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CYCLODEXTRINS AND POLYMERS TOWARDS APPLICATIONS

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Miscellaneous possibilities are known to bring cyclodextrins and polymers together. The polymerization of cyclodextrins leads to polymeric materials that can be used for several applications. The formation of polyrotaxanes due to threading of cyclodextrin molecules onto a polymeric backbone or side chains alters the behaviour of polymers. The permanent fixation of cyclodextrins on the surface of different polymeric materials enables the creation of textile materials with new properties.

Известны разнообразные возможности связывания циклодекстринов и полимеров. Полимеризация циклодекстринов ведет к образованию полимерных материалов, которые могут быть использованы для нескольких целей. Образование полиротаксанов, благодаря волокнистости молекул циклодекстрина на полимерной основе или на боковых цепях, изменяет поведение полимеров. Постоянная фиксация циклодекстринов на поверхности разных полимерных материалов дает возможность создавать текстильные материалы с новыми свойствами.

Հայտնի են ցիկլոդեքստրինների և պոլիմերների կապակցման բազմազան հնարավորություններ: Ցիկլոդեքստրինների պոլիմերիզացիան առաջ է բերում պոլիմերային նյութեր, որոնք կարող են օգտագործվել որոշ նպատակներով: Պոլիռոտաքսանների առաջացումը, շնորհիվ ցիկլոդեքստրինի մոլեկուլի թելատվության պոլիմերային հիմքի կամ կողքային շղթայի վրա, փոխում է պոլիմերների վարքագիծը: Ցիկլոդեքստրինների մշտական ֆիքսացիան տարբեր պոլիմերային նյութերի մակերեսին թույլ է տալիս ստեղծել նոր առանձնահատկություններով մանածագործական նյութեր:

Introduction

The degradation of starch results in formation of cyclodextrins, a process that was presented in the literature more than 100 years ago [1,2]. The structure of the degradation products was determined by Freudenberg [3,4]. Cramer was the first who realized the formation of inclusion compounds in solution with cyclodextrins [5]. At the beginning of the 50th this idea was rather revolutionary. In a lecture given at the First International Symposium on Cyclodextrins Cramer described this state of affairs as follows: "A whole maffia of physicochemists was united against the young greenhorn from Heidelberg. I believe the concept was finally successful." [6].

The formation of complexes with cyclodextrins has been studied with increasing interest since that time [7]. Beside the complex formation, the chemical modification of cyclodextrins also received much interest. Thus a large number of substituted cyclodextrin molecules are already known [8].

Polymeric cyclodextrins. Chemical substances with two or more covalently bounded cyclodextrins are described as polymers. They are synthesized from the reaction of cyclodextrins with bifunctional or multifunctional substances. The synthesis of different polymers with cyclodextrins has already been reviewed in detail [7,8]. Some industrial applications of cyclodextrin containing polymers have also been described [7,9].

The synthesis of cyclodextrin polymers is relatively easy. The hydroxyl groups of the cyclodextrins are located at the upper and lower rim of the torus, see Figure 1. Mainly the reaction of cyclodextrins with epichlorhydrin has been studied.

