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NEW POLYMER BASED MODIFIED CYCLODEXTRINS GRAFTED TO TEXTILE FIBERS; CHARACTERIZATION AND APPLICATION TO COTTON WOUND DRESSINGS

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ABSTRACT

This study describes the use of a new polymer based modified cyclodextrins (CDs) as a finishing agent of natural cotton fibers used in order to obtain wound dressings with improved antibacterial delivery properties. We have first synthesized the per-6-azido-β-CD and after the well-known per-6-amino-β-CD was obtained via the Staudinger reduction. This synthesis was then confirmed by NMR and mass spectrometry characterizations.

This per-aminated primary face CD was then polymerized with a citric acid. The new polymer (polyCTR-CDNH$_2$) yielded a cross-linked polymer that chemically bonded to cotton wound dressing fibers and was resistant to severe water washings.

We report that the grafting rate of polymer of modified CDs functionalizing the cotton dressings was controlled by temperature, curing time and the CDs dilution of the impregnating bath.

The functionalization was then characterized by a topographic study of dressings grafted surfaces which was approached by atomic force microscopy (AFM; non-contact mode). This characterization permitted to evaluate the roughness and the chemical heterogeneity of the grafted dressing surfaces.

The improvement of the hydrophilicity of medical wound dressings is a much sought property. The evaluation of the wetability of treated samples showed a clear enhancement of the hydrophilicity of polyCTR-CDNH2 grafted dressings which are more effective than those treated with the polymer of native CDs. Much more the new polymer caused no yellowing compared with the polymer of unmodified CDs. So the grafting of the new polymer of modified CDs better respected the original properties of treated textiles. Moreover, it can provide a functionalized medical dressing with new added properties. In fact, they can be exploited to complex substances for antibacterial effect or healing purpose to facilitate the cure of wounds. These substances will be stabilized and protected by encapsulation then they will be slowly released in contact with a wet wound.

In conclusion, these results from our study offer an insight into the efficient performance of modified CDs as drug delivery systems for multiple applications in the fields of biomaterials and medical textiles.

KEYWORDS

Cyclodextrin; modified cyclodextrin; polymer; Textile finishing; functionalized dressing

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1. INTRODUCTION

Many researchers have been conducting to develop special functionalized dressings which include hydrocellular dressings (TSUKADA et al., 1992 / FOSTER et al., 1994 / AMEEN et al., 2000), collagen dressings (MIAN et al. 1992 / RUSZCZAK et al. 2003 / SINGH et al. 2011) and silicone dressings (MEULENEIRE 2002 / TIMMONS et al. 2009). Despite these different kinds of dressings they still have deficiencies and they deserve to be better studied to improve their functionalities.
In the present study, we have chosen to graft a new polymer of modified CDs onto cotton dressings, in order to provide them more functionalities, allowed by the improved complexing capacity of modified CDs and the enhanced properties, as hydrophlicity, of their formed polymer.
CDs are torus-shaped starch derivatives that have the capability of forming ‘‘host–guest” compounds with a wide range of organic molecules, such as fragrances and drugs (EL GHOUL et al., 2008). CDs and their derivatives have been used in the textile domain since the early 1980s (SZEJTLI et al., 1982). The permanent binding of CDs onto textile fibers offers the advantage that the inclusive properties of CDs towards bioactive molecules become intrinsic to the modified fibers (POULAKIS et al., 1992 / DENTER et al., 1996 / MARTEL et al., 2006 / EL GHOUL et al., 2010), and gave rise to a new generation of intelligent dressing textiles which presented enhanced capacities of sorption, encapsulation and delivery of active molecules. Therefore By applying polymer of CDs to wound dressing can offer new properties and give us a medical dressing with added value.

The current paper reports the modification of cotton wound dressings by a new polymer based modified CDs. Firstly we have synthesized and characterized the per-aminated CD and then we have applied a polymer of this CD to cotton dressing samples. After the influence of parameters involved in this specific textile processing such as the curing conditions (temperature, time) and the concentration of modified CDs were investigated. Then, physicochemical characterizations were applied in order to define the presence and the effectiveness of the fiber grafting. Finally the efficiency of our new polymer (polyCTR-CDNH2) was compared with a polymer of native CDs (polyCTR-CD) by evaluating the wettability via the measure of contact angle and by conducting a colorimetric study of treated samples.

