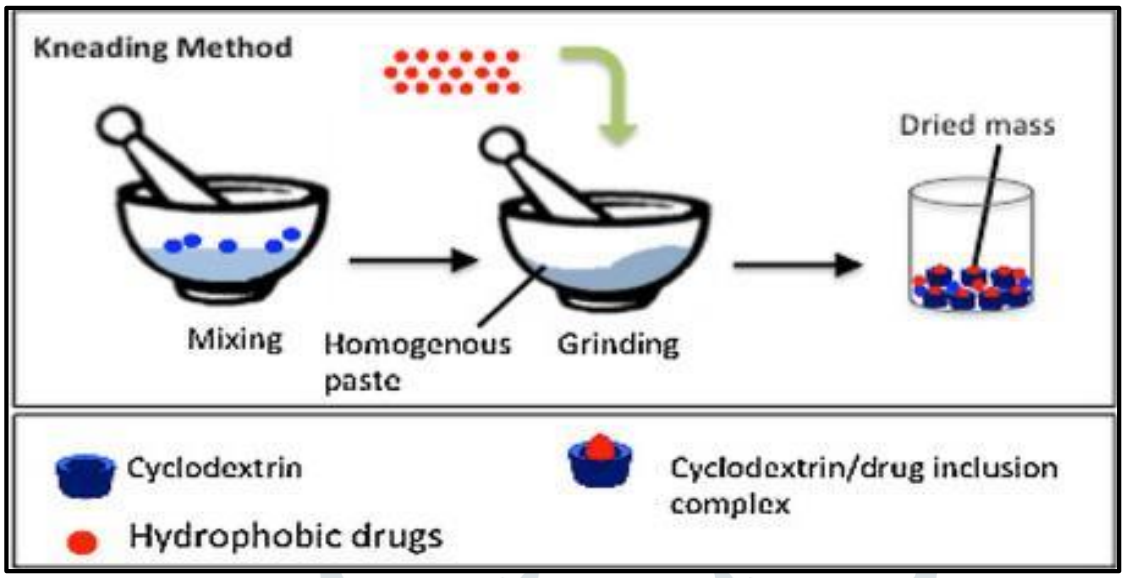


Fig no.4: Kneading method

Solvent evaporation method:

Dissolve drug in organic phase and cyclodextrins in water phase separately in to two miscible solvents, mixing of both solutions to get dispersion of drug and complexing agents and finally evaporating the solvent in vacuum oven to obtain inclusion compound.

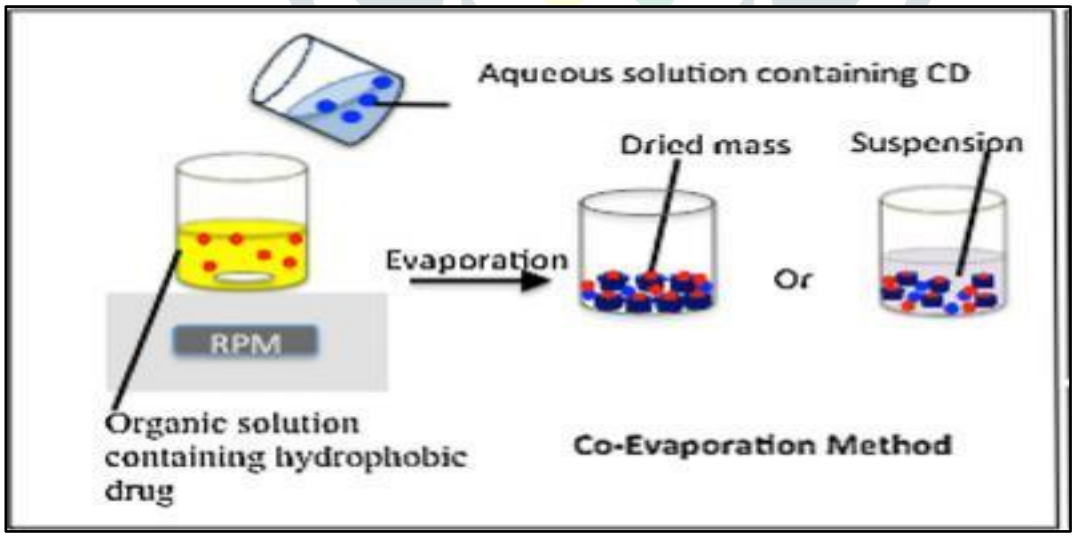


Fig no.5: Solvent evaporation method

Generally, the aqueous solution of cyclodextrins is added to the alcoholic solution of drugs. The resulting mixture is stirred for 24 hours then evaporated under vacuum at 45 ºc. The dried mass is passed through a 60-mess sieve.

