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Molecular Recognition of Cyclodextrins and Their Derivatives

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Abstract: Cyclodextrins and their derivatives have been widely used in many fields such as science and technology as molecular receptors, artificial enzyme models and drug carriers because of their unique structures and characteristics. Cyclodextrins and their derivatives have hydrophobic cavities, so that they can interact with various guest molecules through non-covalent bonds to form "molecular capsules", thus changing the physical and chemical properties of guest molecules.

1. From molecular chemistry to supramolecular chemistry

Supramolecular chemistry is beyond the category of molecular chemistry. As a new chemical discipline, it studies the chemistry of intermolecular interactions and molecular aggregates [1]. The development of supramolecular chemistry benefited from three chemists, C.J. Pedersen, J.M. Lehn and D.J. Cram, and C.J. Pederson discovered the coordination properties of crown ethers. D.J. Cram developed the host-guest chemistry [2]; J.M. Lehn proposed the concept of "supramolecular chemistry" [3]. In 2016, the Nobel Prize in Chemistry Jean-Pierre Sauvage, Sir J. Fraser Stoddart and Bernard L. Feringa were born, and their proposal of "Design and Synthesis of molecular machines" pushed supramolecular chemistry to the academic climax again [4-6].

In recent years, supramolecular chemistry has developed rapidly, and contemporary chemists pay more attention to it [7]. Supramolecular chemistry is closely related to physics, informatics, materials science and life science [8]. A complex and ordered system with specific functions formed by weak intermolecular interactions among multiple molecules is supramolecular system [9-12]. Supramolecular chemistry gives people two important inspirations: First, weak intermolecular interactions can be superimposed and synergistically transformed into strong binding energy under certain conditions; Second, the supramolecular system assembled by molecules can have completely different properties from the original molecules. In recent years, supramolecular chemistry, combined with new materials—C60, carbon nanotubes and gold nanoparticles, has become one of the hot research topics [13].

Cyclodextrins (CDs), a kind of macrocyclic compounds with D-glucopyranose units connected end to end, are the second generation main compounds in supramolecular chemistry research. Since its discovery, this kind of cyclic carbohydrate has attracted more and more attention of scientists. Cyclodextrins and their derivatives are widely used in the field of science and technology, which

may be attributed to the following characteristics of these compounds: firstly, these compounds are relatively easy to obtain semi-natural products; Secondly, this compound has stable chemical properties and can be selectively modified. Third, the cavity of cyclodextrin can provide a space for bonding with the model substrate; Fourthly, cyclodextrin has no toxicity (or low toxicity) and can be degraded in vivo, so it can be used in industrial technology as fat-soluble drug carrier, food additive and cosmetic filler [15]. This paper mainly studies the synthesis, molecular recognition and molecular assembly of cyclodextrin and its derivatives. In the following content, we will mainly introduce the molecular recognition and molecular assembly research of cyclodextrin on pharmaceutical active molecules.

2. Molecular recognition of cyclodextrin and its derivatives

2.1 Basic structural characteristics and physical and chemical properties of cyclodextrin

Cyclodextrins (CDs) are mainly cyclic oligomers linked by α-1,4- glycosidic bonds, and the most common ones are α-,β-and γ-cyclodextrins, which have 6, 7 and 8 glucose units[16]respectively. As shown in fig. 1, cyclodextrin has a truncated cone shape, in which all D- glucopyranose units adopt the conformation [17] of $^4C_1$. The inner wall of cyclodextrin is composed of hydrogen atoms on C3 and C5 and oxygen atoms of glycosidic bond, and the lone pair on oxygen atoms of glycosidic bond points to the inside of the cavity, which makes the inside of cyclodextrin cavity produce high electron cloud density, thus showing some characteristics of Lewis base [18-20].

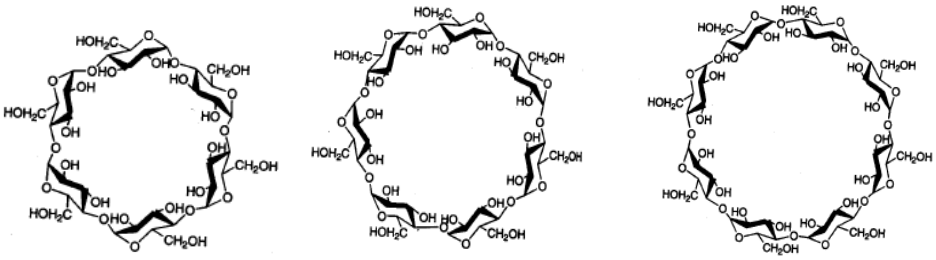

Figure 1: Structure diagram of three kinds of CD

Due to the above structural characteristics, cyclodextrin has hydrophobic cavity and hydrophilic surface, and it can include inorganic, organic, biological molecules and other guest molecules.

α-,β-and γ-cyclodextrins are three common natural cyclodextrins, and their solubility, cavity size, optical rotation and crystal shape are different due to the difference in the number of glucose units.

2.2 Synthesis and Molecular Identification of β-CD

Synthesis of 1.2.2.1 Polyamine Modified β-CD

β -CD has a hydrophilic outer surface and a hydrophobic inner cavity, which can improve the solubility, stability and bioavailability of the guest, and make them widely used in pharmaceutical field, agriculture and food technology. However, the natural β-CD still has great limitations, and its binding ability with the guest molecule is relatively low. Therefore, in order to meet different needs, we need to chemically modify the natural β-CD[24-28]. The modification of cyclodextrin can adopt the following basic strategies: (1) modification from hydroxyl group; (2) changing the hydroxyl groups of cyclodextrin molecules into groups with higher nucleophilicity; (3) selectively converting hydroxyl groups of cyclodextrin molecules into leaving groups; (4) Use other special chemical reactions for modification.

