A new cyclodextrin-grafted viscose loaded with aescin formulations for a cosmeto-textile approach to chronic venous insufficiency

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Abstract Cosmeto-textile applications can be used in the treatment of chronic venous insufficiency in legs by means of elastic bandages loaded with natural products which possess flebotonic properties. We have developed an efficient synthetic procedure for the preparation of β -cyclodextrin (β -CD)-grafted viscose by means of a 2-step ultrasound-assisted reaction. The highly grafted fabric bearing bis-urethane bridged β -CD has been characterized by ATR-FTIR and CP-MAS spectra and by an empiric colorimetric method which used phenolphthalein as the CD guest. We have also developed a suitable cosmetic preparation containing natural substances and extracts (aescin, menthol, Centella asiatica and Ginkgo biloba) to recharge the CD-grafted textile. The efficacy of the new cosmetotextile has been corroborated by in vitro studies of diffusion through membranes, cutaneous permeation and accumulation in porcine skin. Aescin was taken as a reference compound and its concentration in the different compartments was monitored by HPLC analysis. This cost effective cosmeto-textile shows excellent application compliance and is easily recharged and so has the strong base characteristics needed for possible industrial production.

1 Introduction

A cosmeto-textile is a textile containing a cosmetic preparation, mainly for dermatology applications, that releases bioactive compounds when in contact with the skin [1].

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One of the most interesting applications is the treatment of chronic venous insufficiency in legs by means of elastic bandages loaded with bioactive compounds [2]. One of these compounds is aescin, the main active principle of the horse chestnut tree (Aesculus hippocastanum L.), which has shown marked vasoprotecting, anti-inflammatory and circulation boosting properties [3]. In chronic venous insufficiency, aescin's effectiveness and safety [4] have highlighted it as one of the best approaches to support bandage compression therapy [5]. Cyclodextrins (CDs) are the most effective molecular complexing agents. Their cage-like supramolecular structure enables intra- and intermolecular interactions with molecules or ions in a 'host-guest' interaction. As a result of molecular complexation, CDs are widely used in many industrial fields, in particular in cosmetics and household products [6]. The 1st article to describe the use of CDs in textiles was written in the early 1990s [7]. At that time several papers and patents described their application as an additive for industrial processing and in particular for improved fibre dyeing. CD impregnated and/or chemically grafted textiles have been used for the release of active compounds and perfumes [8, 9]. In 1996, monochlorotriazinyl β -CD (MCT β -CD) was presented by Wacker-Chemie as the first reactive CD derivative to be used for permanent cotton fabric surface modification. Analogously to many reactive dyes, it binds the hydroxyl groups of cellulose chains at high temperature via nucleophilic substitution at the chlorotriazine ring [10]. The relatively low reactivity and the high scaling up cost of MCT β -CD stimulated the search for cheaper cross linkers which went back to the pioneering experiments of Szejtli with epichlorohydrin [11]. Diacid and poly(carboxylic acid) have been used as cross-linking agents to graft CDs to polyamide, cotton and wool fibers [12, 13]. A new bioactive textile material for the treatment of venous insufficiency in legs has recently been described by Nichifor et al. [2]. It is a polyamide grafted with a β -CD derivative that can form inclusion complexes with troxerutin.

The aim of this study is to design an innovative approach to the treatment of venous and lymphatic legs based on a synergic combination of a new fabric: a β -CD-grafted viscose loaded with aescin formulations. To this end, we have developed an efficient synthetic procedure to graft the viscose by means of a 2-step ultrasound-assisted reaction; first with hexamethylene diisocyanate then with native β -CD. We have also developed a suitable cosmetic preparation containing natural substances and extracts (aescin, menthol, *C. asiatica* and *G. biloba*) to recharge the CD-grafted textile. The efficacy of the new cosmeto-textile has been corroborated by in vitro studies of aescin permeation and cutaneous porcine skin uptake.

2 Experimental section

2.1 Methods

2.1.1 Viscose grafting

Two grams of viscose fabric was soaked in an anhydrous DMF (120 ml) and hexamethylene diisocyanate (2 ml) mixture and then sonicated for 2 h with an immersion horn (21.0 kHz, 40 W) while being stirred at 80°C under a nitrogen atmosphere in a 250-ml double-necked flask. The reaction was then stirred at the same temperature for 15 h. The viscose fabric was rapidly washed with DMF (100 ml) and soaked in a solution of β -CD (4.9 g) in DMF (100 ml) in a double-necked 250 ml flask. The mixture was sonicated for 2 h with an immersion horn (21.0 kHz, 40 W) while being stirred at 70°C under a nitrogen atmosphere. The reaction was then stirred at 80°C for 30 min. The viscose product was washed with DMF (2 × 40 ml), water (3 × 50 ml) and acetone (3 × 30 ml) and then dried under vacuum at 80°C for 24 h.

