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THE USE OF CYCLODEXTRIN DERIVATIVE CARRIERS IN THE ENCAPSULATION AND CONTROLLED RELEASE OF INSECTICIDES HAS ADVANCED RECENTLY

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ABSTRACT
In light of the ongoing rise in grain output worldwide and the significant financial outlay for a variety of chemical pesticides, herbicides, fungicides, and other treatments. It has unavoidably resulted in issues with food safety and the environment. Current studies indicate that the amount of agrochemicals that contaminate the environment may be greatly decreased by using cyclodextrins and their derivatives to safeguard pesticides. We may make reference to the comparable manner that drug molecules build cyclodextrins and cyclodextrin polymers to form inclusion compounds by using the cavity features of cyclodextrins. In general, β-cyclodextrin and its derivatives are employed as a novel pesticide excipient to enhance pesticide stability, inhibit oxidation and degradation, increase pesticide solubility and absorption, lessen harmful side effects, and cover up medication odors. This study aims to give a comprehensive categorization of β-cyclodextrin polymers, as well as novel synthesis methods and techniques in diverse applications. It also summarizes the latest research advances on β-cyclodextrins and their derivatives in pesticides and other domains. Lastly, new directions for cyclodextrin-like polymer production are anticipated, and significant difficulties raised by the study are thoroughly examined and explored

1. Introduction

Inrecentyears,withtheadjustmentofChina'sagriculturalindustry structureandthegrowingenvironmentalpressure,theuseofpesticides has faced challenges. Some pesticides with disadvantages such as inconvenientuse,hightoxicityandpoorcontroleffecthavebeenaban- donedbypeople.[1–3]Therefore,innovationisalsorequiredinthepro- cessingofpesticideformulations,anditisincreasinglyurgenttodevelop pesticideformulationswithhighefficiency,lowtoxicity,lowresidue, and easy use. As we all know that chemical pesticides are mostly fat-soluble,forfat-solublepesticides,theuseofnovelpesticidesinthe form of cladding can improve its solubility, promote the uniform dispersion of pesticides on a specific surface, so that the utilization rate of pesticides is improved and the amount of pesticide application is reduced.[4–6]At the same time, the amount of pesticides entering the environment is reduced, and the pollution of soil-water systems by pes- ticidesisreduced.Comparedwithotherco-solventsandsynergists,cy- clodextrins (CD) are non-toxic, not easily adsorbed by soil, easy to transportandbiodegradeinsoil,andharmlesstoecosystems.[7]

CDs,includingα-,β-,andγ-CDs, havebecome thecarrierofmany hydrophobicpesticidestoincreasewatersolubility andstabilitydueto thespecialstructureof"hydrophilicoutside,hydrophobicinside"andthe cavityinsidethemolecule.[8–10]Atthesametime,byusingitspropertyof forminginclusioncomplexes,itcancontroltheslowreleaseofactive ingredientsofpesticidestoprolongtheprevention andcontroltime, reducethedosageofpesticidesandreduceenvironmentalpollution. However,ifthedurationofvalidityistoolongandthesolubilityistoo large,itmaycausephytotoxicity.Theapplicationof CDsinpesticidesis of great significance without causing phytotoxicity. After using the pesticide,somepartsofpesticidesareoftennotfullyutilized,whichwill produce decomposition

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metabolites. However, the toxicity of these substancesisrelativelystrong,andtheinclusionof cyclodextrincan makethepesticidestableandslowlyreleased,thusavoidingtheharmof thistoxicsubstancetoplantsandtheenvironment.[11–13]

Incyclodextrinderivatives,aqueoussolutionsof β-CDandHP-β-CD areoftenusedtoabsorbpesticidesandothersmallpolarorganicpol- lutants from contaminated soil and to treat contaminated soils.[14,15]Studieshaveshownthatβ-CDorHP-β-CDincreasesthesolubilityof organicpesticidesinwater,andtheformationofcyclodextrincomplexes doesnotaffectthebiotoxicityofmethylparathion.[16,17]Ithasalsobeen announced that treating crop seeds with aqueous solutions of cyclodex- trin derivatives, or spraying them on the foliage of vegetables, can significantlyincreasetheyieldofwheat,barleyand vegetables.[18–20]In addition,high-gradefeedshavetobesupplementedwithspecialnutri- entssuchasfat-solublevitaminsAandD3inadditiontothebasema- terial,anditisdifficulttomixasmallnumberoffat-solublevitamins evenly into a large amount of base material, which is also prone to deterioration due to light and oxygen.[15,21,22]These problems can be avoidedbyusingcyclodextrinpowderedinclusions,andtheratioofin- gredients is easyto control.Cyclodextrinsand their derivativesalready playanimportantroleineverydaylifeandarestillbeingexploredand researched to make them more applicable.[23–26]

Inlightofthecurrentresearchonβ-CD,asystematicreviewofits polymerformisveryimportant.Polymerization,substitutionandgraft-ingmodificationsofcyclodextrinmonomershaveledtothe formation of highmolecularweightcyclodextrinpolymers(pCDs)containingmultiple CDunitsandcyclodextrinmonomerderivatives.[27–29]Thecombinationof thetwoallowspCDstopossessboththeinternalhydrophobic-external hydrophilicpropertiesandthecavitystructureofCDs,aswellasthe stabilitygivenbypolymermolecules.MoreoverpCDsandfunctional polymericmaterialsarebeingintensivelyresearched,leadingtogreat prospectsfordevelopmentinvariousfields.[30,31]Cyclodextrinmolecules aregroupedintoapolymerstructurebychemicalbondingorphysical blending,andthepolymerwithnumerousCDmatricesinthemolecular skeletoniscalledcyclodextrinpolymers(CDPs).[15,32,33]Forcyclodextrin polymers,thereisnosystematicclassificationprinciplesofar,whichcan bedividedfromthestructure:(1)CDhydrophobiccavityisencasedin tandemtoformanecklace-likeenvelopecomplexonthepolymerback-bone,andtheendisthenterminatedwithamacromoleculargroup;(2) CDisgraftedonthepolymerbranchchaininthefor mofachemical bond;(3)CDandbifunctionalmonomerforlinearpolycondensation,the formationoflinearpolymer;(4)CDasacrosslinkingpointinthecross polymer, forming a three-dimensional network of molecular chains; (5) CD as the core and the polymer chain as the arm to form the star polymer molecule.[18,34]Inthisarticle,wemainlysummarize thesynthesisand applicationofcyclodextrinpolymersaccordingto theirconformation. These cyclodextrinderivativecarriershavebeenwidelyusedin novel pesticide formulations, as shown in Fig. 1. For example, the solubility andstability ofpesticidescan bemaximallyimprovedduetotheamphipathicnature of cyclodextrin. At the same time, it can increase the drug load andenhancethebiologicalactivityofpesticides.Inparticular,cyclodextrin polymer,asacarrierofpesticides,canachieveacontrolledreleaseof pesticidesandsustainablereleasetoreducepesticideloss.