2. MATERIALS AND METHODS

The textile samples used for the different grafting tests are woven cotton wound dressings of 20 threads/cm, having a surface weight of 190 g/m². They are a gift from URGO laboratories (France). β-CD was purchased from Wacker Fine Chemicals (Burghausen, Germany). Citric acid (CTR) and sodium dihydrogen hypophosphite (SHP catalyst) were Aldrich chemicals (Saint Quentin Fallavier, France). The textile finishing equipment consisted of a padder and a thermofixation oven. In standard conditions, the impregnating solution consisted of CTR (100 gL^{-1}), catalyst (30 gL^{-1}), and CD (100 gL^{-1}) in water and with the use of ammonium hydrogen phosphate. Fabrics samples were padded and roll-squeezed, dried (30 min at 104°C) and thermofixed (at variable temperatures and times) and finally washed several times. Virgin and treated samples were dried 40 min at 100°C before being weighted. The weight gain of the fabrics (expressed as %-wt) was measured to evaluate the yield of the grafting rate of the textiles by modified CDs (for each point 10 replicates are used).

For the modification of CD and the synthesis of the per-aminated-CD, Chemicals were purchased from commercial suppliers (Sigma-Aldrich society) and used as received in their highest purity. All solvents were used as supplied without further purification, with the exception of CH_2Cl_2 (distilled from CaH_2). Distilled water was used in all experiments. NMR spectra were recorded with Bruker AV300 spectrometer operating at 300 MHz.

Washing tests were conducting in order to check the permanece of the grafting. They were performed according to the standard ISO1 (washing at 40°C during 30 min in presence of 3 gL^{-1} of detergent and 2 $gL^{-1}$of Sodium Carbonate) and ISO3 (washing at 60°C during 30 min in presence of 3 gL^{-1} of detergent and 2 $gL^{-1}$of Sodium Carbonate).

The surface hydrophilicity and wettability of the treated and untreated samples were determined by measurements of contact angles with glycerol liquid that presents a surface tension of 63.4 mJ/m^2. A digidrop image analysis software from GBX was used. Each point is the average of ten measurements.

In order to study the morphology of dressing fibers and thus assess the impact and the evolution of grafting on the surface, we performed a three-dimensional topographic analysis by atomic force microscopy (AFM). We used the Nanoscope.III instrument (version 3.2) to perform topographic images.

The mass spectrometry characterization was performed via the electrospray ionization mass spectrometer. Tested sample is previously well purified and dissolved in a mixture solution of méthanol/water, to be injected into the capillary needle.

Whiteness index of different samples was determined using a spectrophotometer CM3600 from Konica Minolta (D65/10°), at School of High Studies in Engineering (HEI) of Lille, France.

2.1 Synthesis of per-6-azido-β-CD (on one step approach) (Sheme 1)

To a solution of β-cyclodextrin (1 g, 0.88 mmol) in dry DMF (90 mL), NaN3 (6,81g, 88 mmol) was added and the resulting suspension was stirred at 80 °C for 2 h, under N2 pressure. The reaction solution was cooled to room temperature before 6.91 g (26.4 mmol) of PPh3 was added. Then, a fresh prepared solution of CBr_4 (8.76 g, 26.4 mmol) in DMF (10 mL) was rapidly added. The orange-yellow solution was stirred at room temperature for 18h under N2 pressure. Methanol (5 mL) was added to quench the reaction and the product was precipitated by addition of ethanol (300 mL). The filter cake was then washed with ethanol followed by a 7/3 ethanol/water solution. The product was then dried at 60 °C under high vacuum to yield a stable white powder (1.03 g, 90%).

^{1}H NMR (DMSO-d6): < = 3.32 – 3.42 (m, 14H), 3.55 – 3.62 (m, 14H), 3.72 – 3.82 (m, 14H), 4.97 (d, J = 3 Hz, 7H), 5.78 (d, J = 2 Hz, 7H), 5.92 (d, J = 7 Hz, 7H). ^{13}C NMR (DMSO-d6): < = 51.28, 70.17, 72.3, 72.9, 83.4, 102.1. FTIR: (KBr pellet, cm-1) 3363.6, 2112.9, 1659.9, 1155.2, 1051.4. ESI-MS : Calcd for (M+Na+) C42H63O28Na: 1332.41; Found: 1332.52.