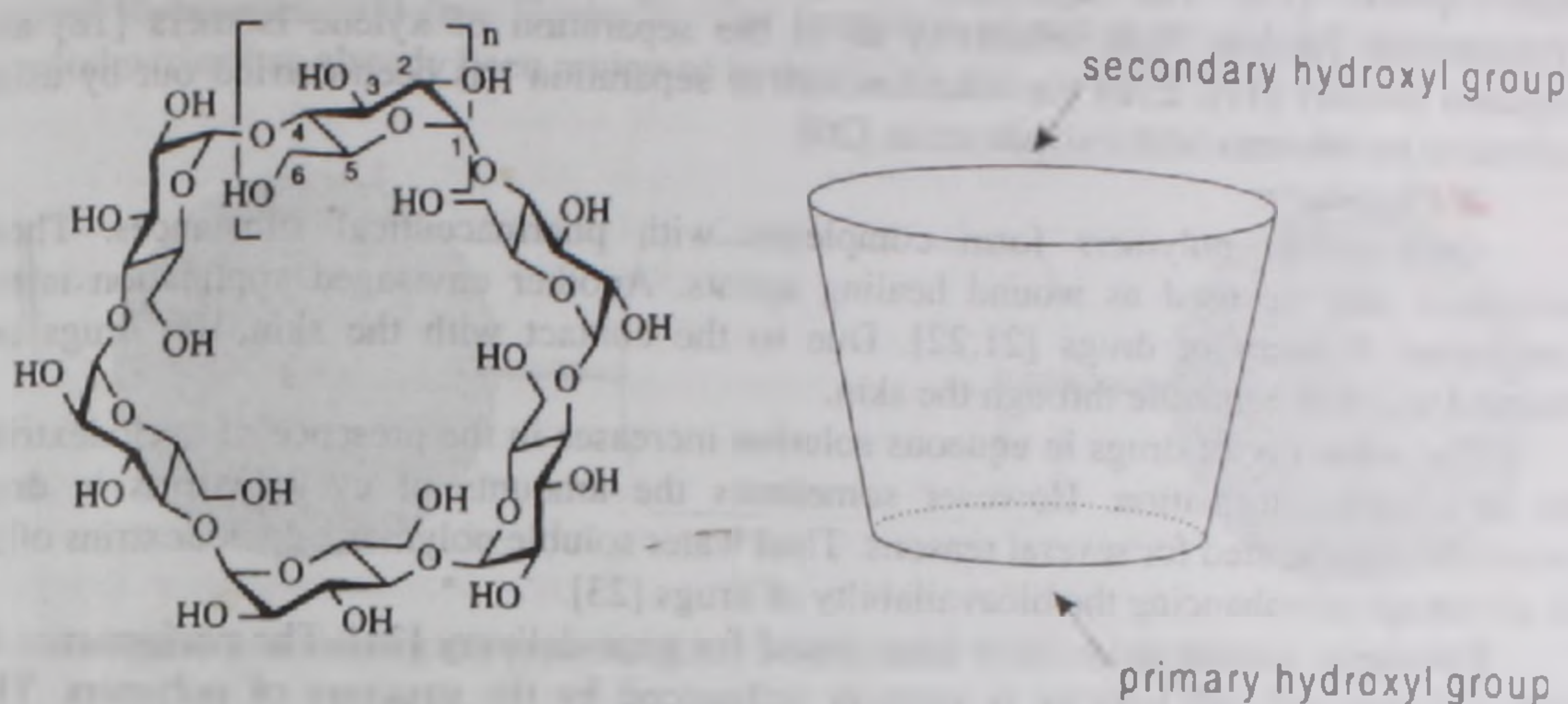

Figure 1. Chemical structure of cyclodextrins (α-CD: n=1, β-CD: n=2; γ-CD: n=3) and the position of the hydroxyl groups.

The behaviour of cyclodextrin polymers varies extremely. They can be arranged in the following manner:

soluble in water,
unsoluble but strong swelling in water,
weak swelling,
solid (foils, fibre, foam).

Even in the cavities of the polymeric cyclodextrins other organic substances are included. In solution the stability of the complexes formed with cyclodextrins in polymers are higher as with the monomeric cyclodextrin. This is due to the simultaneous interactions of at least two cyclodextrin molecules of the polymer with the guest molecule [10,11]. The complex formation between solid cyclodextrin polymers and molecules in solution results in more stable complexes compared with the reaction of cyclodextrins in solution. This effect is caused by the reaction kinetic. The rates of complex formation in homogeneous and heterogeneous systems are similar. However, the kinetics of the dissociation reaction in the heterogeneous system is several orders of magnitude smaller as in solution [12].

Polymers with cyclodextrins are already used in some applications.

1. Analytical chemistry:

Differences of the complex stability of cyclodextrins with organic substances are used for their chromatographic separation. The polymeric cyclodextrins are employed as stationary phase in liquid chromatography [13,14]. The thermal stability of cyclodextrin resins is high enough to allow them acting as stationary phase in gas chromatography [14,15].

Immobilized cyclodextrins are used in affinity chromatography. Using a stationary phase of β-cyclodextrin tetradecasulfate polymer mixed with Cu-Sepharose the purification of fibroblast growth factor has been performed [16].

A significant improvement of separation and catalytic ability of membrane has been achieved by the introduction of cyclodextrin oligomer in the polymeric membrane. In this respect, the preparation of a poly(vinyl alcohol) membrane containing β-cyclodextrin oligomer and its pervaporation characteristics for water-alcohol mixture separation have been reported [17]. The separation of isomers by polymeric membranes containing cyclodextrins features high selectivity as in the separation of xylene isomers [18] and propanol isomers [19]. Even the enantioselective separation has been carried out by using polymeric membranes with cyclodextrins [20].