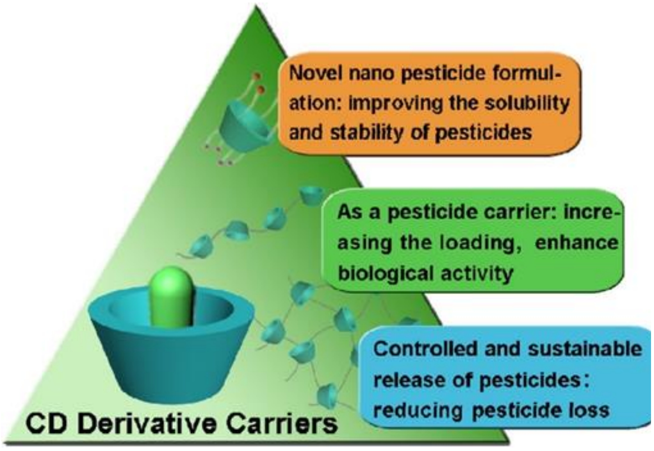

Fig.1.Theapplicationofnovelpesticideformulationbasedonthecyclodextrinderivative carriers.

2. Functionalized cyclodextrins for encapsulation and release of pesticides

Withtheprogressofscienceandtechnology,pesticideshavebeen widelyusedinagriculture,butmostofthemarehydrophobicpesticides andareeasilyadsorbedbysoilcolloids,whichmakestheirtransportand degradation in soil difficult, thus causing the accumulation of pesticide residues.[35,36]β-cyclodextrinhasanimportantapplicationinpesticide formulationsbecauseitformsaninclusioncompoundwithpesticides, whichhasfunctionsofsolubilization,controlledrelease,andimproved stability.[37,38]β-cyclodextrinisapesticideresiduethatcanbeusedin pesticide formulations because of its ability to promote the degradation of pesticide contaminants and its selective recognition of pesticide mol- ecules.[39–41]The solubilizing effect of β-cyclodextrin and its derivatives are closelyrelatedtotheirmolecularstructure. Thedifferent molecular structuresandthecorrespondingwatersolubilitylead todifferentsolu- bilizingeffects oftheformedinclusionsonthe drugs,butallof them improvethewatersolubilityandstabilityofthedrugstoa largeextent.[42, 43]

Compared with β-CD, hydroxypropyl β-cyclodextrin (HP-β-CD), formedbythemodificationofhydroxypropylandnaturalcyclodextrin, has significantly improved water solubility and better toxicological properties. It is an excellent cyclodextrin derivative. Garrido et al. studiedtheencapsulationprocessofaherbicide(terbuthylazine)withnatural andmodifiedβ-cyclodextrininasolidsolutionandaqueoussolution. (Fig. 2).[44]The study of E. Manuela Garrido showed that in the presence ofβ-CD and HP-β-CD, the solubility of terbuthylazine is significantly improved.Atthesametime,theyuseddifferentanalyticalmethodsto preparesolidterbutazine/β-CDandterbuthylazine/HP-β-CDcomplexes bykneadingundertheconditionofamolarratioof1:1.Thismethod reliablyproposesthatthesameefficacycanbeprovidedwithalower doseofterbuthylazinecomplexes,whichwillwell improvetheeffec- tivenessoftheherbicideandtheincreaseinbioavailability.Withthe in-depth researchof functionalized cyclodextrins, the advantages of functionalized cyclodextrins have been well used by many researchers, andinthereportofAlessandra'sgroup,itwasfoundthattheclathrate obtainedbythereactionoftheneutralcrystallineherbicidebentazon (HBtz)withnaturalcyclodextrins(CDs)wassynthesizedinmechanical. Theguestmoleculeisnotpermanentlyboundbutisindynamicequi- libriumwithCD,whichisoneoftheadvantagesofcyclodextrinsbeing exploited. Based on the fact that the inclusion complex will dissociate theagglutinateandreleasetheguest.Afterthat,thewatermoleculesinthe surroundingenvironmentgreatlyincreased.Naturalcyclodextrinβ-CD andγ-CDwereusedtoreactwiththeherbicidebentazontoformnovel clathratesduringtheexperiment[β-CD•HBtz]•6H_2Oand[γ-CD•HBtz]•8H_2O.Thedissolutionrateofallcompoundsandthesolubilityinwater weresubsequentlydetermined,andacleartrendwasobserved.Itis found that this study is the first report about the complexation and sol- ubilitypropertiesofclathratesobtainedbythereactionofbentazonwith a range of natural and modified β-cyclodextrins, such as sulfonyl ether-β-CD(SBE-CD)and2-hydroxypropyl-β-cyclodextrin(2-HP-CD).

Y´an~ez'setal.reportedalowerdissolutionrateandsolubilitycomparedto sodiumbentazonalone,suggestingthatcomplexationhelpsprevent herbicideleachingintogroundwater.Theirresearch provedthatadding insoluble molecules to cyclodextrins is a viableway to overcome the solubility problems of widely used herbicides and allow for the spray-loading process. A large number of experiments have shown that thecloserthecavityvolumeofβ-cyclodextrinanditsderivativesistothevolumeofpesticidemolecules,themoreobviousthesolubilizationeffect; The solubilization capacity of β-cyclodextrin and its derivatives on pes-ticidesincreaseswiththeincreaseofpesticiden-octanol/waterpartition coefficient,indicatingthatthehydrophobiceffectbetweenthecavityof β-cyclodextrinanditsderivativesandpesticidemoleculesisthebasisfor the solubilization effect.