2.2 Synthesis of per-6-amino-β-CD (Sheme 1)

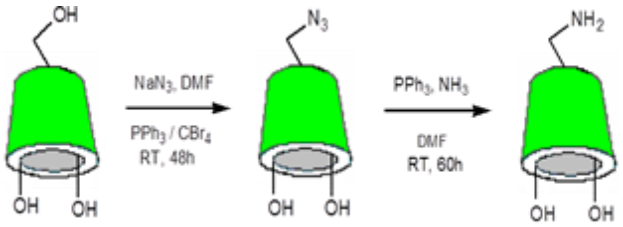
The amino-CD was obtained via the Staudinger reaction or Staudinger reduction. The last mentioned is a chemical reaction in which the combination of an azide with a phosphine or phosphite produces an iminophosphorane intermediate through nucleophilic addition. Combined with the hydrolysis of the aza-ylide to produce a phosphine oxide and an amine, this reaction is a mild method of reducing an azide to an amine. Triphenylphosphine is commonly used as the reducing agent, yielding triphenylphosphine oxide as the side product in addition to the amine.

The heptazide (per-6-azido-β-CD) (153 mmol) was dissolved in DMF (40 mL) and PPh3 (24.2 mmol) was added. The reaction was under N_2. After 2 h, concentred aqueous NH_3 (6 mL approximatively) was added dropwise to the solution. Shortly after the addition of NH_3 solution was complete, the reaction mixture turned to an off-white suspension. It was stirred at room temperature for 24h before the resulting suspension was concentrated under reduced pressure. The product was then precipitate by the addition of EtOH (100 mL). The precipitate was then washed with EtOH and dried under high vacuum to yield a white solid. ^{1}H NMR (D_2O): < = 2.68 – 2.92 (m, 14H), 3.62 (d, 7H), 3.9 (d, 7H), 4.1 (m, J = 3 Hz, 7H), 5.08 (d, J = 2 Hz, 7H). ^{13}C NMR (D_20): < = 40.18, 70.17, 72.3, 72.9, 83.4, 102.

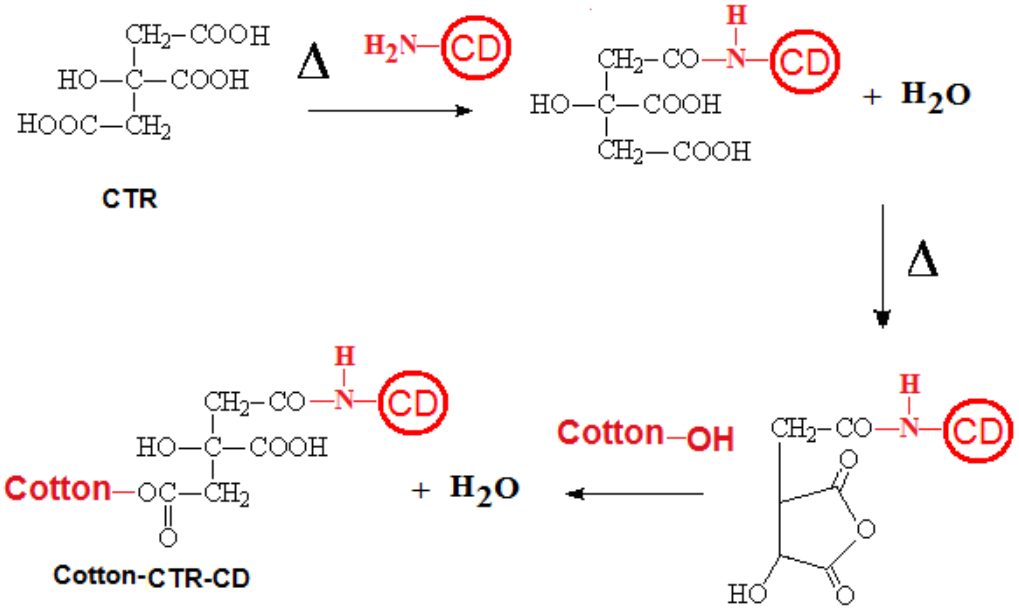
3. RESULTS

3.1 Synthesis of modified CDs and polymers

The hydroxylated per-6-azido-β-CD was prepared by using a one step approach. The native β-CD was reacted with sodium azide and tetrabromomethane in the presence of triphenylphosphine to substitute all the hydroxyl groups on the primary face of CD. After work-up, the well-known per-6-azido-β-CD was isolated as a stable white powder in 90% yield. The per-6-amino-β-CD was then obtained via the Staudinger reduction using triphenylphosphine and a solution of NH_3 (Sheme1). New polymer was then prepared (Sheme2), using the modified CD with an intact secondary hydroxylated face and seven substituted hydroxyl groups by amines functions on the primary face. The polymer was obtained by reacting the modified CD with citric acid and with the presence of ammonium hydrogen phosphate and catalyst (sodium dihydrogen hypophosphite). So it was obtained via a polyamidification (polymer is called polyCTR-CDNH_2).