The attenuated total reflectance micro-Fourier transform infrared (ATR-FTIR) spectra were recorded on an ATR-FTIR Nexus Thermo Nicolet spectrophotometer (ν /cm-1): 3300 (-OH,-NH), 2900 (-CH₂-), 1695 (-NH-CO-O-), 1616, 1537, 1362, 313, 1155, 1017, 992.

The CP-MAS spectra were measured on a JEOL GSE 270 (6.34 T) spectrometer operating at 109.6 MHz. Cylindrical 6 mm o.d. zirconium rotors with a sample volume of 120 ml and with a spin rate in the range 5.5–6.0 kHz were employed. In a typical experiment the CP contact time was 3.5 ms and the recycle time 15 s. CP-MAS: 157.9 (-NH-CO-O-), 105.66, 88.2, 83.9, 75.4, 63.3, 42.9 ($-CH_2-NH-$), 31.7 ($-CH_2-$).

2.2 Cosmetic preparation

2.2.1 Aescin/β-CD-inclusion complex preparation

The inclusion complex $\operatorname{aescin}/\beta$ -CD was prepared in a planetary Ball Mill PM 100 (Retsch). A 1:1 $\operatorname{aescin}(20 \text{ g})$: β -CD (20 g) Mol. ratio was used. The powder mix was milled in the presence of EtOH (15 ml) and 70 ml of balls (diameter 0.5 mm). The mixture was grounded at 450 rpm for 30 min and the rotation was reversed after 15 min. The product was separated from the balls and evaporated under vacuum.

2.2.2 Differential scanning calorimetry (DSC)

DSC analyses were performed with a DSC/7 differential scanning calorimeter (Perkin-Elmer, Monza-MI, Italy) equipped with a TAC 7/DX instrument controller. Melting point and heat of fusion calibration was carried out with indium. A heating rate of 10° C min⁻¹ from 50 to 280° C was used. Standard aluminium sample pans (PerkinElmer) were used. An empty pan was used as the reference standard. Analyses were performed under a nitrogen purge and triple runs were carried out on each sample. The weight of each sample (pure aescin, pure β -CD, complex aescin/ β -CD and physical mixture) was kept constant (0.5 mg).

2.2.3 Emulsion preparation

2.2.3.1 Base emulsion The composition of the base emulsion was as follows: water 2,240 g; Carbopol 15 g; imidazolidinyl urea 9 g; mixture of paraoxybenzoathes in fenoxy ethanol 15 g; triethanolamine 99% 15 g; buthylhydroxyanysole (BHT)1 g; dimethicone 15 g; cethylstearyl alcohol 45 g; almond oil 210 g; glycerol 90 g; Umectol (NMF) 45 g; propylene glycol 180 g. Carbopol was dispersed in water by treatment with Ultra Turrax, then glycerol, Umectol and propylene glycol were added. Cethylstearyl alcohol was melted with BHT, dimethicone and almond oil, then dispersed in the aqueous phase with a Silverson homogenizer. The emulsion was cooled at room temperature and neutralized with triethanolamine. The emulsion was added with the mixture of paraoxybenzoathes in fenoxy ethanol and imidazolidinyl urea and homogenized (Silverson).

2.2.3.2 Base emulsion plus $\operatorname{aescin}/\beta$ -CD complex (1 and 2) To this base cream (96 g aliquots) were added different amounts of the $\operatorname{aescin}/\beta$ -CD complex. The resulting mixture was then dispersed by the Ultra Turrax treatment to obtain emulsions with 2.0% (1) and 4.0% (2) $\operatorname{aescin}/\beta$ -CD complex.

2.2.3.3 Base emulsion plus free aescin (3 and 4) To the base cream (50 g aliquots) were added different amounts of free aescin after prior dissolution in H₂O/EtOH 6:4 (2.5 ml). The resulting mixture was then dispersed by the Ultra Turrax treatment to obtain emulsions with 1.0% (3) and 2.0% (4) free aescin.