The activity of hydroxyl groups on the major and minor surfaces of β-CD is different, so in some

cases, the difference of hydroxyl groups can be used for selective modification. Figure 2 shows the basic laws of the products obtained under different reaction conditions.

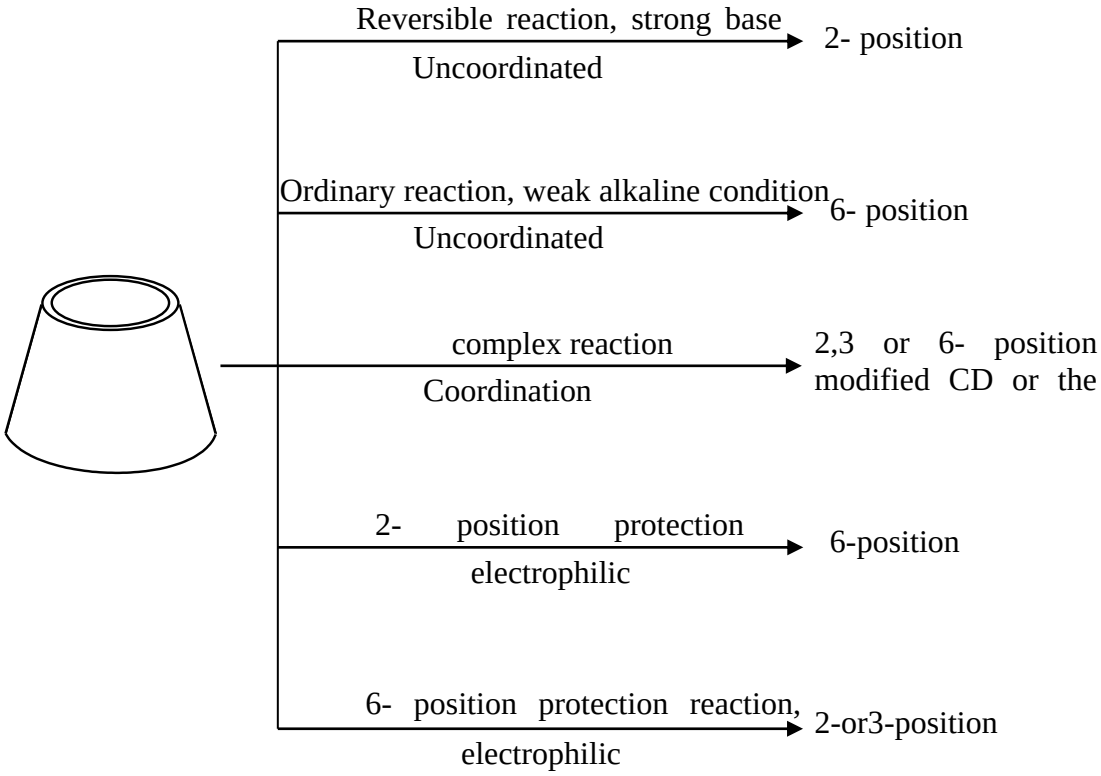

Figure 2: Reaction conditions and products of chemical modification by using the difference of β-CD hydroxyl activity

Polyamine-modified β-CD is a common intermediate used to synthesize chemically modified β-CD. They usually react with electrophilic reagents to produce many β-CD derivatives. Generally, β-CD p-toluenesulfonate is used as the starting material of polyamine modified β-CD, which reacts with sodium azide to form β-CD6-position azide, and then triphenylphosphine is added to react with ammonia water, and the desired target product is successfully synthesized[29]. There is another method to prepare polyamine-modified β-CD: dissolve the mono (6- deoxy -6- p-toluenesulfonyl) -β-CD in DMF, add concentrated ammonia water, and put it into an autoclave for reaction, and successfully obtain the desired mono (6- polyamine -6- deoxy) -β-CD with a yield of 54%[30]. Polyamine-modified β-CD[31]can be prepared by reacting polyamine compounds such as ethylenediamine, diethylenetriamine and triethylenetetramine with β-CD 6-position p-toluenesulfonate. This paper adopts the second preparation method.

Molecular Recognition of 1.2.2.2 Polyamine Modified β-CD

J.-M. Lehn pointed out in his Nobel Prize-winning speech: "Molecular recognition, conversion and transmission are the basic functions of supramolecular species"[34]. The selective bonding of the receptor (host) to the substrate (object) produces a specific function, so we call this process molecular recognition. The process of molecular recognition is similar to the interaction between enzymes and substrates, protein and nucleic acids, hormones and receptors, antigens and antibodies, immunosuppressants and immune parents, which are common in living organisms. In supramolecular chemistry, β-CD and its derivatives belong to a very important class of supramolecular host compounds. These β-CD host compounds have hydrophobic cavities of different sizes, hydrophilic surfaces of different sizes, and chiral microenvironment, which can selectively bond various organic, inorganic and biological molecules to form host-guest or

supramolecular complexes[35]. Therefore, molecular recognition plays an important role in the process of information processing and transmission, the preparation of molecular and supramolecular devices, and it is of great significance in life, becoming the core concept of supramolecular chemistry. Fig. 3 shows a schematic diagram of a typical β-CD molecular recognition process.

