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Exploring multifaceted solicitation of cyclodextrins: An overview

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Abstract
Cyclodextrins are a type of cyclic oligosaccharide produced by an enzymatic starch breakdown. They are extraordinary macrocyclic molecules that have led the way for significant theoretical and practical advancements in chemistry, biology, biochemistry, health research, and agriculture. Their molecular structure comprises of a hydrophobic cavity that can accommodate other molecules to form inclusion complexes through host-guest interactions. As a supplementary dyeing agent and a matrix for dye adsorption, CD serves as a finishing agent until chemical changes are applied, which is investigated in this review. These adaptable supramolecular hosts have grabbed much attention from scientists who want to learn more about them. Cyclodextrins are used in various streams like cosmetics, food and nutrition, textile and chemical industries, and so on due to their ability to create host-guest type inclusion complexes.

Keywords: cyclodextrins, inclusion complex, host and guest molecules, applications, dyeing, bioavailability

Introduction

When cyclic oligosaccharides are joined with six, seven, or eight glucopyranose units linked by-α-(1,4) bonds, cyclodextrin forms. Cycloamyloses, cyclomaltoses, and Schrodinger dextrins are other names for them [1, 2]. They are formed via an intramolecular transglycosylation process resulting from starch degradation by the enzyme cyclodextrin glucan otransferase (CGTase) [3, 4, 5, 6]. Cramer investigated cyclodextrins in 1954. They are torus-shaped cyclic oligosaccharides of six to eight D-glucose units (α =6, β =7, ϒ =8). The carbon atoms C1 and C4 are covalently bonded in the D-glucose units. Cyclodextrins have the potential to act as organic host molecules. One or two guest molecules occupy the interior cavity. Suitable guest molecules, on the other hand, can be employed to thread one, two, or hundreds of cyclodextrin rings. The medication and the cyclodextrin molecule usually have a 1:1 complexation ratio, but 1:2 or 2:1 complexation ratios have also been observed [7]. As the water molecules increases in the surrounding environment causes, such complexes dissociate [8]. Most people utilize it daily. Food, personal care, biotechnology, radiography, agro chemistry, packaging, the textile sector, nanotechnology, and soil and water treatment are all currently impacted. Furthermore, CDs have several distinguishing qualities, including high biodegradability, biocompatibility, and FDA approval, making them both human and environmentally friendly [9, 10, 11]. As a result, this paper provides an overview of the numerous applications of cyclodextrins.

Basic characteristics of cyclodextrins

The three forms of cyclodextrins are α -Cyclodextrin, β -Cyclodextrin, and ϒ–cyclodextrin. It is also known as first-generation or parentcyclodextrins. It is the most extensively accessible, affordable, and practical.Depending on the amounts of cyclodextrin and guest components, it crystallizes into either channel structures or cage structures, the two primary forms of crystal packing.Cyclodextrin derivatives are obtainedby aminations, esterifications, and etherifications of cyclodextrins' primary and secondary hydroxyl groups [12, 13, 14]. The solubility of cyclodextrin derivatives varies from their parent cyclodextrins depending on the substituent. Each derivative has a unique hydrophobic cavity volume that can affect the guest molecules' chemical activity and improve solubility or stability against oxygen or light [15]. Cyclodextrins can be used as a building block to create supramolecular complexes. Their capacity to form inclusion complexes with organic host molecules suggests that they could be used to create supramolecular threads. Catenanes, rotaxanes, polyrotaxanes, and tubes are molecular architectures that can be built this way. Such a building block, which cannot be made by other means, can be used to separate complex molecules and enantiomers, for example.Figure 1 shows the chemical structures of cyclodextrins and their molecular diameters. The cyclodextrins are made up of a torus-like macrocyclic ring with hydrophobic cavities ranging in size from 0.5 to 0.85 nm. [16]. Because of their steric orientation, the individual glucose units' polar–OH groups are on the cylinder's exterior. Because of the secondary C-H bonds, the exterior of the cylinder is hydrophilic, whereas the inside is non-polar and consequently hydrophobic [17, 18]. No harmful symptoms were seen when cyclodextrins were used in textile manufacturing processes.