Scheme 1: Synthesis of Heptakis(6-amino) cyclomaltoheptaose, the modified CD



Scheme 2: Grafting reaction of modified CD onto cotton fibers

3.2 NMR and Mass spectrometry characterization of modified CDs

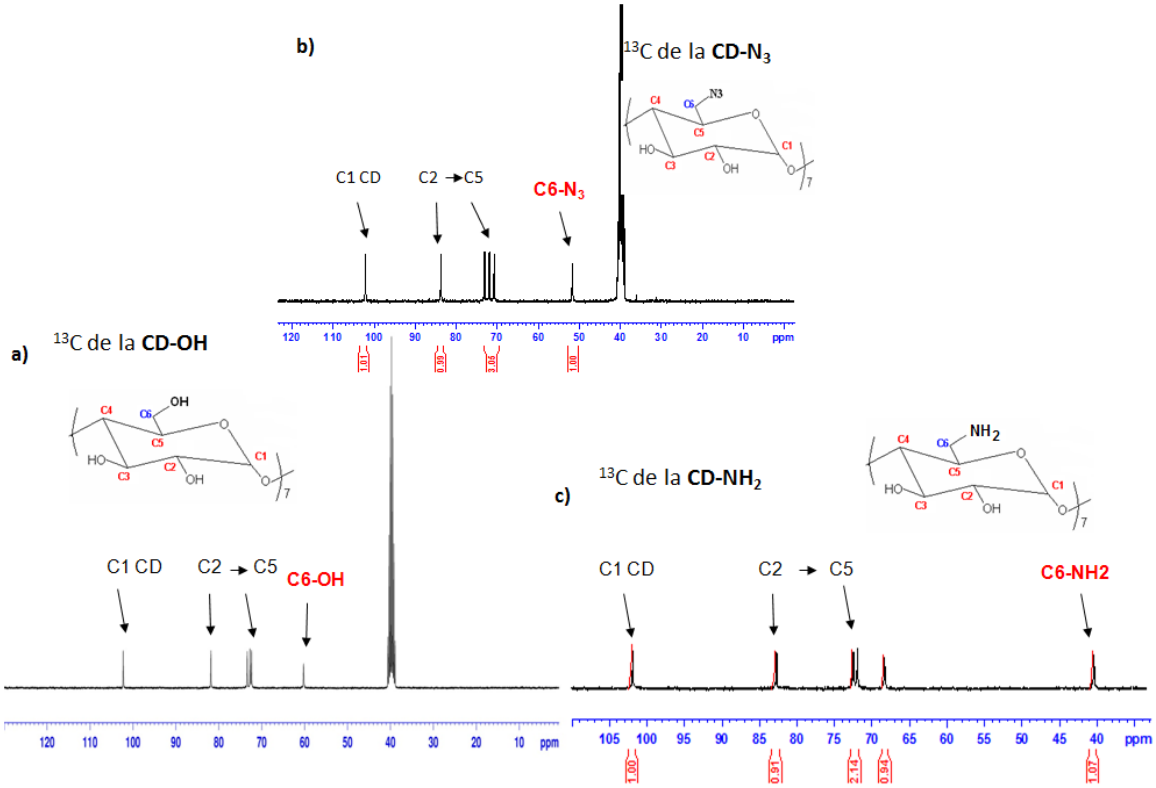


Figure 1: ^{13}C NMR characterization of: a) native CD (in DMSO), b) azido-CD (in DMSO) and c) amino-CD (in D_2O)