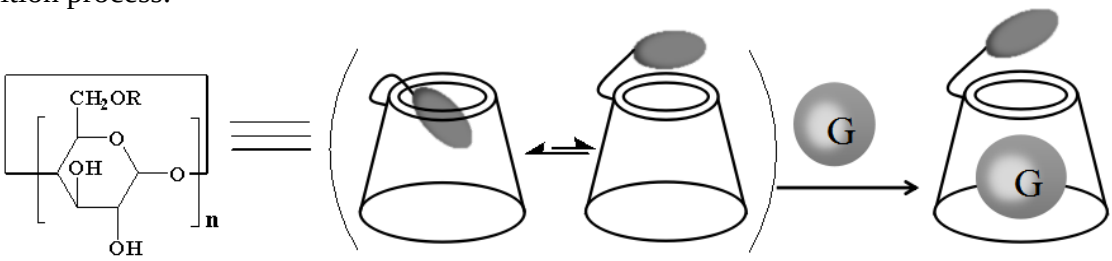

Figure 3: Molecular recognition pattern of β-CD

The inclusion of β-CD on guest molecules is mainly due to the non-covalent bond between molecules, such as hydrophobic interaction; Van der waals interaction; Hydrogen bond; The release of high-energy water in β-CD cavity after coating substrate; The release of tension energy of β-CD-water adduct after the substrate is coated. Interestingly, however, the selective binding of molecular receptors to substrates to form supramolecular systems is a synergistic effect between molecules, that is to say, the binding effect of two molecules is not caused by one kind of weak interaction, but the synergistic result of many kinds of weak interactions.

Polyamine modification of β-CD will produce special molecular recognition effect, because a new "N" recognition site is added based on van der Waals force and hydrophobic interaction between host and guest. Liu Yu et al.[36]determined the inclusion coordination of β-CD modified by diethylenetriamine and triethylenetetramine with a series of naphthalene derivatives, using fluorescence spectrometry titration. The results show that the stability of the required supramolecular complexes is due to the synergistic effect of many weak interactions, in which van der Waals force and hydrophobic interaction play a leading role. Yoshida et al.[37]reported that polyamine-modified β-CD can be protonated and will be positively charged in a certain pH range. The required stability of inclusion complexes is enhanced to some extent, which is attributed to electrostatic interaction or extended hydrophobic microenvironment at the edge of coordination inclusion sites. To sum up, the recognition mechanism of polyamine-modified β-CD molecule[38,39]is determined by the synergy of several weak interactions, such as size and shape matching of host and guest, Van der Waals, hydrogen bond, geometric complementarity and so on. Polyamine modified β-CD can increase recognition sites, and then change the hydrophobicity of microenvironment.

2.3 Application of polyamine modified β-CD in medicine

β -CD and its derivatives are multifunctional carriers, which are generally regarded as non-toxic and non-irritating materials. Therefore, β-CD and its derivatives have been widely used in the fields of medicine, food, cosmetics and consumer goods, other industries (such as spinning and weaving, printing and dyeing, etc.), agriculture, environmental protection, biotechnology, etc.[41], and its consumption is increasing by 20%~30% every year. Among them, in the field of medicine, the research and application of β-CD is the most active, and in the field of pharmacy, the application of β-CD has made great progress[42].

In drug research, the inclusion of β-CD and chemically modified β-CD with drugs can change the solubility of drugs, promote drug absorption and improve drug bioavailability, improve drug stability, mask the bad smell and taste of drugs, reduce irritation and side effects, powder liquid

drugs, and prevent drug interactions[43]. Therefore, with the increasingly mature research of β-CD inclusion technology, more and more drugs have been improved by rationalizing their properties with β-CD inclusion, which has solved some difficulties in preparation production, and many preparations containing β-CD inclusion compounds have been listed, such as prostaglandin E2/β-CD produced in Japan; Garlic oil /β-CD produced in Germany, Hungary and the United States; Piroxicam /β-CD produced in Brazil and France; Corticosterol /HP-β-CD produced in Iceland; Chloramphenicol /M-β-CD produced in Japan; Cisapride /HP-β-CD produced in Belgium and so on.

Polyamine-modified β-CD derivatives have been widely used as drug carriers. Bo. Y's research group prepared a series of amine β-CD- artesunate conjugates (Figure 4), in which artesunate (ATS) was covalently coupled to a primary hydroxyl of β-CD through an amino bond. The results showed that the water solubility of ATS-β-CD conjugate was 26-45 times higher than that of free ATS. The cytotoxicity of ATS-β-CD conjugates was evaluated on human colon cancer cell lines HCT116, LOVO, SW480 and HT-29. The results showed that ATS-βCD had low cytotoxicity[45].

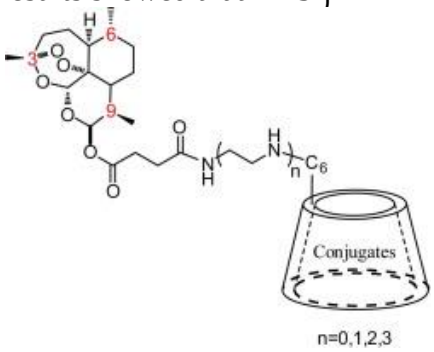

Figure 4: ATS-β-CD bond

In Ren Yufeng's research group, they synthesized tetraethylenepentamine modified β-CD, and included it with oleanolic acid to prepare supramolecular system (Figure 5). The water solubility increased by 2100[46].