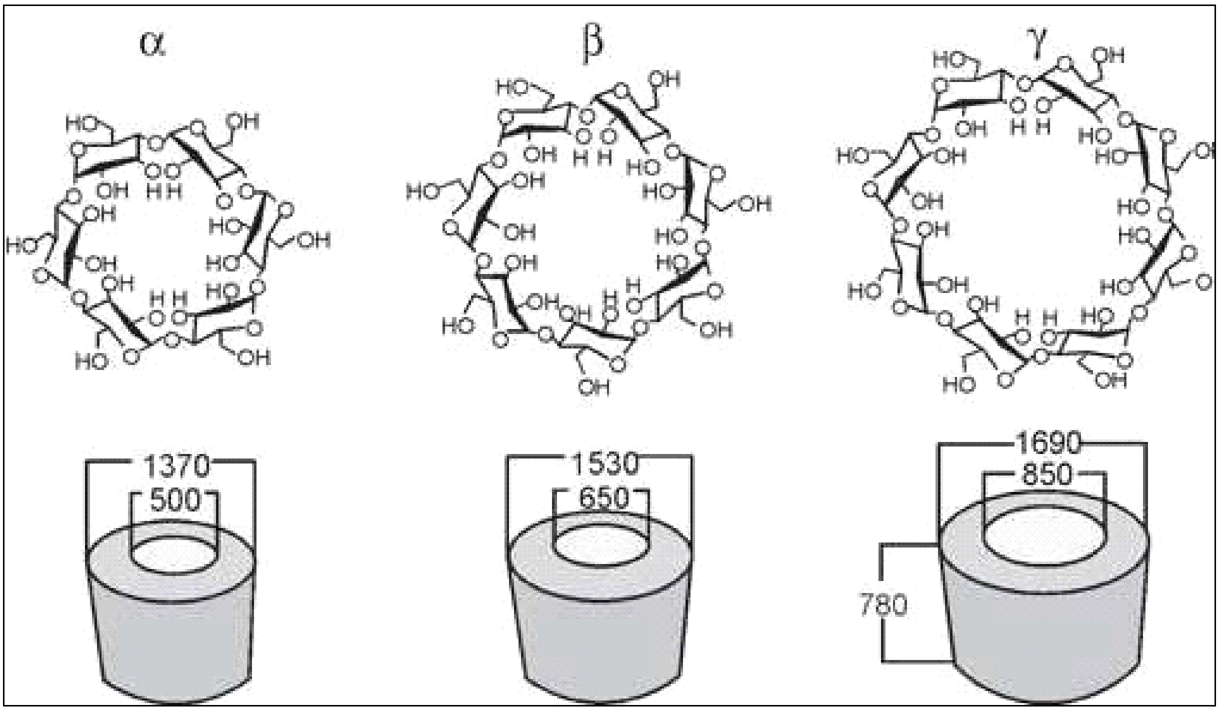

Fig 1: Chemical structures of cyclodextrins and their dimensions in pm

Inclusion compound (IC) formation property of Cyclodextrin

Cyclodextrin's inclusion compound (IC) comprises a torus-like macrocyclic ring with hydrophobic voids that form a complex with organic molecules. Alpha cyclodextrin (α -CD) has a low complexation efficiency; beta-cyclodextrin (β -CD) has an excellent complexation efficiency, and its complexes have minimal water solubility; and gamma-cyclodextrin (ϒ- CD) has a lower complexation efficiency than beta-cyclodextrin (β -CD). The hydrophobic component of the guest molecule is positioned on the inclusion complex's outer surface so that maximal contact with the non-polar cavity is achievable. The geometric geometry of the molecule, rather than chemical interactions, influences the ability of Cyclodextrin to form inclusion complexes. Two essential elements affect Cyclodextrin's capacity to assemble an inclusion complex with a visitor molecule. The size of the Cyclodextrin concerning a few significant functional groups inside the guest molecule determines the first effect, which is steric [19]. If the visitor is the incorrect size, the cyclodextrin chamber will not accommodate them appropriately.The second crucial element is how the system's many components interact at the thermodynamic level (Cyclodextrin, guest, solvent).