Supercritical anti-solvent technique:

In this technique, carbon dioxide is acts as an antisolvent for the solute. The use of supercritical carbon dioxide is advantageous for heat-labile active pharmaceutical ingredients.

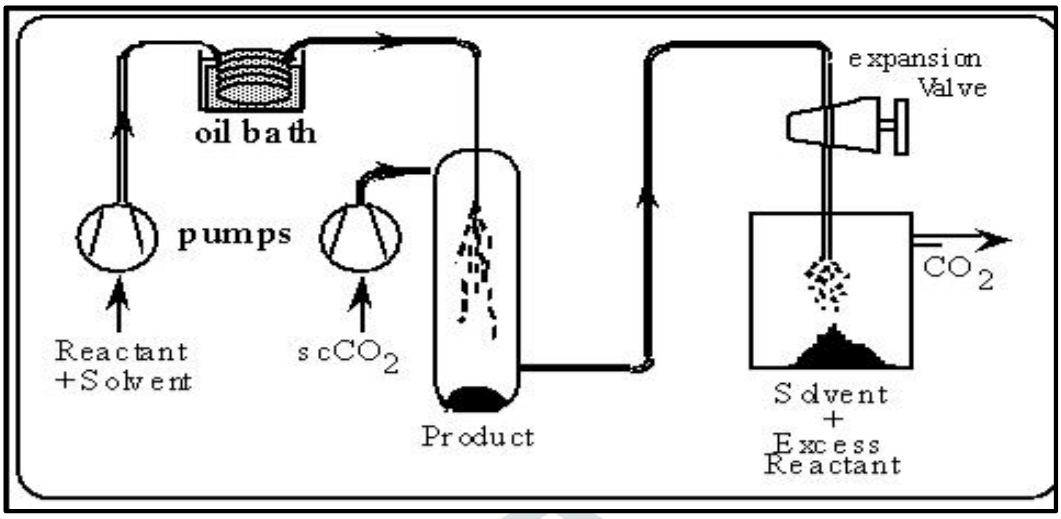


Fig no.6: Supercritical anti-solvent technique.

Supercritical particle generation processes are efficient route for improving bioavailability of pharmaceuticals. In this technique, drug and cyclodextrin are dissolved in solvent then the solution is poured into a pressure vessel, through a nozzle. When the solution is sprayed in to supercritical fluid anti-solvent, the carbon dioxide rapidly diffuses into that liquid solvent as the carrier liquid solvent. the mixture becomes supersaturated and gives precipitation of the solute and the solvent is carried away.

Microwave Irradiation Method:

The cyclodextrin and drug are dissolved in a mixture of water and organic solvent. The mixture is allowed to react for time of about 90 sec to 1min at 60°C in the microwave oven. After completion of the reaction, adequate amount of water and organic solvent mixture is added to the reaction mixture to remove the un-complexed free drug and cyclodextrin. It is filtered and dried in vacuum oven for a sufficient time.

Atomization spray drying method:

Spray dryer used for the formulation of inclusion complexes. In this technique, host and guest molecules dissolved in common solvent and dried by spray drying technique. Different size of inclusion complexes is obtained by checking the size of atomizer or spray nozzle and other parameters such as sample feeding rate and inlet temperature. For volatile substances, this method reduced the losses and not appropriate for highly volatile or thermolabile substances.

Co-precipitation method:

Coprecipitation is used for the formation of cyclodextrin complexes of water insoluble drugs. The guest molecule or lipophilic drugs were dissolved in organic phase (ethanol) and host molecules were dissolved in aqueous phase. Organic phase solution is dissolved in the aqueous phase solution with proper agitation. The solution is cooled and complexes were washed with organic solvent sch as ethanol and dried at 50°C.

Lyophilization method:

This technique is the suitable for the formulation of cyclodextrin complexes of heat sensitive drugs. In this

method, drug and cyclodextrin were dissolved in a suitable solvent such as ethanol with stirring after that the solution was freeze-dried. The solvent was evaporated under the vacuum, and cyclodextrin inclusion complexes is obtained.