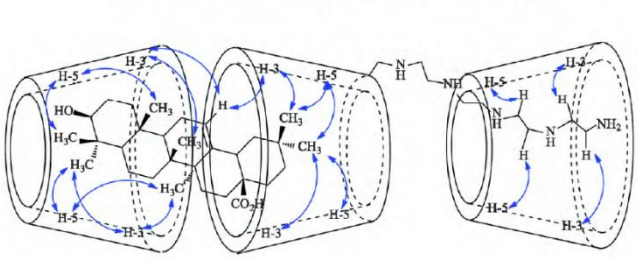

Figure 5: Inclusion mode of β-CD modified by tetraethylenepentamine with oleanolic acid supramolecular system

Our research group[47]prepared three kinds of inclusion compounds of polyamine-modified β-CDs with baicalein (BC) by solution stirring method. The results showed that the antioxidant activity of BC was enhanced after inclusion, and the solubility in water was satisfactory. (Figure 6)

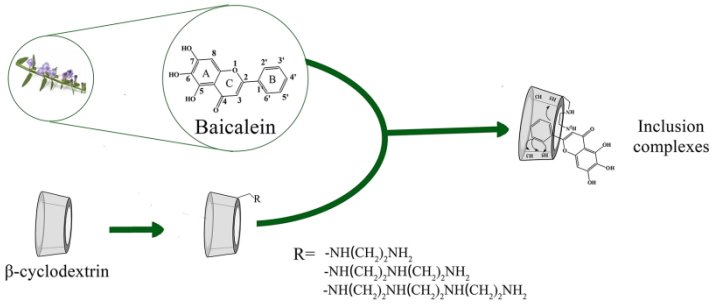

Figure 6: Inclusion complex of polyamine-modified β-CDs with baicalein (BC)

Our research group71) also prepared the inclusion compounds of three flavonoids including taxolL), quercetin (QCT) and morin hydrate (MH) with propanediamine -β-β-CD(DP-β-CD) by saturated aqueous solution method. The water solubility ofL,QCT and MH increased by 70-102 times after forming inclusion compounds with DP-β-CD. In addition, the antioxidant activity of DP-β-CD/L inclusion complex is better thanL. This satisfactory water solubility and high antioxidant activity of DP-β-CD/flavonoids may be useful for their application as herbs or health products. (Figure 7)

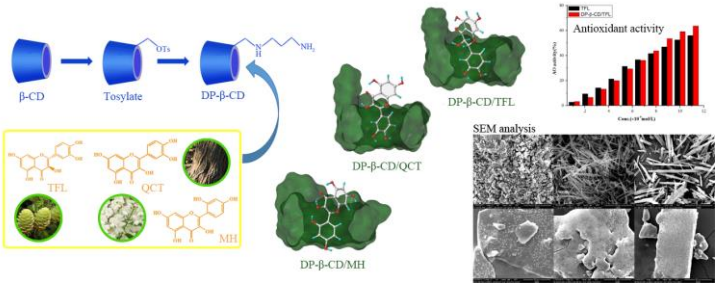

Figure 7: Inclusion compounds of three flavonoids with propanediamine -β-β-CD (DP-β-CD)

3. Molecular assembly research based on β-CD

3.1 The concept of molecular assembly

In recent years, molecular assembly, which is based on molecular recognition and aims at realizing molecular functionalization, has attracted wide attention. Supramolecular assembly is the self-assembly process of spontaneous formation of supramolecular aggregates under equilibrium conditions, which is completed by weak interaction between molecules through non-covalent bonds[1,49-56]. The assembly process and assembly have become important research targets of supramolecular chemistry, and finally supramolecular functional system[57]is formed through molecular assembly. In supramolecular chemistry, the addition and coordination of weak intermolecular interactions, such as hydrogen bond, van der Waals force and hydrophobic interaction, is the prerequisite for realizing molecular assembly, which is completed according to certain directionality and selectivity[58]. There are various kinds of supramolecular self-assemblies in living organisms, which play an important role in the functions of living organisms. This kind of self-assembly usually provides a highly ordered microenvironment and has a special structure. For example, enzymes, biofilms, etc. are typical examples[59-60]that have survived the long-term evolution of living organisms. Therefore, the formation of supramolecular functional systems through molecular self-assembly has attracted more and more chemists' attention and research.

3.2 Polyrotaxane based on β-CD derivatives (quasi-polyrotaxane)

β-CD has a rigid, cylindrical hydrophobic cavity, and can form inclusion complexes with various guest molecules in aqueous solution or solid state, which makes it widely used in supramolecular assembly research as a basic Building Block[62-63]. β-CD-based Polyrotaxane is a supramolecular system made of β-CD molecules penetrating linear molecules and assembled by non-covalent bonds and blocked by blocking agents. The product obtained without blocking or with too small blocking agents is called pseudo-polyrotaxane[64]. Linear macromolecules are usually polystyrene (PS), polyethylene glycol (PEG), polypropylene glycol (PPG), polyethylene imine (PEI), etc., while end-capping agents are some larger molecules.

In 1981, Ogino[65]first reported rotaxane with undecylenediamine as axis and cobalt complex as axis plug by penetration method (as shown in Figure 8). It is found that the length of linear axis has great influence on the synthesis yield of rotaxane, and the highest yield is obtained when diamines containing 12 methylene units and β-CD are used to prepare rotaxane. However, using organic solvent as reaction solvent has great influence on the yield and inclusion rate.

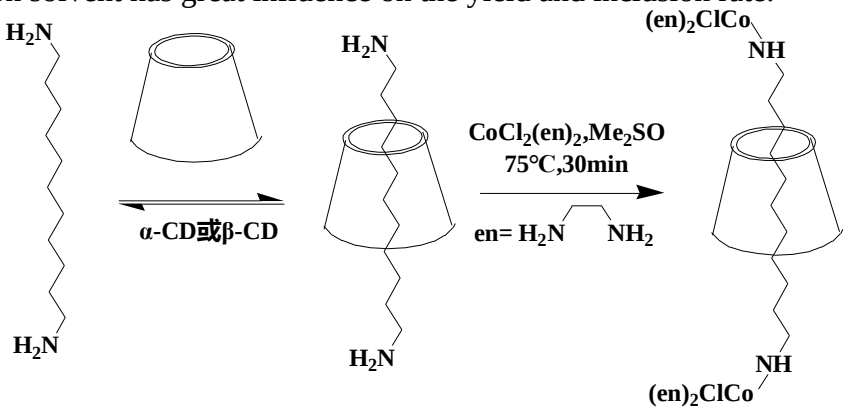

Figure 8: Rotaxane synthesized by Ogino for the first time

Harada et al.[66]from Japan reported for the first time in 1990 that polyethylene glycol (PEG) could be included with α-CD to prepare quasi-polyrotaxane. When the saturated aqueous solution of water-soluble PEG and β-CD was mixed at room temperature, a water-insoluble white precipitate was produced. In the follow-up study, Harada also synthesized PEG-β-CD quasi-polyrotaxane from α-CD and PEG with amine-terminated group, and prepared polyrotaxane[67]with 2,4-dinitrofluorobenzene as end-capping agent (as shown in Figure 9).

