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Cyclodextrin-Based Nanostructures

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1. Introduction

Cyclodextrins are widely used excipients in the pharmaceutical, cosmetic and food industries. These excipients are non-reducing, cyclic oligosaccharides composed of glucopyranose units. They have three widely known derivatives: α-, β- and γ-cyclodextrins, which contain 6, 7 and 8 glucopyranose units. The inner cavity of these molecules is hydrophobic, and their surface is hydrophilic so they are able to complex lipophilic molecules. Due to this property, cyclodextrins are mainly used to increase solubility, mask unpleasant tastes and odors and increase bioavailability. Besides the drug complexation, the hydroxylpropyl-beta-cyclodextrin is applied in the treatment of Niemann Pick Disease type C, because this derivative is able to complex a biological important molecule, the cholesterol. By modifying or coupling cyclodextrin ring with other rings, these excipients can be used to build up larger nanostructures. On the other hand, they have numerous effects on cells.

2. Cyclodextrin-based nanostructures

The modification of the cyclodextrin rings with hydrophobic (aliphatic) chains can yield amphiphilic cyclodextrins. This type of cyclodextrins can self-assemble into water-soluble aggregates, like micelles. These cyclodextrins have two groups: the polysubstituted and the monosubstituted amphiphilic cyclodextrins. In the case of polysubstituted derivates, we can distinguish some subgroups, such as medusa-like, bouquet-like and skirt-shaped according to the position of substitution groups. In the case of monisubstituted amphiphilic cyclodextrins these excipients obtained by appending a single anchor. The aim of this derivatization is to improve cell targeting. This group has also some sub-groups, such as "Lollipop", "Cup and Ball" and lipid-like amphiphilic cyclodextrins. α-, β- and γ-cyclodextrins can form aggregates and bind together by hydrogen bonds and by intermediate water molecules. These wormlike, self-assembled aggregates called "poly-CD". Polypseudorotaxane is a single polymer chain, which is made by mixing of concentrated solution of α-cyclodextrin with the polymer polyethylene-glycol or β-cyclodextrin with poly-(propylene-glycol). Polyrotaxane is the modified derivative of polypseudorotaxane: the two ends of the polymer chain are linked to two bulky end groups. In this case, the cyclodextrin rings are prevented from dethreading.

Today another investigated area is the polymerizationof cyclodextrins. Dependig on the chemical structure; we can talk about grafted, conjugated or polymerized cyclodextrins.

These modifications can increase the usability of CDs. Polymerized cyclodextrins can be divided into three groups: soluble cyclodextrin polymers, insoluble cyclodextrin polymers and nanosponges. The soluble CDPs and nanosponges have higher ability to increase the solubility of the APIs than free cyclodextrins, while the insoluble type starts to conquer the solid phase extraction and analytics area.

The conjugated and grafted cyclodextrin have opportunity to develop sensitive, smart drug delivery systems that can respond to many external influences such as pH, thermo or photo stimuli. The acrylamide, acryl acid or poly(ethylene glycol) influences the swelling ratio during the heating or cooling thereby regulate the drug release. The pH sensitive carriers use to treat tumor dis-

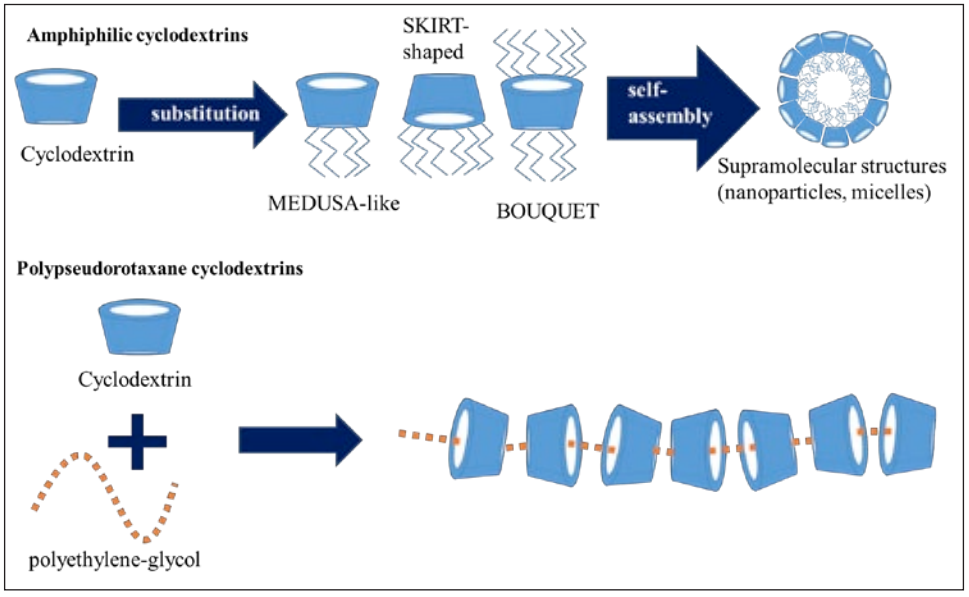

Figure 1

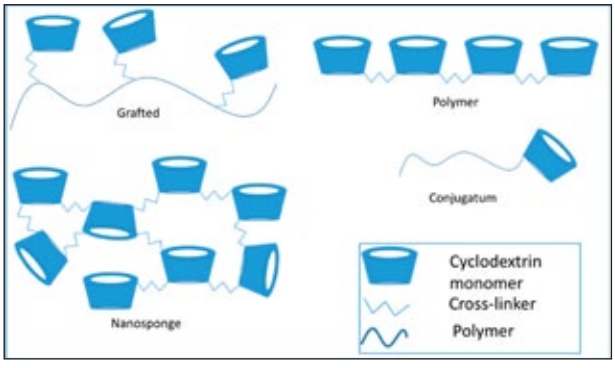

Figure 2

eases, because of the different pH micro area around the cells. Furthermore, it has ability to avoid the API damage in the low stomach pH. The application of mucoadhesive CDs may be beneficial in stomach also, these carriers are conjugated with alginate or chitosan, or thiol group is bonded to the native CD ring to increase the residual time on the mucosa layer. The photo responding polymers leak the API from the drug delivery system, if they are exposed by light.

3. Conclusion

The research of the newly synthesized, polymerized and modificated cyclodextrins attracted more interest in the last 5-10 years. They have adanced efficacy to complex drugs and have responsive abilities.

4. Acknowledgements

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