A positive net energetic driving force must pull the guest into the Cyclodextrin for a complex to form. As a result of these dimensions, Cyclodextrin typically has room for both larger molecules like macrocycles and steroids and low molecular weight molecules or substances with aliphatic side chains [20, 21, 22]. Molecules significantly longer or more significant than the cavity can form an inclusion complex if a particular group or side chain is entrapped in the hole. A 1:1 combination between Cyclodextrin and Ibuprofen, for example, could include. Nicotine creates a compound with beta-cyclodextrin. This feature can be used in cigarette filters to filter out the majority of the nicotine and tar.Allicin, a component of garlic with antibacterial properties, forms stable compounds with cyclodextrins. Between cyclodextrin and nitro-glycerine, an explosive-proof crystalline compound forms. Water molecules are displaced from the hydrated hydrophobic cavity by the less polar guest molecules, resulting in the inclusion of guest molecules in Cyclodextrin. This feature is critical in the application of Cyclodextrin in odor-free textile finishes. The organic components of sweat are complexed by the fixed cyclodextrins when they come into direct contact with the skin. Under these conditions, enzymatic breakdown of sweat components is impossible; hence, no disagreeable odor develops, reducing odor emission [23]. Because cyclodextrin complexes of scents and perfumes are stable over time, they can be used in washing powder and other products for cleaning and caring for textiles to keep them smelling fresh. [24]. For technological and geotextile developments, the complexation of fungicidal and bactericidal chemicals into cyclodextrins fixed to fibers may be significant. The growth of fungi in the microscopic cavities of the fibers induced by water penetration is inhibited after the modification process of these textiles.

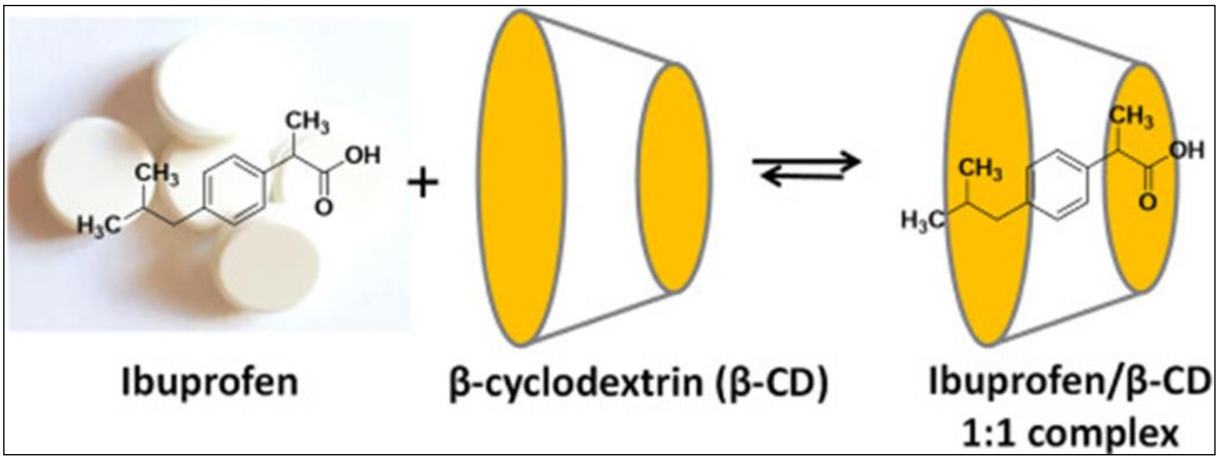

Fig 2: Structure of cyclodextrins and development of inclusion complex

Applications for cyclodextrins in various contexts

Since Cyclodextrin surrounds each guest molecule separately, each guest molecule seems to be micro-encapsulated under a microscope. (derivative). This can result in beneficial modifications in the guest molecules' chemical and physical properties.