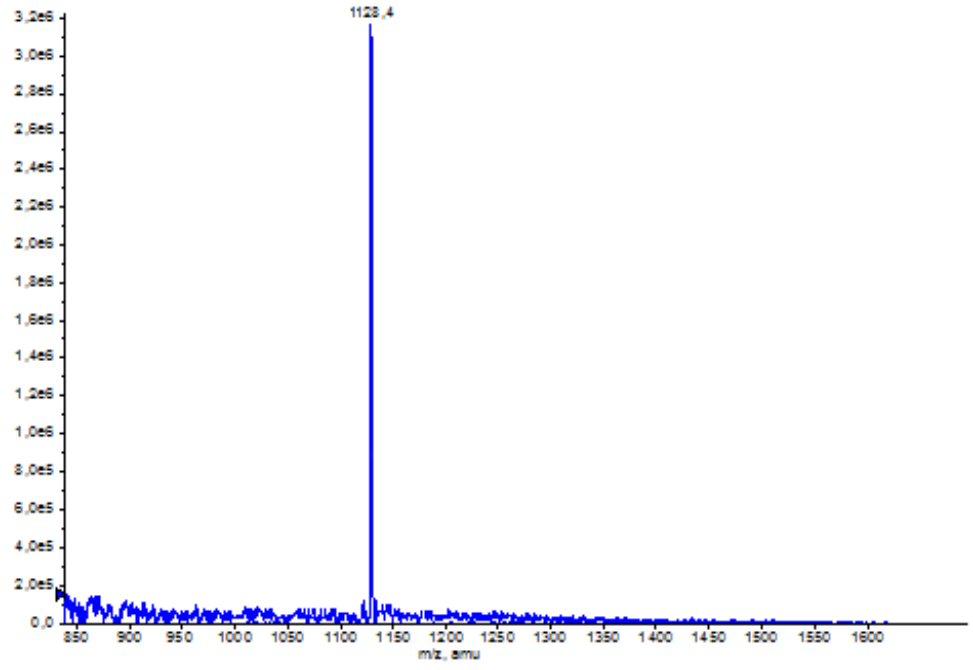


Figure 2: Mass Spectrometry of aminated CD

NMR analyses were conducted in deuterated DMSO for the native and azido-CD, which are soluble only in DMSO or DMF deuterated solvents. Aminated CD is not soluble in DMSO, but soluble only in D2O.

NMR characterization showed the presence of all the picks characteristic of the synthesized CDs. So the evidence of the exact structure was well defined. Quantitative ^{13}C NMR analyze in figure 1, proved the quantitative modification of the cyclodextrin derivative. Firstly, a new important protocol of synthesis of the azido-CD was developed in one step. After we was obtained the aminated CD by substituting the azide groups by the amine ones in the C6 position of the primary face of CD (peak at 51 ppm was substituted by a new peak at 41 ppm us showed in figure 1).

In addition, the mass spectrometry characterization, in figure 2, came to confirm the purity of synthesized per-6-amino-CD and showed that all the seven azide groups in position C6 were substituted by the amine groups. The theory mass is 1128.5 $gmol^{-1}$ and the mass found here is 1128.4 $gmol^{-1}$.

3.3 Preparation of wound dressing samples functionalized with modified CDs

The treatment of wound dressings by the polymer of modified CDs resulted in the weight increase of samples. As there was a weight increase noticed when CTR or CDs were used separately in the treatment of cotton dressings, we deduced that there was a covalent bonding between the fiber and CDs. So, the reaction happened through the polyesterification between CTR and hydroxyl groups of cotton fabric and through the polyamidification between CTR and the 6-per-amino-CDs (Sheme2), to result to the formation of crosslinked polymer. The polymer was covalently bonded to dressing cotton fibers. This functionalization mode was resistant; as we could observe no variation of the grafted samples weight upon different washing standard tests (figure 3).

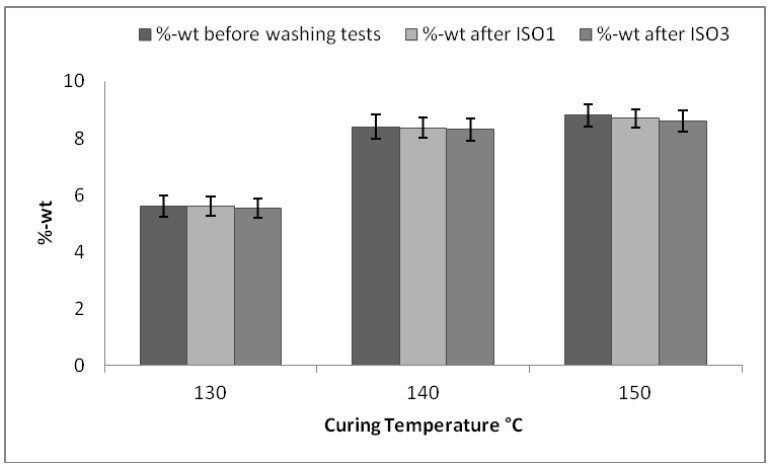


Figure 3: Washing fastness of grafted cotton dressings according to standard tests ISO1 and ISO3

The study of the influence of the variation of time and temperature of curing on the grafting rate allowed us to settle the standard conditions of grafting, which were 140°C during 20 minutes. The study of the variation of the curing time on the grafting rate (figure 4) showed the weight increase of samples according to the duration of fixation. So the grafting rate increased progressively with the curing time. And a pseudo plateau of values was reached at 20 minutes of curing. The same tendency was observed when we varied the temperature of curing (figure 5). The grafting rate increased progressively with the temperature and from a temperature of 140°C we could observe the constancy of the evolution.