2.2.3.4 Complete formula emulsion (5) The complete formula emulsion was obtained by adding the following active substances to the base emulsion (percentages refer to the final preparation): escin/ β -CD 1%; Menthol 1.6%; dry *C. asiatica* extract 0.35%; dry *G. biloba* extract 0.35%; Menthyl lactate 0.54%; Umectol (NMF) 1.5%; Tea Tree oil (*Malaleuca* oil) 0.01%. The choice of the components was made on the combined basis of a literature study and our previous experiences in the field [14–16].

2.3 Aescin quantitative analysis by HPLC

The quantitative analysis of β -aescin was performed by HPLC (Waters pump 1525EF, Waters diode array 2967), with a RP-18 column (150 mm × 4.6 mm, 5 µm) and CH₃OH/H₂O (65/35) with 0.1% CF₃COOH as mobile phase. The elution time was 0.1 ml/min, λ max was 219 nm. A standard solution of aescin (98 µg/ml) in EtOH/ water (4:6) was diluted 1:2, 1:5, 1:10 and used for the calibration curve.

2.4 Test of aescin diffusion through membrane

The test was performed using a system with 2 horizontal cells: one for the donor phase (12 ml) and one for the receptor phase (20 ml). The 2 cells are separated by a cellulose membrane, cut off 1200–1400 Da (Spectra/Por CE) and the receiving phase was constituted of water/eth-anol (6:4). The four donor phases tested were: emulsion with $aescin/\beta$ -CD complex 2% (1), emulsion with $aescin/\beta$ -CD complex 4% (2), emulsion with free aescin 2% (4) and the complete formula emulsion ($aescin/\beta$ -CD complex 1%) (5).

Both cells were stirred in the dark for 24 h. The samples were taken out from the receiving phase at scheduled times (after 1.5, 3, 4.5, 6, and 24 h) and the receiving phase was substituted with an equal volume of fresh receiving phase at each of these times. The samples were analyzed by TLC and HPLC. The TLC eluant was a AcCN/water (98/2) mixture with a drop of acetone. Plates were revealed by immersion in sulphuric acid (5.0% in ethanol) and heated on a hot surface.

The results are the mean of 2 different measurements that in all cases are coincident or very close.

2.5 Permeation test and uptake on porcine ear skin [17]

Tests were carried out in vertical Franz cells with donor and a receiving compartments (6 ml is the volume of the latter) and in between a diffusion area of 1.3 and 1.6 cm². A thin layer of skin of about 1 mm, made up of the epidermis and part of the dermis, was obtained through the use of bistouries and of dermatome. This was frozen and stocked at -20° C. At the moment of use the thin layer of skin was defrosted for immersion in physiological solution, dried with filter paper and cut to dimensions suitable for the Franz cells.

The pieces of porcine skin were laid out in such a way that the horny layer was in contact with the donor phase and the dermis in contact with the receiving phase. The mixtures in both cells were stirred for 24 h. At scheduled times all the receiving phase was removed and substituted with a fresh phase. A H₂O/EtOH (6/4) mixture was used as the receiving phase, while the following preparations were used as the donor phase: emulsion with $\operatorname{aescin}/\beta$ -CD complex 2% (1), emulsion with $\operatorname{aescin}/\beta$ -CD complex 4% (2), emulsion with free $\operatorname{aescin} 1\%$ (3), emulsion with free $\operatorname{aescin} 2\%$ (4), complete formula emulsion ($\operatorname{aescin}/\beta$ -CD complex 1%) (5).

Receiving phase samples were removed after 4, 6 and 24 h and analyzed by HPLC in order to evaluate skin permeation. The process to determine aescin uptake on porcine skin was performed at the end of the 24 h. The skin taken from the cell was washed with a physiological solution/EtOH (6:4) mixture dried and cut up. It was then put into a closed bottle containing 5 ml of H₂O/EtOH (6/4) and magnetically stirred for 6 h. The supernatant was centrifuged (20,000 rpm for 15 min) and analyzed by HPLC. This experiment allowed the amount of aescin which accumulates in the porcine skin to be determined. The method used was in accordance with the guidelines published by Diembeck et al. [18]. The results are the mean of three different measurements and error bars are reported in the graph.

2.6 Release of aescin from the CD-grafted viscose fabric

The CD-grafted viscose fabric (0.5 g) was soaked in a H_2O /EtOH (6/4) solution of aescin 4% and magnetically stirred for 3 h. The textile was wringed and placed in a drier under vacuum overnight. The release of aescin from the fabric was evaluated by HPLC analysis. For this purpose, the sample was placed in H_2O /EtOH 6:4 (15 ml) and magnetically stirred for 24 h. Samples (1 ml) were taken after 4, 6, and 24 h and analyzed by HPLC. The results are the mean of 3 different measurements and error bars are reported in the graph.