2. Pharmacy:

Cyclodextrin polymers form complexes with pharmaceutical substances. These complexes may be used as wound healing agents. Another envisaged application is the transdermal delivery of drugs [21,22]. Due to the contact with the skin, the drugs are liberated and will penetrate through the skin.

The solubility of drugs in aqueous solution increases in the presence of cyclodextrins due to complex formation. However sometimes the amounts of cyclodextrins in drug formulation are limited for several reasons. Thus water soluble polymeric cyclodextrins offer the advantage of enhancing the bioavailabilty of drugs [23].

Polymeric cyclodextrins have been tested for gene delivery [24]. The performance in DNA delivery and cell toxicity is strongly influenced by the structure of polymers. The incorporation of β-cyclodextrin in the polymer backbone decreases significantly the toxicity of polymers.

3. Food Science:

Since insoluble cyclodextrin polymers can easily be removed from food, they are not really food additives. Insoluble cyclodextrin polymers are used to remove the bitter component of orange and grapefruit juices [25]. The browning of food products is caused by the enzymatic oxidation (e.g., chlorogenic acid). In order to prevent this undesired reaction, the chlorogenic acid may be removed from juices using polymeric cyclodextrins [26].

4. Environmental:

The formation of dye complexes with cyclodextrins is well known [27]. Using insoluble polymer resins with cyclodextrins makes possible the removal of dye molecules from aqueous solution [28]. The polymeric cyclodextrins form complexes with different types of dyes. Consequently, such a method has been proposed for the decolorization of waste water from the dye house.

The removal of other organic compounds from aqueous solution is possible too. Thus aromatic substances like benzene or phenol [29], different substituted chlorophenols and nitrophenol [30] or even trichloroethylene [31] are complexed by insoluble cyclodextrin polymers. Even the removal of the polar urea from aqueous solution has been presented in the literature [32].

Nonionic surfactants like alkylphenol ethoxylates have been employed in many industrial processes. Their biodegradation leads to the formation of several biorefractory metabilites. Some of them are acute toxic or endocrinic [33]. The removal of alkylphenol ethoxylates from aqueous solution is difficult. Polymeric cyclodextrins offer simple means for complexation of nonionic surfactants. The polymeric material can easily be regenerated by extraction with alcohols [34].

Rotaxanes and polyrotaxanes with cyclodextrins. Another way to synthesize polymers containing cyclodextrins was accomplished much later. The formation of a complex between α-cyclodextrin and polyethyleneglycol bisamines followed by a reaction of the amino end groups with 2,4-dinitrofluorobenzene leads to polymeric materials with threaded cyclodextrin molecules [35,36]. The cyclodextrins are arranged like pearls on a string formed by the polymer chain. These cyclodextrins are unable to thread from the polymer chain although they are not fixed by chemical bonds. According to Schill these molecules formed from an axis and a wheel held together without any chemical bonds are called **Rotaxanes** [37] (see Figure 2). The formation of rotaxanes and polyrotaxanes with cyclodextrins has already been reviewed in detail [38-41].