- Oxygen- and light-sensitive CD molecules are stabilized
- Modification of the visiting molecules' reactivity in terms of chemicals
- Increased solubility of compounds
- Protection against microbial degradation
- Cyclodextrins' catalytic activity with guest molecules

Because of these characteristics, cyclodextrins and their derivatives are suitable for application in analytical chemistry, food, medicines, agriculture, and toilet paper [25]. The capacity of CDs to form inclusion complexes with a broad range of chemicals makes them useful for various applications. The numerous uses of CDs are compiled in Figure 3.

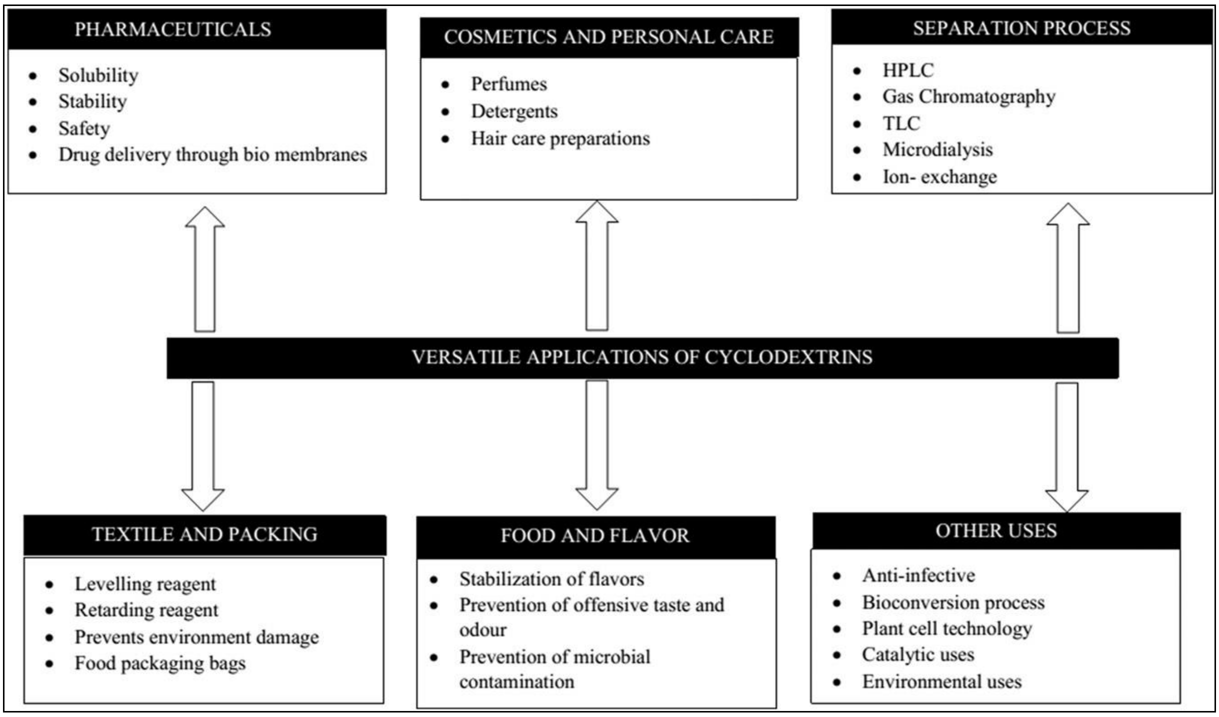

Fig 3: Versatile applications of cyclodextrins.

CDs are essential to the development and processing of textiles. They have a wide range of uses and great potential, and they offer right away chances to make eco-friendly products and textiles.

With dyeing, finishing, and water treatment being the most frequently used in the textile sector, cyclodextrins can be employed in a wide range of applications, including spinning [26], pre-treatment, dyeing [27], finishing, and color removal.

1. Dyeing Process

As a dyeing aid, cyclodextrins can combine with the dye [28, 29] or modify the surface chemically [30] during the dyeing process. With textile dyes, CDs can create a variety of inclusion complexes (Table 1), which change their properties and immediately affect dyeing quality. Cyclodextrins can therefore be employed as auxiliary materials in the dyeing process.