Inthestudyofgreenherbicides,Gaoetal.usedwaterasablank controltodeterminetheeffectofwater,β-CD,cyanazine,β-CD/

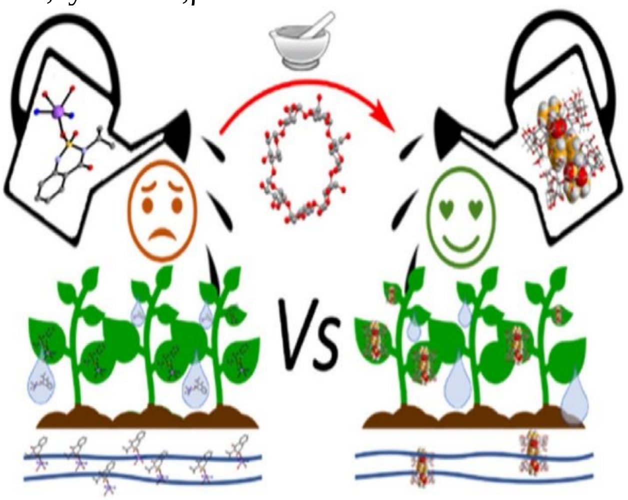

Fig. 2.Themechanochemicalsynthesis ofinclusioncomplexesobtainedbyreactingtheneutralcrystallineherbicidebentazon(HBtz)withnativecyclodextrins(CDs).Copyright 2021, American Chemical Society.

cyanazinemixtureandcyanazine-β-CDclathrateonthechlorophyll contentof barnyardgrass,asshownin Fig.3, aftersprayingβ-CDaqueoussolution and spraying water, the chlorophyll content in barnyard grass wasaboutthesame,whichcouldexcludeβ-CDwithoutherbicidal

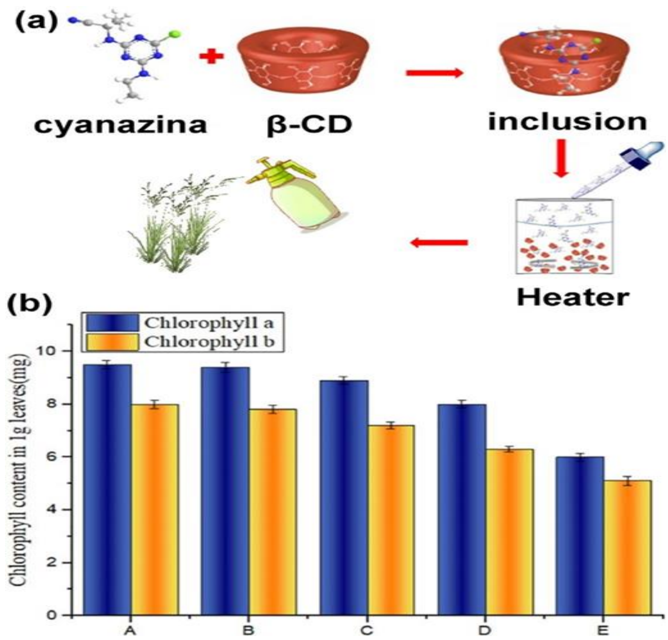

Fig.3.(a)synthesizedclathrateofcyanazine-beta-cyclodextrin(cyanazine-β-CD) clathrate via coprecipitation. (b) the result of chlorophyll content: (A)water; (B) β-CD; (C) cyanazine; (D) physicalmixture; and (E) the clathrate.Copyright 2020, with permission from Elsevier.

activity.[45]When spraying the mixture and the complex, the chlorophyll contentwassignificantlyreduced,whilethechlorophyllcontentofthe sprayedcomplexwasthelowest,whichisagoodproofthattheclathrate has the strongest herbicide activity. Experiments have shown that clathrateshaveasignificanteffectonimprovingthephysicalproperties ofherbicides,includingimprovingthewatersolubility,thermalstability andbiologicalactivityofherbicides.Theresultswerecomparedbythe watersolubilityandthermalstabilityofβ-CDagglutinatewithHP-β-CDagglutinate,respectively.Although,itsphysicalandchemicalproperties arenotverygood.Thelowcostofβ-CDanditsadvantageofstillhaving practicaleffectsintheapplicationwasworthyofourattention.However, thisstudyhaslaidthefoundationfortheresearchandapplicationof cyclodextrinderivationto a certain extent.

Weed eradication aims to prevent weeds from competing with variouseconomicandfoodcropsforresources,resultingincroplossanddeath. However,duringcropgrowth,theinfectionofvariouspathogenswill poseagreaterthreat.Inthisregard,Jietal.reportedthatasupramo-lecularcomplexwassynthesizedbyadamantane-functionalized1,3,4- oxadiazole, to facilitate β-cyclodextrin-adamantane host-guest in-teractions. The complex was developed to manage refractory plant bac- terial diseases and enhance biological activity. The ecologically friendly and biocompatible supramolecular complexes are shown in Fig. 4.[46]Xanthomonas oryzae pv. oryzae (Xoo), Xanthomonas citri (Xac) and *Pseudomonassyringae*(Psa) areconsideredby experts in the field of plant protectionasthethreemosttypicaldestructivebacterialstrainsamong thetoptenpathogens,whichareextremelysusceptibletoparasitizing plants and once the plants are infected they get bacterial wilt, citrus ulcerand kiwifruit ulcer disease. In preliminary inhibition screening studies byJi,mostoftheadamantane-modified1,3,4-oxadiazolesshowedsignifi- cant biological activity against the three typical destructive plant pathogens.

Invivoinhibitiontestsinthisstudy,yieldedoptimalconditionsfor thepreparedsupramolecularcomplextosignificantlyalleviatedisease symptoms and improve control of rice leaf blight (34.6–35.7%(III18) ~ 40.3–43.6% (III18@β-cd) and kiwifruit ulcer (41.0–42.3% (ThisstudybyJinotonlyprovidesnewperspectivesforpestcontrol without causing additional environmental damage but also for the preparation of eco-friendly and biocompatible supramolecular compo-sitions.Thehigherthebiologicalactivityofthepesticideformulation towardthetarget,thebetter,andthelesstoxictoenvironmentalor-ganisms.Thebiologicalactivityandtoxicityofpesticidesencapsulated bycyclodextrinderivativesarepoorlyreportedandthemechanismof action is still unclear, so a lot of research work is needed to provide theoreticalguidancefortheapplicationofencapsulation.