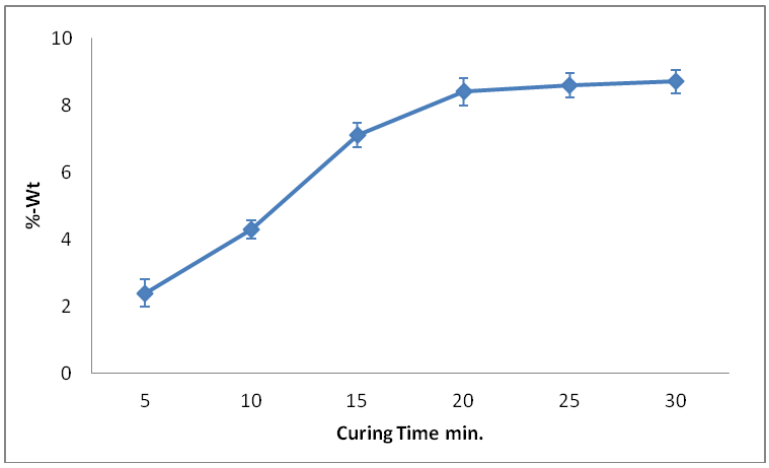


Figure 4: Influence of curing time on the grafting rate of Cotton wound dressing samples; curing at 140°C.

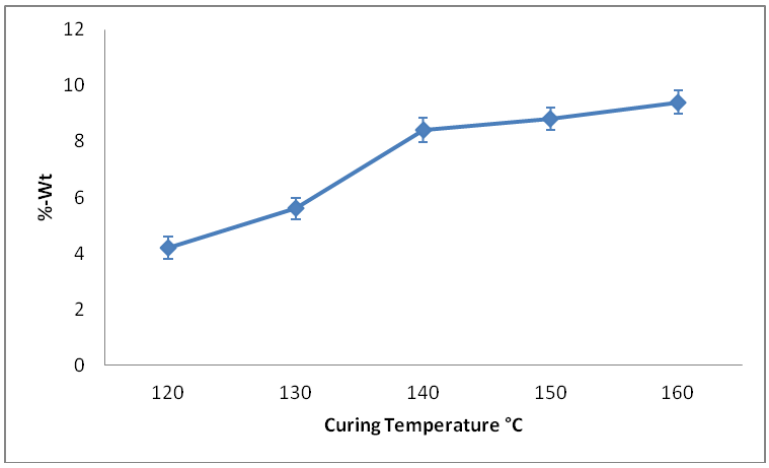


Figure 5: Influence of curing temperature on the grafting rate of Cotton wound dressing samples; curing time 20 min.

The study of the variation of the concentration of the modified CDs with a temperature of curing of 140°C and during 20 minutes permitted us a perfect control of the grafting rate.

As reported in figure 6, the grafting rate of dressing textiles treated with derivative CDs was perfectly proportional to the concentration of the reactants in the impregnating bath. The results showed that the reaction of grafting is easily controllable and that a precise modification rate could be reached by adjusting the impregnating solution and the curing conditions.

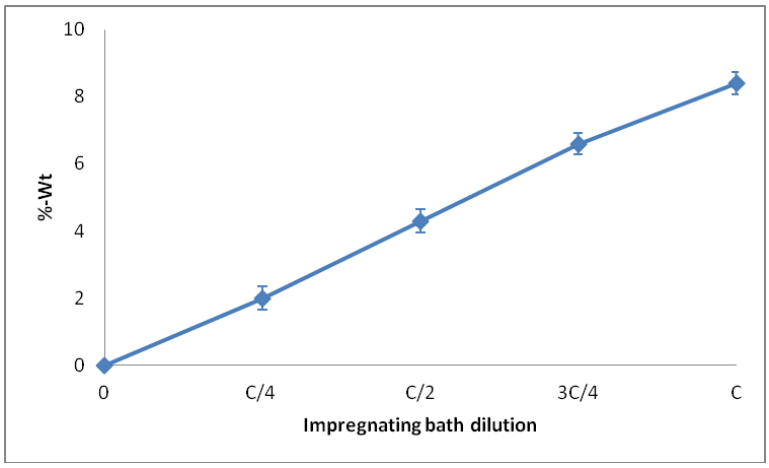


Figure 6: Grafting rate of the dressing samples with modified CD as a function of the concentration of the impregnating solution; [C] corresponds to [CTR] = 100 g L^{-1}, [catalyst] = 30 g L^{-1}, [CD] = 100 g L^{-1}, temperature =140°C and curing time = 20 min.