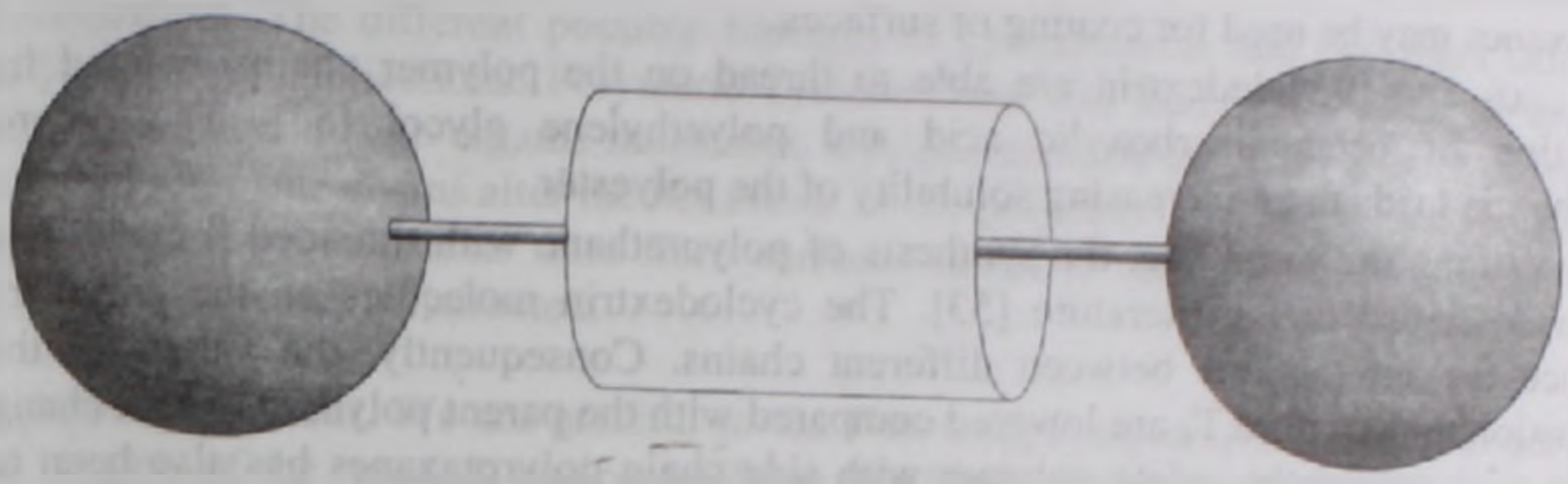

Figure 2. Schematically presentation of a rotaxane.

Mixing polyethylene glycols with α-cyclodextrin already results in the precipitation of the corresponding complexes [42]. β-Cyclodextrin does not form insoluble complexes with polyethylene glycols [43]. However, a complex formation takes place in solution [44]. Polypropylene glycols form solid complexes with β-cyclodextrin [45].

Using α-cyclodextrin polyrotaxenes with polyethylene glycol the cyclodextrin molecules can be crosslinked using epichlorohydrin. After dethreading from the polyethylene glycol chain pure cyclodextrin tubes are obtained [46]. Their schematic structure is given in Figure 3.

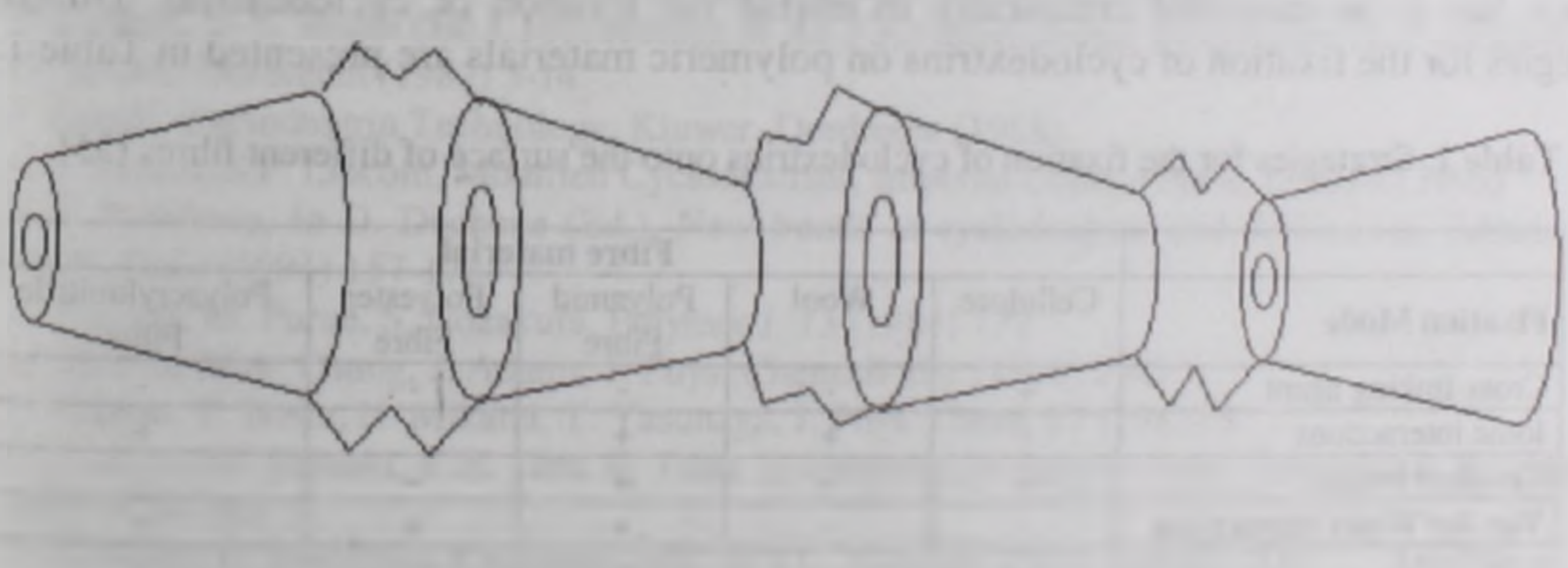

Figure 3. Schematic structure of cyclodextrin tubes.