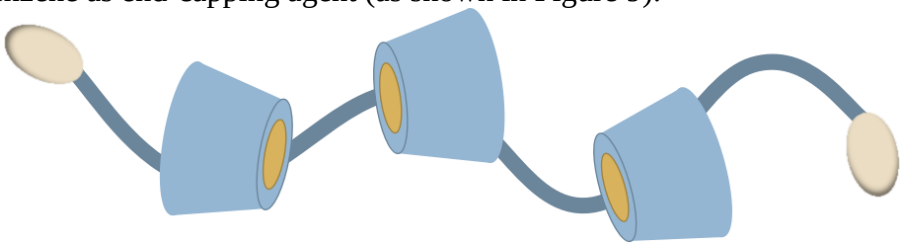

Figure 9: Structure diagram of polyrotaxane

3.3 Application of β-CDS polyrotaxane in biomedical field

In recent years, intelligent drug carriers with different properties and shapes formed by self-assembly of β-CD have emerged continuously. Self-assembled polyrotaxane based on β-CD is a highly functional molecule, which is composed of β-CD or modified β-CD and guest molecules. Because of its water-solubility and less toxic and side effects, it has been applied in the research of

drug controlled release. Yu et al.[68]synthesized β-CD polyrotaxane (PR) with PPG as the axis. Using β-CD-N3 as the end-capping group, the succinate-based taxol derivative (PXT) was linked to PR through hydroxyl groups and hydrophilic spacers on polyrotaxane, which increased the drug loading rate and further accelerated the release of PTX through esterase catalysis. In vitro experiments proved that PR-PTX complex was easily internalized by tumor cells and retained the pharmacological activity of PTX (Figure 10).

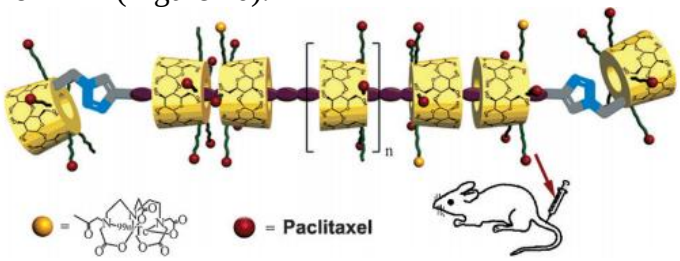

Figure 10: Synthesis and antitumor activity of paclitaxel -β-CD polyrotaxane

Lai Chunli et al. [69] prepared polyrotaxane-camptothecin conjugate by polymerization with β-CD polyrotaxane as carrier, which improved the shortcomings of poor water solubility, low drug loading and low bioavailability of camptothecin. (Figure 11)

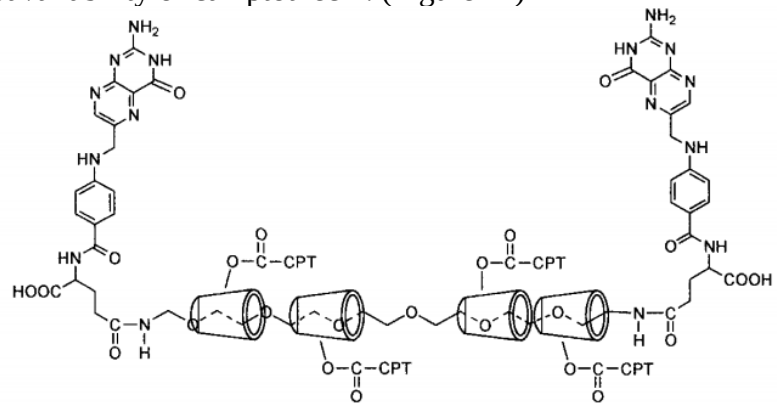

Figure 11: Structure of polyrotaxane-camptothecin conjugate

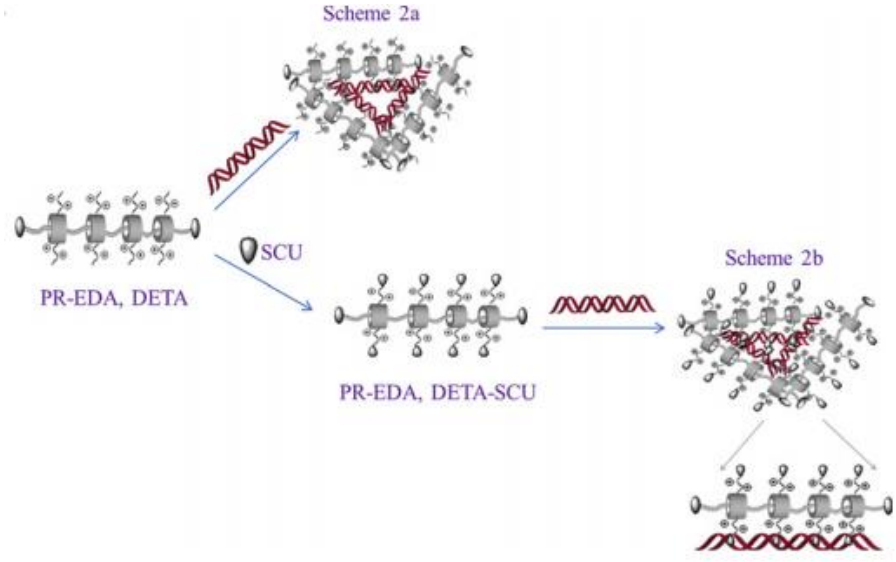

Figure 12: Synthesis and antitumor activity of paclitaxel -β-CD polyrotaxane

Yang et al.[70]designed and prepared two new types of scutellarin grafted cationic polywheel