3.4 Topographic study (AFM)

The topographic study of dressing textiles grafted surfaces was approached by atomic force microscopy (AFM non-contact mode) which enabled us to evaluate the roughness and the chemical heterogeneity of grafted surfaces. As illustrated in figure 7 we noticed a clear modification in the topography of surfaces of the grafted dressing fibers with the polyCTR-CDNH2. This revealed the presence of the modified CDs polymer deposed on the surface and the permanence of the graft even after sever washing cycles.

The image of the virgin fiber, showed a smooth surface with streaks oriented along the axis of the fiber. The calculated roughness of the fiber is low (3.2 nm). However the topographic image of the grafted fiber, has many more bumps, due to the increased presence of CD polymer. The surface has an average roughness of 10.2 nm.

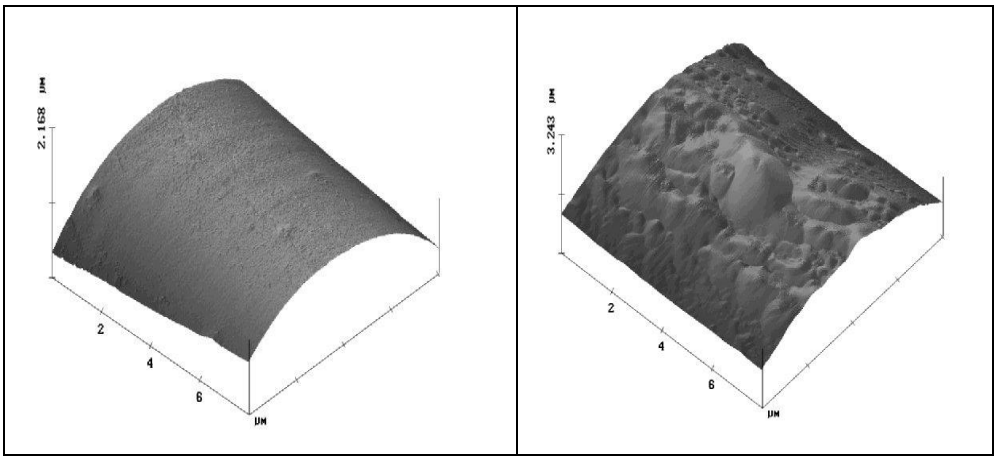


Figure 7: Fibers of virgin (on the left) and grafted (7.6%-wt) dressings observed in AFM

3.5 Contact angle and wettability

The hydrophilicity is a very important property of dressings to be more efficient in the treatment and the cure of wounds. We compare here our polymer of modified CDs with a polymer of native CDs. For the two applied polymers we have used the same condition of temperature and time of curing (140°C during 20 minutes) and we have adjusting the concentration of the impregnating bath to obtain practically the same grafting rates for each measurement of the contact angle.

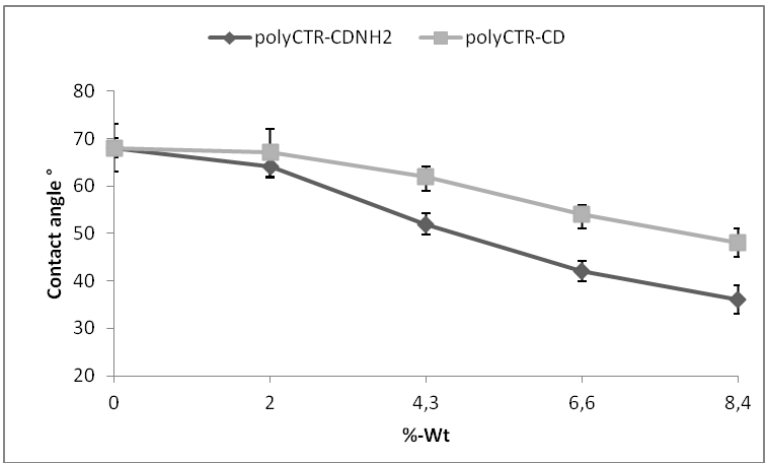


Figure 8: Wetting angles of virgin and grafted cotton dressings with PolyCTR-CDNH2 and PolyCTR-CD according to the grafting rate

Figures 8 reports that for the two polymers, the polyCTR-CDNH2 and the polyCTR-CD, the contact angles decreased with the increase of the amount of fixed CDs. So, the wettability of the treated cotton dressings, increased with the grafting rate. We can notice that the polymer of modified CDs offers more hydrophilicity to the treated dressings compared to the polymer of native CDs. This can be explained by the presence of amine and amide groups in the case of polyCTR-CDNH2.