Table 1: Examples include using coloring CDs as a chemical modifier and a textile assist.

Utilization of cyclodextrins	Fibre	Dye
Auxiliary agent	Polyester	Disperse,
		Synthetic
		Disperse Orange 30, Disperse Blue 79,
		Disperse Red 167,
	Polyamide 6	Disperse Red 60
		Synthetic
		Disperse
	Nylon, polyester, and cotton	Synthetic, reactive, and dispersed dye
	Cellulose Acetate	Azodisperse
	Polyacrylic	Basic Blue 4
	Cotton	Direct
	Wool	Natural (Bixa Orellana)
Chemical modification	Polyester	Pigment inks carbon black, magenta, Yellow and cyan
		Disperse Red 60, Disperse Yellow, Disperse Blue 56, Disperse Red 343
	Cellulose Acetate	Disperse Red 60 and 82
	Vinyl on fiber	Reactive Red 2
	Cotton	Acid
	Cotton and cotton/polyester	Basic Red14, Basic Blue3, Basic Yellow 24and13

1.1 Cyclodextrin as an Adjunct Dyeing Agent

The textile industry may accept if innovative auxiliaries are utilized in low quantities, are biodegradable, and do not degrade effluent quality. CDs are biodegradable and improve the biodegradability of several hazardous organic compounds [31, 32]. They also do not cause difficulties in textile effluents. They are used because they combine with dyes to generate compounds that can enhance washing processes and color consistency [33]. On the other hand, Cyclodextrin's ability to function as an auxiliary substance depends on the formation of the CD: dye complex. If it is not created, the dyeing quality will not improve. The usage of cyclodextrins can aid in the resolution of these dyeing issues.

1.2 Dyeing Chemical Modification

Cyclodextrins are polymers that can elicit this chemical modification when incorporated into a fiber [34, 35]. Depending on the procedures used after alteration, this inclusion may be seen as a finishing step or a pre-treatment for dying. The cellulose acetate cloth (38.5 percent acetyl) was treated with monochlorotriazinyl—Cyclodextrin (MCT— CD) to increase its dye capacity as part of the padding procedure by Raslan *et al*. [36] to enhance the dyeing process.As a result, dyeing at lower temperatures allowed scientists to achieve enhanced dye diffusion into the fiber and improved color intensity.

CDs with personal care, toiletry, and cosmetic products

Recent research in cosmetic preparations has shown that CDs can effectively prevent the vaporization of perfumes, air fresheners, and detergents by obtaining controlled fragrance release from the presence of complicated ingredients. The key benefits of CDs in this context are stability, odor control, and process optimization by converting a liquid in a gradient to a solid state (Del Valle, 2004). The following is a list of CD's primary roles in cosmetic preparations.

Table 2: Allegations of cyclodextrins in cosmetics recently.

Drugs	Cyclodextrin used	Work done	Conclusion
Lemon grass volatile oil	β –CD and HP- β -CD	The formation of microparticles	Improvement in efficacy
Octyl p-methoxy cinnamate (OMC)	β –CD	Preparations for using sunscreen	The lipo/OMC system proved to be the most effective releasing method.
Phenylenediamine isomers (PDI)	β –CD	Detection of PDI in hair dyes	A good approach was devised.

1. Oxidation and light protection
Cosmetics are shielded from oxidation and light damage when a CD is present. Pure skin oil does not change whether exposed to light or oxygen for a month.If not, the oil's terpenes will generate the skin irritant p-cymene when they combine with oxygen and light. [37, 38]. Because of the CD complexation, skin oil is resistant to light and oxygen. As a result, the risk of undesirable chemicals being produced is eliminated. Furthermore, skin-based oil's antibacterial and anti-inflammatory characteristics do not change after the complex is formed.

2. Preventing evaporation losses
CD complexation helps to keep volatile chemicals stable by reducing their evaporation. Powders or liquid formulations can be used to include the complexes. Perfume compounds in solid form are now being used in perfumes. The use of these suspensions on the skin provides the requirement for a long-lasting effect by allowing the odors to depart gradually.