(PR-EDA-SCU and PR-DETA-SCU), using scu as the extension surface, and combining β-CD molecules of PR-EDA and PR-DETA, PR-EDA -SCU and PR-DETA-SCU were concentrated with satisfactory pDNA. (Figure 12)

4. Conclusion

Cyclodextrins have hydrophobic cavities and hydrophilic surfaces. Therefore, it has unique inclusion properties and can form inclusion complexes with various guest molecules through weak interaction, so as to change the physical and chemical properties of guest molecules At the same time, because of the low toxicity and water solubility of cyclodextrin, the inclusion complex formed by cyclodextrin and hydrophobic small pharmaceutical molecules can be dissolved in water, thus improving the solubility of drugs, increasing the stability of drugs and improving the bioavailability and curative effect of drugs. And many chemical reactions can be carried out in water to make the whole reaction environmentally friendly.

Acknowledgments

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References

[1] Liu Yu. Nanometer Supramolecular Chemistry, Chemistry and Application Publishing Center of Chemical Industry Press, 2004.
[2] Lehn J M. Supramolecular chemidtry--scope and perspectives molecules, supermolecules, and moleculars devices (nobel lecture). Journal of Inclusion Phenomena. 1989. 27:299-308.
[3] Hagbani T A, Nazzal S. Curcumin complexation with cyclodextrins by the autoclave process: method development and characterization of complex formation [J]. International Journal of Pharmaceutics, 2017, 520(1–2):173-180.
[4] Krakowiak K E, Bradshaw J S, Dalley N K, et al. Preparation and cation complexing properties of some macropolycyclic ligands[J]. Journal of Organic Chemistry, 1992, 57(11):3166-3173.
[5] Li Wenlin, Li Meilan. Present situation and progress of supramolecular chemistry [J]. Guangdong Chemical Industry, 2009, 36(9):80-81.
[6] Cram D. The design of molecular hosts, guests, and their complexes [J]. J. Angew. Chem., 1988, 27(8): 1009-1020.
[7] Sigurdsson H, Stefanson E, Gudmundsdoir E, et al. Cyclodextrin formulation of dorzolamide and its distribution in the eye after topical administration[J]. Journal Controlled Release, 2005, 120(1):255-262.
[8] Uekama K. Design and evaluation of cyciodextrin-based drug formulation [J]. Chemical & Pharmaceutical Bulletin, 2004, 52(8):900-915.
[9] Konno A, Misaki M, Toda J, et al. Bitterness reduction of narngin and limonin by β-cyclodextrin[J]. Agricultural and Biological Chemistry, 1986, 46(9):2203-2208.
[10] Tong L H, Hou Zh J, Inoue Y. Molecular recognition by modified cyclodextrins inclusion comlexation of β-cyclodextrin 6-O-monobenzoate with acyclicand cyclic hydrocarbons [J]. Journal of the Chemical Society, Perkin Transactions 2, 1992, 4(7):1253-1257.
[11] Sun Mo. Construction of supramolecular polymer of β-CD and porphyrin and its magnetic resonance imaging study [D]. Nankai University, 2014.
[12] Szejtli JJ. Introduction and general overview of cyclodextrin chemistry [J]. Chemical Reviews, 1998, 98(5): 1743-1754.
[13] Ramos Cabrer P, AlvarezParrilla E, Meijide F, et al. Complexation of Sodium Cholate and Sodium Deoxycholate by β-Cyclodextrin and Derivatives [J]. Langmuir, 1999, 15(17):5489-5495.
[14] Stid J.W., Atwood J.L. Supramolecular Chemistry [M]. Beijing: Chemical Industry Press, 2006.
[15] Zhang Laixin, Hu Xiaobing. New progress in synthesis and application of new supramolecular compounds [J]. Applied Chemical Engineering, 2013, 42(10): 1907-1909.
[16] Kong Rui, Shi Dongjian, Liu Rongjin, et al. Research progress of β-CD supramolecular assembly [J]. Polymer Bulletin, 2012, (12): 36-43.
[17] Breslow R, Dong SD. Biomimetic reactions catalyzed by cyclodextrins and their derivatives[J]. Chemical Reviews,