These tubes may be considered as a new class of cyclodextrin polymers. These cyclodextrin tubes are expected to form complexes. Only recently, the reactions between the tubes from α-cyclodextrin and alkyl sulfonates have thoroughly been studied [47]. The stability of the complexes formed depends upon the number of the methylene groups of the alkyl chain.

In general. the formation of two different types of polymeric rotaxanes with cyclodextrins are possible. The cyclodextrins are located on the polymer main chain [48] or in side chains [49]. The presence of threaded cyclodextrin molecules changes the physical behaviour of the polymeric material.

Thus polyamide rotaxanes obtained by solid state polycondensation of α-cyclodextrin complexes with different amino acids are soluble in water [50,51]. After dissolution of these polyrotaxanes in few cases a slow formation of a precipitate is observed depending on the chemical structure of the amino acids. Bulky substituents at the amino acids prevent the cyclodextrin molecules from dethreading. Due to their solubility in water these polyamid rotaxanes may be used for coating of surfaces.

α- and β-cyclodextrin are able to thread on the polymer chain obtained from the reaction of octanedicarboxylic acid and polyethylene glycol [52]. The polyrotaxane formation leads to an increasing solubility of the polyester.

Along the same line, the synthesis of polyurethane with threaded β-cyclodextrin has been described in the literature [53]. The cyclodextrin molecules on the polymer chains reduce the interactions between different chains. Consequently, the values of the glass transition temperature T_g are lowered compared with the parent polyurethane. A change in T_g value of a polymethacrylate polymer with side chain polyrotaxanes has also been reported [54]. The presence of the threaded cyclodextrin molecules reduces the mobility of the polymer segments.

The threading of cyclodextrins onto polymers leads to new polymeric materials with almost unknown properties. Though the preparation of these polymers is relatively easy, there is no information on the behaviour of fibres made out of these polymers.

Surface modification of fibres with cyclodextrins. A further possibility to obtain polymers with cyclodextrins is their fixation on the surface of a polymeric material like fibres or fabrics. Without any chemical modification, cyclodextrins are only bounded to cellulosic materials using epichlorhydrin [21] or other bifunctional reactants. In the case of all other synthetic polymers, either cyclodextrin derivatives have to be used or the fibre surface has to be modified chemically to enable the fixation of cyclodextrins. Different strategies for the fixation of cyclodextrins on polymeric materials are presented in Table 1.

Table 1. Strategies for the fixation of cyclodextrins onto the surface of different fibres [55].

	Fibre material				
Fixation Mode	Cellulose	Wool	Polyamid Fibre	Polyester Fibre	Polyacrylonitrile Fibre
Cross-linking agent	+	-	-	-	-
Ionic interactions	-	+	+	-	+
Covalent bonds	+	+	+	-	-
Van der Waals interactions	-	-	+	+	+

A cyclodextrin derivative with a reactive group (e.g., the monochlorotriazinyl group) is able to react with the hydroxyl groups of cellulosic fibres like a reactive dye [56, 57]. Permanent fixation on fibres made from polyester is only possible with cyclodextrin derivatives with long alkyl chains or other hydrophobic groups. Comparable with disperse dyeing, the hydrophobic part of the substituted cyclodextrins migrates into the fibre above the glass transition temperature. The polar cyclodextrin molecules remain on top of the fibre surface [58]. After graft polymerization of glycidyl methacrylate onto polypropylene fabrics α-, β- and γ-cyclodextrin are coupled with the epoxide group [59,60].

With cyclodextrins fixed onto the fibre surfaces, such textile materials get new properties. As for instance the comfort of clothing increases. The organic components of sweat are complexed and therefore the possibility of body odour development is reduced. The chemical analysis of sweat components can also be used for medical applications. The identification of organic compounds from patients enables new ways in medical diagnosis. Various aspects of textile materials permanently finished with cyclodextrins have been reviewed very recently [61].

Conclusions. The different possible linkages of cyclodextrins and polymers offer a large varity of new applications. Polymeric cyclodextrins will mainly be used as strong complex forming agents with organic molecules. Cyclodextrins threaded on a main polymer chain or in polymer side chains alter the behaviour of the polymers compared with polymers. The attachment of cyclodextrins onto fibre surfaces modifies only the surface area. The polymer properties remain unaffected.

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