3. Removal of noxious odors
CD powders are used in hair care preparations and for smell control in things like diapers, menstrual products, and paper towels to lessen the volatility of pungent mercaptans. CDs are a significant component in dishwashing and laundry detergents, as they disguise odors in laundered things (DelValle, 2004). Dihydroxyacetone has an unpleasant smell that is difficult to cover up with perfumes. CD complexation decreases this smell. It functions as a tanning agent. A more uniform tan is produced by the delayed release of di-hydroxyacetone from the complex brought on by this CD complexation [39]. Ultra sun Self-tan (Ultrasun) and Self Action Super Tan for Face include this CD complex (Estee Lauder).CD is also used in deodorants to fight the unpleasant odor brought on by perspiration microbial breakdown. The newest studies on the use of cyclodextrins in cosmetics are listed in Table 2.

CDs in the nutrition sector
In order to eliminate bitter tastes, unwanted chemicals like cholesterol, microbiological contaminations, and browning reactions, the food, and nutrition business must also use CDs as flavor stabilizers or food additives (Astray *et al*., 2009). By molecularly encapsulating lipophilic food ingredients with CD, which increases the physical and chemical stability of colorants, flavors, unsaturated fats, and vitamins, a longer product shelf life can be attained. (2002) Singh *et al*. The primary goal of using CDs in food processing and as food additives are: To prevent the deterioration of lipophilic dietary components caused by oxygen, light, or heat. Protection against unfavorable changes in perfumes, tastes, vitamins, and essential oils [40]. To achieve a regulated release of specific meal components. In food-packaging materials, the CD has a dual purpose. To begin, CD reduces all residual organic volatile pollutants in packing materials**.** Second, using CD enhances the sensory qualities while maintaining the quality and safety of food by improving the barrier properties of packaging materials, such as diffusion rate and transmission rate.

Table 3: Studies on the application of cyclodextrins to flavors and food

Food products	Cyclodextrin used	Work done	Conclusion
Cholesterol	β -CD	Investigation of the features of inclusions and the factors that influence encapsulation and stability.	Cholesterol has been successfully eliminated from new food products.
Fat-containing meal	α-CD	In healthy adults, CD's impact on post-meal reactions is immediate.	Post-meal blood triglyceride levels were found to have significantly decreased.
Ginseng solution	β -, ϒ -CDs	Ginseng sensory characteristics and flavor masking research.	Consumer-friendly beverages can be made using CDs dissolved in water and ginseng-based energy drink base solutions.
Goat milk and its yogurt	α -, β -, ϒ -CDs	The impact of CDs on the taste of goat milk and yogurt.	β–CD was the most efficient at masking the goaty flavor in yogurt while retaining the nutritional benefits.

1. Technological and food quality advancements
Cyclodextrins or their appropriate complexes can often enhance critical physical properties of food goods. For instance, water retention, emulsion stability, texture, etc."Beta-cyclodextrin is not a tasteless or merely mildly pleasant material in and of itself. It has a lower taste threshold than sucrose. The sweetness of Beta-cyclodextrin cannot be overlooked when it is utilized in food processing. The sweetness of sucrose and -Beta cyclodextrin are additive. Stable water-in-oil emulsions, like those found in salad dressings, can be created using Cyclodextrin. Cyclodextrins can improve the consistency and flavor of soy sauce and the stability of natural food coloring additives., Beta-cyclodextrin polyrner [41, 42] can remove phenylalanine and tyrosine from casein hydrolysates with high selectivity for phenylketonuric dietetic meals.