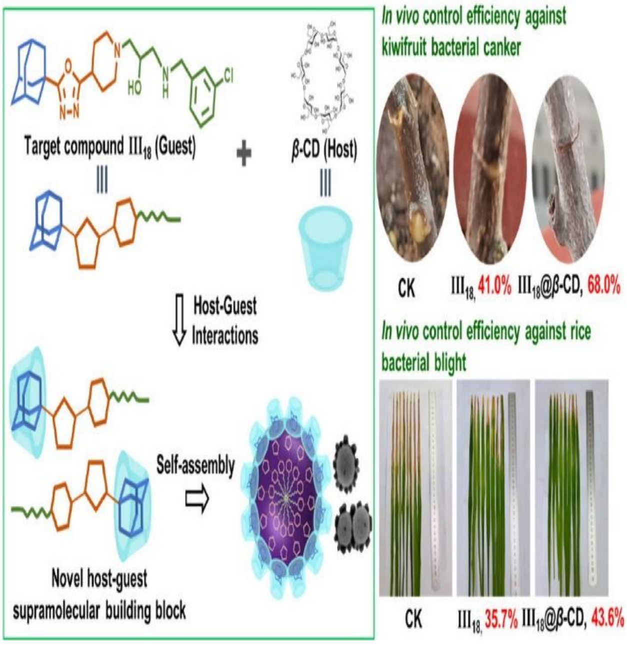

Fig.4.The formation of supramolecular complexes via β-cyclodextrin—adamantane host—guest interactions prepared 1,3,4-oxadiazole. Copyright 2022, AmericanChemical Society.

3. Linear cyclodextrin polymer for loading and releasing of pesticides

Cyclodextrinpolyrotaxaneisoneoftheimportantmembersofsu- pramolecular chemistry. Due to its low toxicity, size controllability and structuraluniqueness. It hasarousedtheinterestof a widerange ofre- searchers and rapidly emerged.[47–50]Like a string of "pearl chains", rotaxaneisasupramolecularsystemcomposedofaringedhostmolecule (pearl)andalonglinearguestmolecule(axis)passingthroughitsinner cavity.Atbothendsofthelonglinearmolecule,anend-sealingagent (stopper)isconnectedtopreventtheslippageofthe macrocyclichost molecule.[13,51]

β-CDhasabettersealingeffectthanα-CDandγ-CD.Inpractice,the polymersweuseusuallyblockcopolymers,wherethedifferentchain segments have a certain selectivity for cyclodextrin. For example, poly-caprolactone (PCL) and polytetrahydrofuran (PTHF) block copolymers canforminclusioncomplexeswiththreedifferent cyclodextrins.The researchers believe that in α-cyclodextrin inclusion complex, only the twoendsofthePCLchainsegmentspenetrateintothecyclodextrin cavity. In β-cyclodextrin inclusion complex, both PCL and PTHF segmentsenterthecyclodextrincavity.However,in theγ-cyclodextrininclusion complex, two PCL and PTHF chain segments enter the cyclodextrin cavityduetothelargestinnerdiameterofthecyclode xtrincavity.Asweknow from the previous descriptions, the matching of the inner diameter size ofthe cyclodextrin to the spatial dimensions of the polymer molecular chainisthemostimportantfactorinthepreparationo fpolymersandcyclo- dextrin inclusions. When the diameter of the polymer chain is matched withtheinnerdiameterofcyclodextrin,theinclusi oncomplexcanbe formed.Iftheinnerdiameter ofthecyclodextrinistoolarge,thepolymer molecular chain entering it can easily slip out. Because polymer molec- ularchainsdonoteasilyenterthecavityanditisdiffi culttoforman inclusionscomplex.Thehydrogenbondinteractio nbetweencyclodex- trinandpolymermolecularchainisalsoafactoraffec tingtheformation ofinclusioncomplex.Theformationofhydrogenbon dsiswellfacilitated for the formation of inclusion complexes between cyclodextrins and polymers of different molecular sizes.

Atpresent,CD- basedpolyrotaxanes(PRs)areahotresearchtopicin supramolecularchemistry.Varioustypesofhost- guestmoleculesare usedtopreparePRswithdifferentstructuresandshapes. Theabovework ispartoftherecentprogressinthefield,andthestruct ureandperfor- mancearedifferentfromthetraditionalPRsystem, whichgreatlyen- richesandpromotesthedevelopmentandapplicat ionofPR.Onthis basis,functionalmaterialsdevelopedinmolecular machines,molecular recognition,self- healingmaterials,stimulus- responsematerialsand otherapplicationfieldshavebeencontinuouslydeep enedandimproved. Rshaveshownexcellentperformanceandbroadde velopmentspacein theseapplicationfields.However,mostofthedrug systemsbasedon cyclodextrin(quasi)rotaxanesareonlyinthestageofb asicexperimentalresearch.Itisnecessarytoaccelerat etheresearchprogressofitsrelatedtheories and its utilization as the novel nano-pesticide carrier, to obtain a better pesticide control and release system with higher loading and encapsulation rate.

In recent years, the multifunctional residence of hyperbranched polymers, represented by dendrimers, has gained attention.[52,53]On the otherhand,withthedevelopmentofdrugdeliveryc arriers,combining thetwotoformsupramoleculargraftpolymershasbe comethematerial ofchoiceforbiomedical,tissueengineeringanddru gdelivery.Although various polysaccharide polymers have been developed for drug delivery applications,amongthemCDsarestillpreferredbec auseoftheirmany important properties in drug delivery such as high load efficiency, easy accessibility and extremely solubility properties.[54]Cyclodextrin grafted polymers are also known as chandelier cyclodextrin polymers, in which thecyclodextrinisusuallyattachedtoabranchchai nofalinearpoly- mer.[55–57]Thereareusuallytwomethodsofsynthesis:1)cy clodextrin reacts with active monomer to generate monomer containing CD struc- ture,andthenthesemonomersarepolymerizedbyi nitiatortoforma linearpolymer.[58]Asa result,CDprimitiveexistsinthepolymerasside grouporbranchchain;2)Inthedirectpolymerizatio nofcyclodextrins withpolymers,themostcommonoperationistheg raftingofβ-cyclo- dextrinsontocellulosemoleculestoproduceβ- CD/cellulose,whichis usedtoadsorbphenolsfromindustrialandagricultu ralwastewater.[59]