3.6 Colorimetric study

The treatment of dressing textile with the polymers of CDs and specially the curing conditions can damage the original properties of fibers and causing a yellowing on the textile. Therefore we have conducting a colorimetric study according to the curing temperature to better fixing the different parameters of grafting. The results in figure 8 revealed that the whiteness index decreased slightly and progressively with the augmentation of the curing temperature and especially from a temperature of 160 °C. We can observe that in the case of the PolyCTR-CDNH2 graft, there is no yellowing observed with a curing temperature inferior or equal to 140 °C. But in the case of dressings grafted with the PolyCTR-CD the decrease of the whiteness index is presented form a temperature of 140 °C.

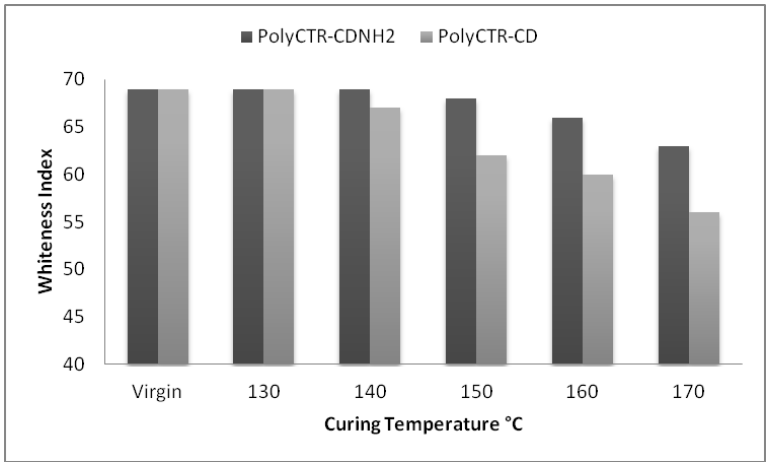


Figure 9: Colorimetric measures of the whiteness index of cotton dressings treated with the PolyCTR-CDNH2 and the PolyCTR-CD, according to the curing temperature

These results in figure 9, show that the polymer of modified CDs caused less yellowing than the treatment with the polymer of native CDs, even with high temperatures of curing. These better results with the PolyCTR-CDNH2 can be explained by the less severe conditions of polymerization in the case of this polymer (nature of reactional medium, pH…), and the use of ammonium hydrogen phosphate, that protect well the dressings from the higher temperature of curing in the case of the new polymer.

4. CONCLUSION

We have first successfully realized a new protocol of synthesis of modified CDs. This modification applied in the optic to polymerise the new CD at more soft conditions compared to the native CD and to have a new polymer with more efficient properties.

This study showed the possibility to finish wound dressing cotton textile with new polymer based primary face modified cyclodextrins.

The study of different parameters permitted us to determine the optimal conditions of grafting. Therefore the grafting rate can be controlled by the curing conditions and by the concentration of the impregnating solution containing the different reactants.

This new polymer grafted to the dressings may offer new properties of encapsulation and permit to obtain amine and amide groups on the textile surface.

The different characterizations of grafted dressing samples showed the permanence of the functionalization and revealed that the graft respected the original properties of the treated samples.

The tests of wetting angles showed a more improved hydrophilicity of dressings treated with the PolyCTR-CDNH2 compared with the case of polymer of native CDs. A very important property sought for medical dressings. In addition the polymer of modified CDs caused less yellowing than the treatment with the polymer of native CDs. The best control of the conditions and parameters of grafting with the new polymer can be so considered as promising way to drug delivery systems that will find multiple applications in the fields of biomaterials and medical textiles.

This succeeded functionalization may offer good new opportunities to dressings to be more effective with high added value. The good results obtained with the new polymer of modified CDs can provide new possibilities to improve the effectiveness of grafted wound dressings. These promising results will be more showed in a next article with a full comparison between the polymer of the modified CDs and the others classical CDs and with an application of antibacterial active ingredient.

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LIST OF ABBREVIATIONS

AFM: Atomic Force Microscopy

CD(s): Cyclodextrin(s)

CTR: Citric Acid

DMF: dimethyl formamide

DMSO-d6: deuterated Dimethyl sulfoxide

D_20: deuterated water

EtOH: Ethanol

FTIR: Fourier transform infrared spectroscopy

NMR: Nuclear Magnetic Resonance spectroscopy

PolyCTR-$CDNH_2$: polymer of CTR and aminated CD ($CDNH_2$)

PolyCTR-CD: polymer of CTR and native CD

SHP: sodium dihydrogen hypophosphite

%-wt: weight gain (grafting rate)

PPH3: triphenylphosphine