Tobacco products containing cyclodextrins

Typically, tobacco scents are blended directly into the tobacco. These volatile fragrance compounds are eventually lost during processing and storage. The fragrance component remains intact in cyclodextrin inclusion complexes until it is freed by burning the tobacco. Menthol can be stabilized by its Beta-cyclodextrin complex in menthol cigarettes. A crystalline molecule is created when nicotine and beta-cyclodextrin combine. Cigarette smoke filters can also benefit from Cyclodextrin's ability to beta-complex. A significant amount of nicotine and tar can be eliminated from inhaled smoke by impregnating the cellulose filters of cigarettes [43, 44]. Smoke filters can also be made from cyclodextrin polymers. The beginning and last thirds of the filter are made up of the middle of a cyclodextrin-powder polymer made from a raw cyclodextrin conversion mixture. Smoke passing through this filter has a considerably different gas chromatogram from a control.

CDs and the Environment

CDs are essential for developing and removing heavy metals, organic pollutants, and the solubility of organic pollutants from soil, water, and the atmosphere in the field of environmental science (Gao & Wang, 1998).CDs are also employed in the water treatment sector to enhance the stability, encapsulation, and adsorption of pollutants [45, 46, 47]. After treating wastewater with β-CD, all hazardous aromatic hydrocarbons, such as phenol, p-chlorophenol, and benzene, are reduced to significantly lower levels than before (Singh *et al*., 2002).Additionally, CDs clean up gaseous waste from the organic chemical sector (Szejtli,1989).In soil improvement testing, a variety of CD solubility-enhancing techniques is used. Increased biomass output and enhanced hydrocarbon utilization as a carbon and energy source are the results of β-CD, which promotes the breakdown of several hydrocarbon classes that affect growth kinetics [48, 49]. Because of characteristics including affordability, biocompatibility, and rapid degradation, the CD has developed into a powerful tool for bioremediation (Singh *et al*., 2002). The employment of CDs in producing insecticides is evidence that they play a significant role in environmental protection.

Anti-infective properties of CDs

Apart from their use in improving the efficiency of antibiotics by encapsulation, CDs have recently been described for direct antimicrobial usage. The anti-infective capabilities of CDs are mainly attributable to their effectiveness in inhibiting pore-forming bacterial toxins, which are comparable in symmetry to the target pores.[50].Investigations have been conducted into using CDs as anti-infectives, newly found CD-based inhibitors of several bacterial toxins, and molecular insights into toxin inhibition. (Karginov, 2013). Given that at least one CD derivative can precisely inhibit a variety of pore-forming toxins, a new class of CD derivatives as broad-spectrum antibiotics against different pathogens is short to be created**.** Table 4 demonstrates how CDs can boost the efficacy and complexity of current anti-infective medications.

Table 4: Cyclodextrinasanti-infectives

Drugs	Cyclodextrin used	Work done	Conclusion
Artemisinin (AN)	β -CD	Based on primary microparticles containing the AN/–βCD complex, an agglomerated powder dosage form has been created for oral administration.	It increased drug bioavailability.
Norfloxacin	β CD	At the molecular level, the solid-state properties of βCD and Norfloxacin complexes.	Improved knowledge of molecular fragments.
Voriconazole (VA)	HP- β CD, 2-O-methyl- β CD,	The effect of CD complexation on the solubility, dissolution rate, and VA's chemical stability was investigated.	2-O-methyl- βCDwas discovered to be a more effective solubilizer.
Zaltoprofen (ZP)	2-HP- β CD,	creation of a gel combining a drug with a complex carbomer and additional excipients	There is no skin irritation.

CDs' function in catalysis

Catalytic reactions are one of the most potential applications of CDs. They can act as enzyme substitutes. These are produced on the primary or secondary face of naturally existing CDs by switching different functional groups or adding reactive groups [51, 52, 53]. The substituted groups attached to the CD molecule act as a bridge for chemical recognition, allowing the modified CDs to hydroxylate selectively and hydroxyl methylate phenol. This makes them useful as enzyme mimics. The resulting CD derivative dramatically boosted catalytic activity by acting as a transaminase mimic and catalyst for converting phenyl pyruvic acid to phenylalanine (Singh *et al*., 2002). CD's involvement in the catalytic reaction can entirely block it or improve it by building inclusion complexes with the catalyst (Singh *et al*., 2002)

Agriculturalapplications

1. Pesticide formulation

Pesticide complexation has effects that are comparable to those seen in medication formulations:

a. Stabilization of labile chemicals to prevent them from decomposing too quickly (by light, oxygen, heat, etc.)
b. The transformation of (volatile) liquids into microcrystalline (persistent) compounds has a territorially limited, long-term effect.
c. Water solubility, absorption, and biological effects can all be improved by increasing water solubility.
d. Improved safety in handling, transportation, and applying highly dangerous or explosive compounds.
e. The complexed material is only released when it comes into contact with water (e.g., a complexed soil insecticide gets released only after rainfall or watering, etc.).