Thegraftingprocessofβ- cyclodextringraftedpolymersalsohassome influencingfactors.Forexample,Mietal.usedβ- Cyclodextringrafted hyperbranchedpolymers(CD- HBP)graftedpolymerasasorbentand combined high-performance liquid chromatography, realizing the pyre- throidsmeasureinenvironmentalwatersamples. Theysuccessfully synthesizedanewsorbentCD- HBPandoptimizedtheexperimental factorsaffectingtheextractionefficiencysuchasextractiontime,pH value,ionicstrengthanddesorptionconditions.Theresultsshowedthat thisreactionprocesswassimple,cost-effectiveandreproducible.[60]The linearity of the three pyrethroids was good. The linearity of cypermethrin rangedfrom10to500ng/mL,andthatofcyhalothrinandpolyethrin rangedfrom5to500ng/mL.Thismethodhasadetectionlimitof 1.0ng/mlto2.1ng/mlunderthemostsuitableconditions.Theextrac-tionrecoveriesofthethreetargetanalyteswereintherangeof83.1%– 91.6%. In addition, the relative standard deviations (intraday and interday)werelessthan6.0%.Therapidandefficientextractioncapa- bilityofCD-HBP-DSPEwasbasedontheeasybindingandseparationofCD-HBPafterinteractionwiththetarget.Therapidadsorptionand desorption processes established in this experiment provide a good linearrange,reproducibilityandhighextractionefficiencyinaveryconvenientway. Without exception, the above grafting CDP systems make use of theself-assemblyfunctionofCD,whichismainlyusedtobuildhigher-level assemblyandspecificidentification,andimprovetheloadingcapacity, adsorption capacity and targeting function of target molecules. There arenumerousreactivehydroxylgroupsontheoutsideofcyclodextrin,whichcanbedirectlyusedasreactivegroupsforpolycondensation.Theformedpolycondensationiscalledcyclodextrinlinearpolycondensation,andthe hydroxylgroupcanalsobemodified(suchasmethylation,sulfonation, aldehydetization) to form polymers. If the hydroxyl group is directly usedasthereactiongroup,thereactiondegreeshouldbestrictlycontrolledto prevent cross-linking.[55,61]

CDgraftingofHApolymershasbeenaverytediousprocessinsome paststudies,requiringatime-consumingmulti-stepprocessforsynthe-sis.[62]Singhetal.showedthatthiscouldbedoneinaone-stepchemical cross-linking reaction and that reaction parameters such as reaction timeandtheratioofHA:DPC:β-CDcouldbevariedinthesyntheticrouteto obtain different polymer derivatives to optimize VE complexation. HA-β-CD is an advanced drug delivery agent in studies where an increasein the β-CD ratio with a grafted supramolecular host molecular backboneimproves the loading capacity and water solubility of VE. As shown in the schematic diagram of HA-β-CD polymer for delivery of tocopherols (vitamin E) (Fig. 5). Direct condensation of the reactive hydroxyl group onthe outsideofthe cyclodextrinresultsin acondensation thatisoften referredtoascyclodextrinlinearcondensation.In additiontodirect condensation of the hydroxyl group, the hydroxyl group can also be modified (e.g. methylated, sulphonated, aldehydized) and then condensedtoformapolymer.Chengetal.firstreacted β-CDwithamino acids to produce β-cyclodextrin derivatives and then reacted them with polyethylene glycol to obtain linear β-cyclodextrin polymers with side chainscontainingfunctionalgroupcarboxylates, whichwereinvesti-gatedusingcamptothecinastheloadingdrug.Inthismethod, β-CD-diaminoacidswithbifunctionalgroupsarefirstsynthesizedand usedasmonomers,whichcanbedirectlyusedtoconstructlinearpoly- mers with simple operation. Cheng's study provides a good reference to breakthroughs in the application of linear cyclodextrins in practice.[63]It isworthnotingthatexpertsinthefieldhavenoticedthis,andthey have used effective methods to subtly circumvent the synthesis difficulties of suchβ-cyclodextrinpolymers,sothatitcanbebetterusedin practical applications.

4. Cross-linked cyclodextrins for encapsulation and release of pesticides

Cross-linkedpolymersofCDarethemostwidelystudied classof CDPs,ofwhichepichlorohydrin(EPI)cross-linkedCDsarethemost common.[64]Duetothehighdegreeofcross-linkingofCDmolecules,the cavities of CDs are retained intact but their movement is restricted comparedtograftedCDPs,sotheyareusuallyusedfor theadsorptionof smallmolecules.Itdoesnothavetheself-assemblyfunctionlikepoly(- rolane) and grafted polymers. The use of EPI to crosslink CDPs have beendiscussed in detail in the literature.Herewe focus on breakthroughs in thefieldofCDcrosslinkedpolymersinrecentyears,including structural modulation, design of material dimensions, and their application in practice.[65–67]Forexample,Dangetal.preparedtwoCDpolymersfrom β-CDandγ-CDusinghexamethylenediisocyanate(HDI)asa cross-linker.[68,69]

InthestudyofWangetal.,2-hydroxypropyl-β-cyclodextrinpolymers cross-linkedbypolyacrylicacidweresuccessfullypreparedbyesterifi- cation reaction, and the successful preparation of 2-hydroxypropyl- β-cyclodextrin polymers was demonstrated by infrared spectroscopy, X- raydiffractionandX-rayphotoelectronspectroscopy,andtheformation ofacross-linkednetworkinthepolymers.Thecross-linkedpolymerwas synthesizedto improvethesolubilityandimpactoftheantifungalac-tivityofpolymyxin(Fig.6).Tofurtherextendtheapplicationofthe2- hydroxypropyl-β-cyclodextrin cross-linked polymer, they used chitosan and β-CD-EP composite films as a plant protection material for the controlledreleaseofcarbendazimtoprotectoilseedrapefromSclerotiniasclerotiorum(Lib.)deBary.Theresultsobtainedwerethattheβ-CD-EP/ carbendazimandchitosan film significantly prolonged the effectiveness of carbendazim at a concentration of 100 μg/ml compared to the sprayingof 500μg/mlcarbendazim.[70]Wangetal.successfully prepared 2-hydroxypropyl-β-cyclodextrinpolymers by esterification and found by the characterisation that they formed a cross-linked network in the polymers.Whentheyusedthiscross-linkedpolymertoremoveibuprofen from aqueous solutions, they found that the amount of ibuprofen adsorbedwasnot onlypH-dependentbutalso increasedwiththe initial concentrationandtemperature.Theadsorptionwasthenfollowedby10 adsorption-desorptioncyclesusinga5%ethanol/watersolutionasthe eluent.Thedatashowedthatthepolymercouldbereusedwithoutany significant loss of the original adsorption capacity. This research result provides a new direction for the application of cross-linked cyclodextrin polymers.Thedegradationeffectsoftitaniumdioxideandβ-cyclodextrin crosspolymersonpesticideswereanalyzed,andthe effectsofcatalyst amountandreactiontimeonexperimentaleffects werestudied.The experimentalresultsshowedthatthereactiontime of8h,titanium