1998, 98(5):1997-2012.
[18] Szejtli J. Cyclodextrins and their inclusion complexes in the biotechnology and chemical industry. Magyar Kemilusok Lapja, 1990, 45(3-4):98-106.
[19] Nascimento C S Jr, Anconi C P, Dos Santos H F, et al. Theoretical Study of the alpha-cyclodextrin dimer Cyclodextrin Dimer. Journal of Physical Chemistry A 2005, 109(14):3209-3219.
[20] Khan M Z, Chuaqui C A. ChemInform Abstract: Cyclodextrin Chemistry: Synthesis of Cyclodextrin Derivatives, Complexation, and γ-Radiation Effects [J]. Cheminform, 1991, 22(5).
[21] Szejtli J, Cyclolab B H. Chemistry, physical and biological properties of cyclodextrin [J]. Supramolecular Chemistry, 1996, 3:5-40.
[22] Liu Y, Chen G S, Chen Y, et al. Synthesis of Tripeptides as Potent Yersinia Protein Tyrosine Phosphatase Inhibitors [J]. Bioorganic & medicinal chemistry letters, 2005, 15:4037-4042.
[23] Harata K. Structural Aspects of Stereodifferentitation in the Solid State [J]. Chemical Reviews. 1998, 98(3): 1803-1828.
[24] Valerian TS, Kenny BL. Cyclodextrins: introduction [J]. Chemical Reviews, 1998, 98(5): 1741-1742.
[25] Szejtli J. Cyclodextrins in Chemical Technology [M]. Cyclodextrin Technology. Springer Netherlands, 1988: 365-410.
[26] Ivan M. Savic, Ivana M. Savic-Gajic, Vesna D. Nikolic, Enhencemnet of solubility and photostability of rutin by complexation with β-cyclodextrin and (2-hydroxypropyl)-β-cyclodextrin[J]. Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2016, 86(1):1-11.
[27] Brewster M E, Neeskens P, Peeters J. Solubilization of the anti-HIV drug candidate, loviride, using beta- and gamma-cyclodextrin derivatives [J]. European Journal of Pharmaceutical Sciences, 2004: S47-S47.
[28] Zhao Minggang. Synthesis and properties of new ββ-CD derivatives [D]. Shandong: Shandong University, 2007.
[29] Petter R C, Salek J S, Sikorski C T. Cooperative Binding by Aggregated mono-6-(alkylami-no)-β-cyclodextrins[J]. Journal of the American Chemical Society, 1990, 112(10): 3860-3868.
[30] Sun Jing, Zhang Wenzhi, Bai Liming, et al. Preparation of mono -6- oxo-p-toluenesulfonyl -β-β-CD [J]. Journal of Qiqihar University (Natural Science Edition), 2016, 32(3):58-60.
[31] Liu Y, Li X Y, Guo D S, Chi H. Synthesis of L-cystine modified cyclodextrin monomers and dimers with primary-side versus secondary-side and their molecular binding behaviours. Supramolecular Chemistry, 2008, 20(7): 609–617.
[32] Liu Yu, You Changcheng, Zhang Hengyi, Molecular Recognition and Assembly of Supramolecular Chemistry-Synthetic Receptors [M]. Nankai University Press, Tianjin, 2001.
[33] Liu. Y, You C C, Wada T, Inoue Y. Molecular recognition of fluorescent dyes with novel triethylenetetraamine te thered Bis(β-cyclodextrin) and selectivity by Tether Ligation[J]. Tetrahedron Lett. 2000, 41:6869-6873.
[34] Lehn JM. Perspectives in supramolecuar chemistry from molecular recognition towards molecular information processing and self-organization [J]. Angewandte Chemie-International Edition, 1990, 29(5):134-149.
[35] Ke C F, Yang C, Liang W T, et al. Critical stereocontrol by inter-amino distance of supramolecular photocyclodimerization of 2-anthracenecarboxylate mediated by 6-(ω-aminoalkylamin-o)-γ-cyclodextrins[J]. New Journal of Chemistry, 2010, 34(7): 1323-1329.
[36] Liu Y, Chen G S, Chen Y, et al. Inclusion complexes of paclitaxel and oligo(ethylenediamino) bridged bis(β-cyclodextrin)s: solubilization and antitumor activity[J]. Bioorganic & Medicinal Chemistry, 2004, 12(22):5767-5775.
[37] Takenaka Y, Nakashima H, Yoshida N. Fluorescent amino-β-cyclodextrin derivative as a receptor for various types of alcohols having cyclic and macrocyclic rings [J]. Journal of Molecular Structure, 2007, 871(1-3):149-155.
[38] Qi A D, Li L, Yu L. Molecular Binding Ability and Selectivity of Natural α -, β -, γ -Cyclodextrins and Oligo(ethylenediamino) Modified β -Cyclodextrins with Chinese Traditional Medicines[J]. Journal of Inclusion Phenomena & Macrocyclic Chemistry, 2003, 45(1-2): 69-72.
[39] Ramos Cabrer P, AlvarezParrilla E, Meijide F, et al. Complexation of Sodium Cholate and Sodium Deoxycholate by β-Cyclodextrin and Derivatives†[J]. Langmuir, 1999, 15(17).
[40] Ma X, Yang B, Zhao Y, et al. Host–Guest Inclusion System of Scutellarin with Polyamine-β-Cyclodextrin: Preparation, Characterisation, and Anti-Cancer Activity[J]. Australian Journal of Chemistry, 2015, 68(6): 946.
[41] Prabu S, Sivakumar K, Nayaki S K, et al. Host-guest interaction of cytidine in β-cyclodextrin microcavity: Characterization and docking study [J]. Journal of Molecular Liquids, 2016, 219:967-974.
[42] Zhao Q, Chen Y, Sun M, et al. Construction and drug delivery of a fluorescent TPE-bridged cyclodextrin/ hyaluronic acid supramolecular assembly [J]. Rsc Advances, 2016, 6(56):50673-50679.
[43] Hădărugă D I, Hădărugă N G, Bandur G N, et al. Water content of flavonoid/cyclodextrin nanoparticles: Relationship with the structural descriptors of biologically active compounds [J]. Food Chemistry, 2012, 132(4): 1651-1659.
[44] Li Zhiwen. Study on the interaction of several new PPT supramolecular systems with BSA and DNA [D]. Yunnan