Pesticides are available in both solid and liquid forms. Cyclodextrin complexes, microcrystalline molecules that are mildly soluble, can be used in solid formulations and concentrated aqueous suspensions [54]. It should be noted, however, that the complex's guest material is just 5 to 25%.The DDVP (O, O-dimethyl-2,2-dichlorovinyl-phosphate) -beta-cyclodextrin complex is an excellent illustration of how CD complexation can convert a short-lived liquid into a long-lived solid substance. etc. Despite not having a gas impact, the chemical performs well as an acaricide and contact insecticide [55, 56]. The complex only killed 38% of the dried-bean beetles, while the conventional Petri dish method using 0.1% DDVP on an etched glass plate killed 80% in 20 minutes. In contrast to the complex, which killed 70% of the beetles after two days and 300 minutes of contact time. The variations are considerably more noticeable at 0.01 percent DDVP concentration.

2. Complexes of Cyclodextrin in animal diets

Isomerization, hydro vitamin production, oxidation, and photochemical processes all reduce the activity of fat-soluble vitamins during storage [57]. This issue also exists in pharmaceuticals, but it is more prevalent in vitamin formulations used in animal husbandry. These goods are combined to form a mass of feed spread over a vast area. Vitamin breakdown is significantly faster in these conditions than in the tidy form. Microencapsulation using gelatine or similar materials is the most common method of vitamin stability**.** Animal husbandry is currently experiencing difficulty with meals manufactured from premixes that include all the necessary vitamins, minerals, and nutrients but could be tastier to the animals [58, 59]. This is especially true when calves are being weaned. Calves' fodder consumption can be significantly increased by using the anethole-β-cyclodextrin inclusion complex as an aromatizer. For instance, cyclodextrin complexes are a free-flowing, light powder that blends effortlessly into premix or feed. Anethole is squandered in other ways or quickly oxidizes after being homogenized.

CDs' chances in the future

The introduction of improved formulation techniques using CDs may also aid in the future demand for currently available derivatives and the medication administration of protein, peptide, and oligonucleotide dosage forms. [60]. CDs prevent the formulation of insulin from degrading physically and chemically. (Brewster *et al*., 1989).It is, therefore, responsible for maintaining the stability of insulin formulations. Because CDs interact with readily available hydrophobic amino acid residues to stabilize the protein structure, in this case [61]. In addition, the ability of CD to form complexes reduces the immunogenicity of oligonucleotides and other adverse effects of oligonucleotide dispersion, such as the effect of macromolecules on platelets.

Conclusion

Pharmaceuticals and other businesses frequently use CDs, which are well-known worldwide. The CD's benefits have been linked to its propensity for building inclusion complexes with various therapeutic substances. The CD serves as the host in this drug-CD interaction, while the drug molecule serves as the guest, fitting entirely or part of the way into the lipophilic cavity of the ormacomplex**.** Since cyclodextrins may form complexes with a range of organic compounds, it aids in modifying the molecule's apparent solubility, improving the compound's stability in light, heat, and oxidizing conditions, and reducing volatility. Due to these characteristics, it is gaining importance in the food, pharmaceutical, agricultural, and textile industries. CDs can also be used to increase penetration. The hydrophobic CDs help medicines pass through cellular membranes more easily. By enhancing enantioselectivity, CDs have improved biocatalysis reactions. More small and large-scale studies and research on CDs should be carried out to look at their involvement in various other fields, given the vast range of uses of CDs in bioprocesses.

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