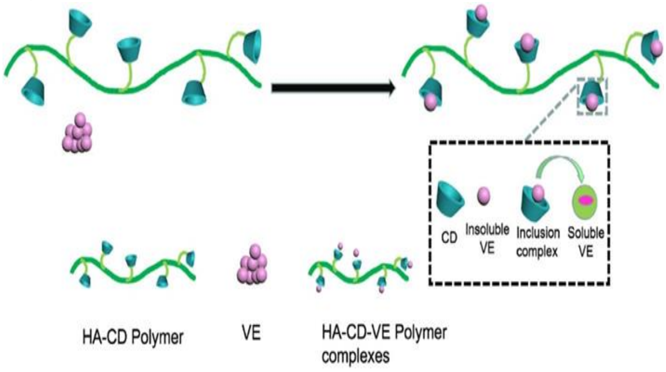

Fig.5.HA-CDgraftedpolymercomplexefor VEencapsulation

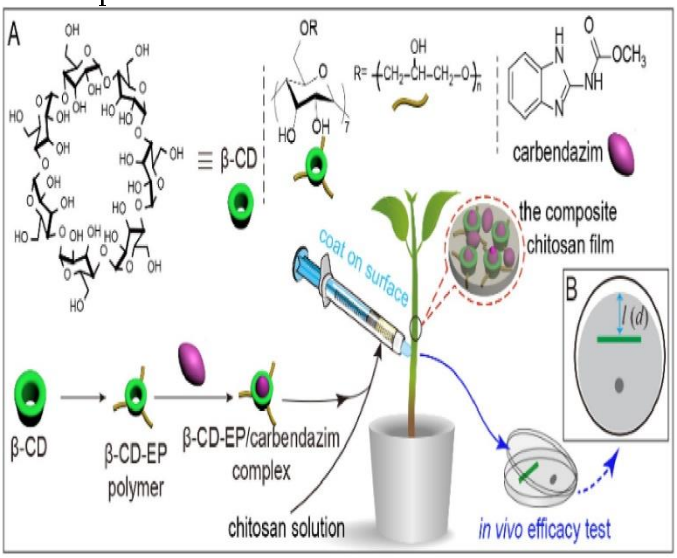

Fig. 6.(A)theillustrationofthestructureofthe(β-CD-EP)/carbendazim complexandtheutilizationtestofvivoefficacy.Copyright2017,withpermissionfromMDPI(Basel, Switzerland).

dioxide0.3g,andβ-cyclodextrincrosspolymer0.1gwasthebestcom-bination,andthemaximumremovalratewas98.6%.

Nanopesticideshavehigherutilizationefficiency,reducedenviron- mentalpollutionandslow-releasepropertiescomparedtomanycon- ventionalpesticidesintermsofuseandefficacy.Basedonthepositively chargedofPolydimethyldiallylammoniumchloride(PDADMAC)and negativelychargedinclusioncomplexSuenbutyl ether-β-cyclodextrin (SCD), Shi et al. prepared antifungal nanoparticles (TEBNPs) loaded withtebuconazole by making use of the principle of electrostatic self-assemblyofthetwo.[71]TEB,asshowninFig.7(a),isa highlyefficientmodern triazole fungicide with high efficiency, low toxicity and broad spectrum antifungalactivity.TEBhasbroadprospectsforthe controlofseveral grain diseasessuch asrice blast, rootrot, sharpeye andsmut.It is usuallyusedasanemulsifierconcentrate,whichisashorteffectivetimeofTEB andamuchlowerutilizationefficiency.Researchers havefoundthatCD

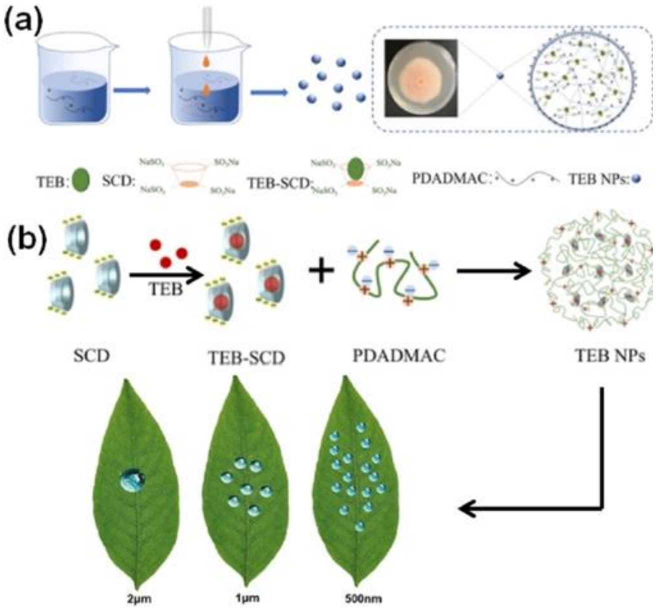

Fig. 7. (a) Schematic representation of the antifungal tebuconazole NPs syn- thesis.(b)Electrostaticself-assemblyprocessofPDADMACloadingtheTEBNPs.Copyright 2022, with permission from Elsevier.

monomers can be easily modified by carboxyl groups, sulfonic acid groups,etc.Thismodifiedcyclodextrinhasmanyadvantagesovernat- uralcyclodextrins,assulfonylether-β-cyclodextrin(SCD)hasahigh negative charge density and acts as an anionic component during self-assembly. Polydimethyldiallylammonium chloride (PDADMAC), a positivelychargedpolymer,issafeandnon-toxicintoxicitytests,soit acts as a cationic component in electrostatic packaging. Shi used SCD andPDADMACtoprepareNPsbyelectrostaticself-assembly.Complexesof SCD and TEB were prepared by freeze-drying. After the preparation of the clathrate, the TEB-SCD solution was placed in PDADMAC solution ofdifferent concentrations. The characterization demonstrated that the positivelychargedPDADMACandthenegativelychargedTEB-SCDag- glomeratesweretightlycross-linkedbyelectrostaticaction.Fig.7(b)of NPs prepared by detailed electrostatic self-assembly method. Shi dis- solvesPDADMACin20mlofdistilledwater.Atthesametime,theSCD and TEB-SCD complexes were dissolved in 5 ml of distilled water, respectively, and then dropped into PDADMAC solution while stirring in magneticstirringat2400rpm.Aftermixingfor10 min,thespeedis adjustedto9600rpmandcontinuedtostirfor30min.Thefinalcon- centrationsof2.4–4.8mg/mLand3.2–4.8mg/mLwereobtainedwith PDADMACblankNPsandTEBNPs,respectively.Cross-linkedcyclo- dextrinpolymer,as theearliestand most studiedcyclodextrinpolymer, endowsthestimulationresponsefunctionofcross-linkedpolymerto cyclodextrin polymer, which will be a good strategy to solve some problemsintheapplicationofpesticides.Thesestudiesaresummarized systematically.Ontheonehand,wecanbetterunderstandtheresearch progressandsomeproblemsthatdonotexistatpresent.Ontheother hand,theexpertswhostudycyclodextrinshaveprovidedgoodexperi- ence in modification.
Inagriculture,waterandfertilizerinteracttopromotecropgrowth.
Shenetal.preparedthedouble-meshhydrogelWSFwithCMCandAl^{3+}insteadofthe previouslyusedsodiumalginateandCaCl2,respectively,as