Normal University, 2017.
[45] Yang B, Zhao Y L, Yang X, et al. Scutellarin-cyclodextrin conjugates: Synthesis, characterization and anticancer activity [J]. Carbohydrate Polymers, 2013, 92(2): 1308-1314.
[46] Ren Yufeng, Niu Raomei, Wang Zhi, et al. Preparation and characterization of β-CD inclusion compound of oleanolic acid and ursolic acid [J]. Journal of Kunming University of Science and Technology (Natural Science Edition), 2017(3):89-95.
[47] Du J J, Zhao L J, et al. Preparation, characterization, solubilization and antioxidant activity of polyamine modified β-cyclodextrins with baicalein inclusion complexes [J]. Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2018, 47(18):847-858.
[48] Yang S L, Zhao L J, et al. Inclusion complexes of flavonoids with propylenediamine modified β-cyclodextrin: Preparation, characterization and antioxidant [J]. Journal of Molecular Structure, 2019, 1183(3):118-125.
[49] Shuai X, Merdan T, Unger F, Kissel T. Supramolecular gene delivery vectors showing enhanced transgene expression and good biocompatibility [J]. Bioconjugate Chemistry. 2005, 47(18):322-629.
[50] Harada A, Okada M, Kamachi M. Complex formation between poly (oxytrimethylene) and cyclodextrins [J]. Acta Polymerica, 2010, 46(6):453-457.
[51] Shigekawa H, Miyake K, Sumaoka J, et al. The molecular abacus: STM manipulation of cyclodextrin necklace [J]. Journal of the American Chemical Society, 2000, 122(22): 5411-5412.
[52] Harada A, Li J, Kamachi M. Supramolecular Assemblies of Cyclodextrins with Polymers and Preparation of Polyrotaxanes [M]. Ordering in Macromolecular Systems, 1994.
[53] Miyauchi M, Harada A. Construction of supramolecular polymers with alternating α-, β-Cyclodextrin units using conformational change induced by competitive guests [J]. Journal of the American Chemical Society, 2004, 126(37): 11418-11419.
[54] Okada M, Harada A. Poly (polyrotaxane): photoreactions of 9-anthracene-capped polyrotaxane [J]. Macromolecules, 2003, 36(26): 9701-9703.
[55] Liu Y, Liang P, Chen Y, et al. Interlocked Bis(polyrotaxane) of Cyclodextrin−Porphyrin Systems Mediated by Fullerenes [J]. Macromolecules, 2005, 38(22): 9095-9099.
[56] Slowing I I, Vivero-Escoto J L, Wu C W, et al. Mesoporous silica nanoparticles as controlled release drug delivery and gene transfection carriers [J]. Advanced Drug Delivery Reviews, 2008, 60(11):1278-1288.
[57] Brieuc G, Sophie M, Vincent L, Jean-jacques R. How to modulate the chemical structure of polyoxazolines by appropriate functionalization [J]. Macromolecular Rapid Communications, 2012, 33(19):1600-1612.
[58] Dam HH, Caruso F. Modular click assembly of degradable capsules using polyrotaxanes. [J]. Acs Nano, 2012, 6(6): 4686.
[59] Allen TM, Cullis PR. Liposomal drug delivery systems: From concept to clinical applications[J]. Advanced Drug Delivery Reviews, 2013, 65(1): 36-48.
[60] Liu Y, Yu L, Chen Y, et al. Construction and DNA Condensation of Cyclodextrin-Based Polypseudorotaxanes with Anthryl Grafts [J]. Journal of the American Chemical Society, 2007, 129(35): 10656-10657.
[61] Li J, Ni X, Leong KW. Injectable drug-delivery systems based on supramolecular hydrogels formed by poly (ethylene oxide) s and α-cyclodextrin[J]. Journal of Biomedical Materials Research Part A, 2010, 65(2): 196-212.
[62] Li J, Li X, Ni X, et al. Self-assembled supramolecular hydrogels formed by biodegradable PEO–PHB–PEO triblock copolymers and α-cyclodextrin[J]. Biomaterials, 2006, 27(22): 4132-4140.
[63] Wang J, Li L, Zhu Y, et al. Hydrogels assembled by inclusion complexation of poly (ethylene glycol) with alpha-cyclodextrin [J]. Asia-Pacific Journal of Chemical Engineering, 2009, 4(5): 544-550.
[64] Li X, Xiao J, Wang X, et al. pH-responsive pseudorotaxane between comblike PEO-grafted triblock polymer and α-cyclodextrin [J]. Colloid and Polymer Science, 2014, 292(12): 3243-3249.
[65] Zhou Z, Li X, Chen X, et al. Synthesis of ionic liquids functionalized β-cyclodextrin-bonded chiral stationary phases and their applications in high-performance liquid chromatography.[J]. Analytica Chimica Acta, 2010, 678(2):208-214.
[66] Harada A, Li J, Kamachi M. Double-stranded inclusion complexes of cyclodextrin threaded onpoly(ethylene glycol) [J]. Nature, 1990, 370(6485): 126-128.
[67] Harada A, Li J, Kamachi M. Synthesis of a tubular polymer from threaded cyclodextrins[J]. Nature, 1993, 364(6437): 516-518.
[68] Yu S, Zhang Y, Wang X, et al. Synthesis of paclitaxel-conjugated β-cyclodextrin polyrotaxane and its antitumor activity [J]. Angewandte Chemie International Edition, 2013, 52(28): 7272-7277.
[69] Lai Chunli, Lai Le, Zhao Jianbin, et al. Preparation of polyrotaxane-camptothecin conjugate and its antitumor effect [J]. Journal of Pharmacy, 2010(7): 920-925.
[70] Qin Q, Ma X, Liao X, et al. Scutellarin-graft cationic β-cyclodextrin-polyrotaxane: Synthesis, characterization and DNA condensation [J]. Materials Science and Engineering: C, 2017, 129(71): 1028-1036.