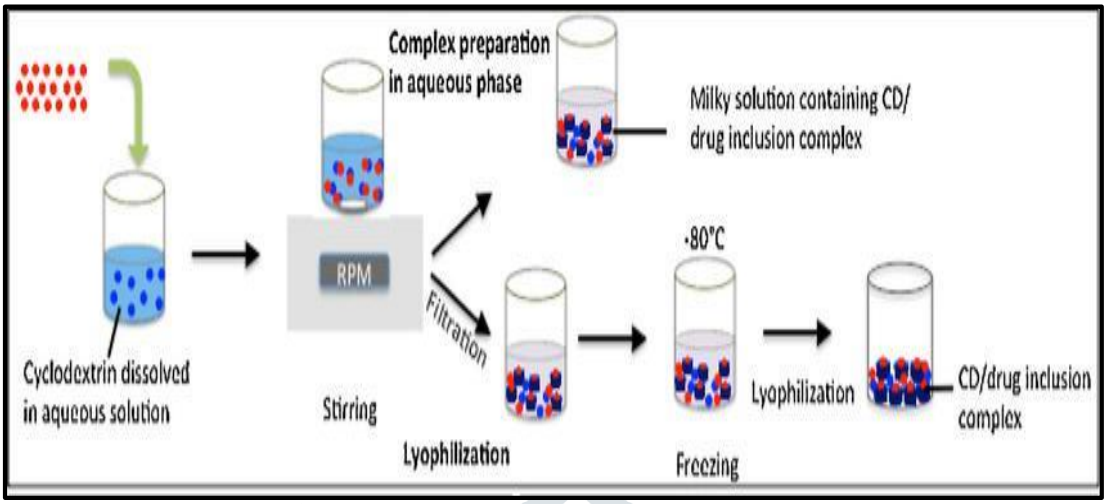


Fig no. 7: Lyophilization/ spray drying method.

Characterization of cyclodextrin complexes[9]

1) **Percentage practical yield**:

   The efficiency of the process is determined by the yield of the process. Percentage practical yield is calculated to know the percent efficiency. It helps in selection of appropriate method of production.

   % Practical yield =

   (Practical mass inclusion complex)/(Theoretical mass)×100

2) **Entrapment Efficiency**:

   Entrapment efficiency evaluates about the amount of drug entrapped into the host molecules. Higher entrapment efficiency implies the more amount of drug entrapped in the host molecule. Entrapment efficiency in cyclodextrin complexes mainly depends on the size of the guest molecules and cavity size of host molecules

3) **FT-IR spectrum**:

   The infrared spectra of the inclusion complexes are analyzed and compared with the spectra of the pure compounds. FTIR spectra indicate the type of intramolecular interaction between the drug and host. Which are in the range of 4000-400 cm-1.The formation of H-bonding between the drug and cyclodextrin is indicated by shifting in the peaks toward higher or lower wave number in inclusion complexes.

4) **DSC analysis**:

   The thermal behavior of drugs such as melting point and heat change formulation is indicated by DSC analysis. Changes in the melting point during the formation of inclusion complexes shows the entrapment of the drug molecules into the cavity of cyclodextrin. The thermogram obtained from the DSC is also explains the crystal behavior endothermic or exothermic reaction and formation of new compound.

5) **Scanning Electron Microscopy**:

The surface morphology of different formation is examined by scanning electron microscope. The SEM experiments were conducted to visualize the changes in the surface morphology of inclusion complex. It displays shape of the inclusion complexes and also confirmed the surface morphology of inclusion complexes.

6) **In-vitro Drug Dissolution Study:**

Dissolution studies are used to evaluate the aqueous solubility of drug with time in a suitable dissolution medium. The outcomes from solubility studies indicated the performance of the inclusion complex when compared to pure drug.

Acknowledgment

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References

[1] Vikas *et al*. 2018. Cyclodextrin complexes: An Approach to Improvement the Physicochemical Properties of Drugs and Applications of Cyclodextrin Complexes, Asian Journal of Pharmaceutics,12 (2).

[2] Keshav, J. *et al*. 2017. Review on solubility: A mandatory tool for pharmaceuticals, International Research Journal of Pharmaceutics, 8 (11).

[3] Tripathi KD. Essentials of medical pharmacology. Sixth edition. Jaypee Brothers Medical Publishers (P) Ltd. p (521-538).

[4] Carrier, R. Miller, A. Ahmed, I. 2007. The utility of cyclodextrins for enhancing oral bioavailability, Journal of Controlled Release Control Release,123:78–99.

[5] Radhouan, M. Radhouan, A. 2015. Application of cyclodextrin: formation of inclusion complexs and their characterization, International journal of Advanced Research,3(2):1030-776.

[6] Cheirslip, B. Rakmai, J. 2016. Inclusion complex formation of cyclodextrin with its guest and their applications. Bio. Eng. Med.,2:1–6.

[7] Jambhekar, S. Breen, P. 2016. Cyclodextrins in pharmaceutical formulation I: Structure and physicochemical properties, formation of complexes, and types of complexes. Drug Discovery Today,21: 359–362.

[8] Loftsson, T. Duchene, D. 2007. Cyclodextrins and their pharmaceutical applications, International Journal of Pharmaceutics,329:1–11.

[9] Singh, R. Bharti, N. Madan, J. Hiremath, N. 2010. Characterization of cyclodextrin inclusion complexes−a review. Journal of Pharmaceutical Science Technol, 2:171−183.