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Volume : 50, Issue 1, No. 1, January 2021

shown in Fig. 8. They believe that the reason why urea release is hindered isduetothehighspecificsurfaceareacharacteristicsofHNT,which allowsureatobeeasilyattachedtothecavityofHNTor adsorbedontheHNT surface. Comparing the cumulative release rate of the WSF prepared bytheirnewmethodwiththatoftheWSFsynthesizedbycomparing sodiumalginateand$CaCl_2$,theformerresultsinadecreaseinthecu- mulativereleaserate.[72]InGaoetal.'sstudy,greenglycineionicliquid functionalizedβ-cyclodextrinpolymer(AAIL-β-CDCP)wassynthesized. AAIL-β-CDCPrapidlyadsorbedpyrethroidpesticidesandtheadsorbed moleculescouldberesolvedwithmethanol,resultinginanovelsolid

Fig.8.(a)Thepreparationprocedureandschematic illustrationofthestructureoftheWSF,(b)Cr(%)of ureafromtheWSFwithoutHNTsandtheWSFwith HNTsindistilled water. Copyright 2020, with permission from Elsevier.

phaseextraction(SPE)method.Theyfoundthatthelinearrangeswere 0.025–20.00 mg/mL and 0.03–25.00 mg/mL for cypermethrin and phenothrin,respectively,withdetectionlimitsof0.020mg/mL-1and 0.023 mg/ml-1, respectively, under their optimized experimental con- ditionsandafter10replicateapplications.hasbeen usedforthedeter- minationofpyrethroidsinteaandtomatosamples withrecoveriesof 92.0–100.6%andRSDsof2.1–4.2%.[73]Inrecentyears,cross-linkingCDP hasmaderapiddevelopmentandbreakthroughsin theapplicationof green cross-linking agents, the preparation of green cross-linking agents,andthestructure(specificsurfacearea)andthree-dimensionalmacro- scopic morphology (bulk high strength) of polymers.

Theexplorationofreformulatingregisteredactiveingredientsto develop micro/nanoscale pesticidesystemshas attractedconsiderable interestinimprovingtheefficacyofpesticides.InthereportbyLiuetal. they controlled the release of imidacloprid (IMI) by preparing function- alizedhollowcarbonmicrospheres(HCMs)forinfraredphotoresponsive pesticidedeliverysystems.(Fig.9).[74]UnlikethecommonlyusedSiO2 templatemethod,HCMswerefabricatedusing$CaCO_3$asthetemplate and dopamine as the carbon source. A novel infraredlight-responsive pesticidecarrierwassuccessfullyformulatedbythemwithfunctional- izedHCMs.Thepreparationofthislight-controlledpesticiderelease system(HCMs/IMI/PEG/α-CD)requiredtheadditionofimidacloprid (IMI) to HCMs, followed by coating with polyethylene glycol (PEG) and α-cyclodextrin(α-CD).Inthissystem,PEGchainscanpenetrateintothe cavitiesofα-CDandformagelnetworktolockthepesticideinside.The HCMsareagoodphoto-thermalresponsivematerialandwheninfrared lightstimulatesthepesticidecarriertogenerateheat,thegelnetwork structure is disrupted and the solids are released. To investigate whetherthecontrolofcornborerbyHCMs/IMI/PEG/α-CDisinfluencedbylight, the results of bioactivityexperiments showed that the combination of irradiationwithinfraredlightresultedina40%survivalrateofcorn borer,a125%increaseincontrolcomparedto90% withHCMs/IMI/- PEG/α-CD alone.

5. Star cyclodextrin polymers for encapsulation and release of pesticides

In this section, a comprehensive account of the preparation of cyclodextrin-centred star-shaped polymers and their application in pesticide synergism, pesticide residue detection and biology are reviewed.[75,76]According to the different principles of preparing star polymers,thesynthesismethodscanbedividedint

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otwotypes:"arm initiation" and "nuclear initiation". The cyclodextrin derivative is used as aninitiator,andacyclodextrinstarpolymercanbe preparedbyboth methods.Theseexcellentpropertiesarecyclodextrinstarpolymerswith a wide range of application prospects and development potential. (Fig. 10).[77–79]

Inthesynthesisofhyperbranchedpolymers,Wanetal.firstmodified the hydroxyl group of β-CD by the ROMBP method to obtain β-CD-HPG.[80]The hydrazine-terminated β-CD (named β-CD-HPG-EBA-HH) was subsequentlysynthesizedusingthehydroxylgroup,whichhastheadvantage offorminghydrazonebondswithEPI,whichisknowntobesensitiveto pH.Basedonthesecharacteristics,theyinvestigated theeffectofpHon thereleaseofthedrugfromthedrug-loadedpolymercomplex(β-CD- HPG-EBA-HH)byEPI.WhileLiangetal.usedtheRAFTarm-firstmethodto form linear arms using butyl acrylate and the 4-allyl variant of Prioleneasmonomers,andreacted1,6-hexanedioldiacrylateasacross-linking agentinacascademicroreactorsystem,thestar-shapedmacromole- cules were synthesized.[81]To consistently prepare star-shaped products withdifferentarmcompositions,Liangetal.carefullyexaminedthe polymerizationkineticsineachstep,optimizedthereactionflowand adjustedthe reactionformulations.The optimized syntheticroute elim-inatedthetediousintermediatepurificationstepand resultedinapoly-merproductwithafairlyhighstaryield(>70%),molecularweight(Mw, LS>100kg/mol)andthenumberofarms(>30).Avarietyofemulsions (includingtwotypes,i.e.oil-in-waterandoil-in-water)wereformed usingstarproductswithdifferentamphiphilicstructuresasemulsifiers. Inthiscontinuousflowmode,theresearcherscontrolthearmandcore structurebyadjustingtheresidencetimeandflowrate ratioateachstep to tailor the star-shaped polymer with significant functionality.

Multiplearmstarblockco-polymerswiththermo-responsiveprop-ertieswereobtainedbyVrijsengroup.Abromine-functionalβ-cyclo- dextrin core is used as a multi-initiator in combination with light-mediatedatomtransferradicalpolymerizationincore-advancedpoly-mersynthesismethods.Inthisstudy,di(ethyleneglycol)ethylether acrylate (DEGA) and 2-hydroxyethyl acrylate (HEA) with excellent biocompatibilitywereselectedasthearmsofthestarpolymer.Ithas been shown that the overall LCST of the polymer can be reduced by using cyclodextrinsasthecorecomparedtolinearpolymers.[82]Basedonthe chemistryweknowthattheLCSTofstarpolymerscanbeadjustedby changingtheratioofthetwohydrophilicstructuralblocks.Jeroenetal. havesynthesizedathermosensitive21-armstarconsistingofahydro- phobic PMA inner block and a thermosensitive HEA:DEGA outer block by adjustingthearmstructureblockcopolymer.Theadditionofhydro- phobic dyes to various star polymer solutions and their dissolution showedthatthesolubilityofthedyesincreasesinthe presenceofther-mosensitivestar(block)copolymers.Atpresent,theapplicationofstar cyclodextrin polymer in agriculture mainly focuses on temperature response.Aseriesofstar-shapedpolymersbasedonβ-CD,2-(2-methox-yethoxy)ethylmethacrylate(MEO_2MA)and*tert*-butylacrylate(tBA) weresynthesizedviaatomtransferradicalpolymerization(ATRP)bySugroup.[83]It shows that, 48% of IMI changes from β-CD-PMEO_2MA micellepromotedthepenetrationofIMIintotheleavestopreventcottonaphids at27°C.Thereisonlyonecyclodextrinunitinthestarcyclodextrin polymer. To realize its practical application, the polymer chain grafted on cyclodextrinisthemainresearchtarget,soitisvery necessaryto

Industrial Engineering Journal
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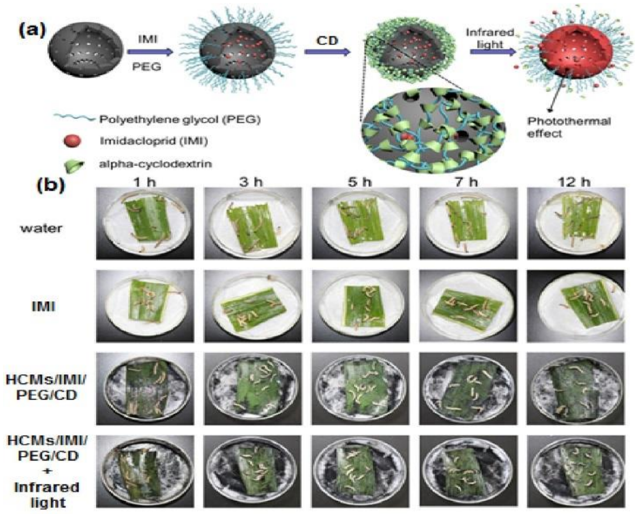

Fig.9.Schematicdiagramoftheprocessforpreparationofthepesticidedeliverysystemandinfrared-light-controlledpesticidereleasebythephotothermaleffectofHCMs. Copyright 2021, American chemical society.

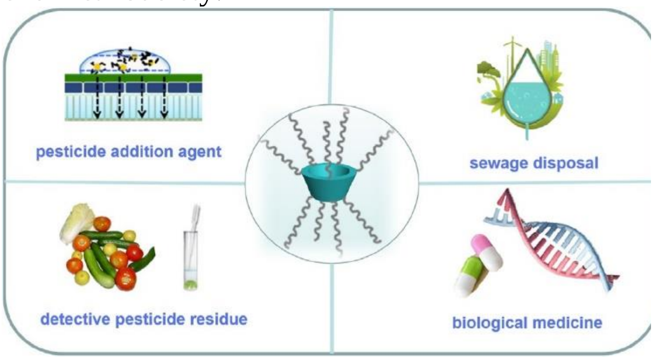

Fig.10.Applicationclassificationofstarcyclodextrinpolymers.

innovateandimprovetheoriginalsynthesismethod.

Compared with linear polymers, star polymers can achieve versatilityinasmallerspaceinparticular,cyclodextrinhasthemolecularstructure ofmultiplehydroxylgroups(primaryandsecondaryhydroxylgroups) and hydrophobic cavities. The reaction characteristics of the multiple hydroxylgroupsmakecyclodextrinitselfcanbeusedasthecoreofthe starpolymer.[84,85]Moreimportantly, thehydrophobiccavityofcyclo- dextrin has supramolecular inclusion for a wide range of guest molecules, which gives the inclusion function of polymer molecules containing cyclodextrin. Therefore, cyclodextrin-based star polymers have broad application prospects in molecular recognition, novel macromolecular constructionanddrug-controlledrelease.

6. Conclusions

Withthedevelopmentoffunctionalmaterials,independentCDmol- ecules can no longer meet the needs of current practical applications. Theexcellent physicaland chemical propertiesof CD havegradually shown itsadvantagesinthedevelopmentofpolymermaterials.Whenthead-vantagesofbotharecombined,thescopeofpracticalapplicationsis furtherexpandedandnewopportunitiesforCDsareopenedup.Someof the advantages are like a sustainable source of raw materials, low cost, multiplesynthesismethodsandasimplesynthesisprocess.Inpractical applications, not only the outer hydrophilic and inner hydrophobic cavity structure and chiral characteristics of CD's polymer are utilized, butalsoitshighphysical-mechanicalstrength,hardness,andthermal stability are exploited. With the expansion of application requirements andthedeepeningofinterdisciplinary,avarietyofnewsingle-molecule functionalized β-cyclodextrin or β-cyclodextrin functionalized polymers havebeenemerging.Predictably,functionalized β-cyclodextrinsmay become a general trend. In the future, it will have great application po- tential in the pharmaceutical chemical industry, energy saving and environmental protection, biocatalysis, green agriculture, etc.

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