2.7 In vitro efficacy of CD-grafted fabric compared to pristine viscose

The experiments were performed using a system including 2 glass cells (similar to Franz cells) as depicted in Fig. 1. The upper cell was empty and the receiving cell was filled with H₂O/EtOH 6:4. A membrane of porcine ear skin covered with 1 ml of the $\operatorname{aescin}/\beta$ -CD complex 4% (emulsion 2) emulsion and fabric were placed between the 2 cells. In the 1st test we used the CD-grafted fabric, while in the 2nd we used the pristine viscose. The porcine ear skin had been treated with the same procedure as previously described in the permeation and uptake of aescin section (2.6). Samples of the receiving phase were taken after 4, 6 and 24 h and analyzed by HPLC. An equal volume of solvent mixture was refilled each time. The skin permeation of aescin was determined by HPLC. Aescin uptake by the porcine skin was determined after 24 h as described in 2.6.

At the end of the experiment, the amount of aescin accumulated in the CD-grafted viscose or adsorbed onto the viscose pristine was determined by HPLC after it had been extracted from the cut fabric with $H_2O/EtOH$ 6:4 as previously described for the porcine skin.

This experiment allowed the level of aescin diffusion through skin, in the presence of either the CD-grafted fabric or the pristine viscose, to be evaluated. This test confirmed the higher performance of the CD-grafted fabric. The results are the mean of 3 different measurements and error bars are reported in the graph.

2.8 In vitro efficacy of cosmeto-textile

The fabric was rolled out onto a portion of porcine ear skin with the aim of evaluating the efficacy of the cosmetotextile in terms of skin permeation and the complexation ability of the CD-grafted viscose. The emulsion tested was the complete formula emulsion (emulsion 5). The experiment was performed using the same glass cells (Fig. 1) and

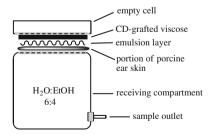


Fig. 1 Two-glass cells system for permeation and accumulation measurements $% \left({{{\bf{n}}_{\rm{s}}}} \right)$

the same procedure as described in the section "in vitro *efficacy of CD-grafted fabric compared to viscose pristine*" (2.8). The results are the mean of 3 different measurements and error bars are reported in the graph.

3 Results and discussion

3.1 Synthesis of β -CD-grafted viscose

In recent years the cosmeto-textiles market has been searching for new CD-grafted materials, with a higher load of CD units, to be used as functional fabrics of all types (socks, girdles, underwear) and for all purposes (antibacterial, slimming, anti-odour, hydration) [19].

In this piece of work we have prepared a model of a viscose fabric bearing covalently bounded CDs which are able to release their active compounds to treat venous and lymphatic insufficiencies of the lower legs. CDs make inclusion complexes with lipophylic molecules which are then gradually released. The 2-step synthesis of β -CD-grafted viscose is depicted in Scheme 1. Diisocyanate mainly reacts with the hydroxyl groups of the fabric that only carry a single functional group, enabling a 2nd reaction with the CDs to form a bis-carbammate aliphatic bridge between viscose fibers and CD units.

The reaction was performed in anhydrous DMF under nitrogen atmosphere. After work up and drying we observed a 13% weight increase over the initial untreated fabric. In accordance with the literature [20], we empirically evaluated the content of bounded CDs to the viscose with a colorimetric method employing phenolphthalein in a 0.1 M sodium carbonate solution. CDs can form inclusion complexes with phenolphthalein, sequestering it from the bath. An UV-Vis analysis of the solution gave an indirect estimation of the amount of CD bound to the viscose. By comparing the absorbance of 2 solutions (20 ml) in which 2 pieces of fabric were soaked, namely plain viscose and β -CD-grafted viscose, we estimated CD loading of about 15% (considering a 1:1 phenolphthalein/CD complex). The β -CD-grafted viscose was characterized by FT-IR analysis. Figure 2 shows 2 superimposed spectra: plain viscose (black line) and β -CD-grafted viscose (grey line). A diagnostic signal for the latter is visible at 1695 cm^{-1} (urethane carbonyl stretching).

The structure was also confirmed by CP-MAS spectra (solid state NMR) by comparing it with the spectrum of pristine viscose (Fig. 3). β -CD-grafted viscose shows characteristic signals at 175.9 ppm (carbamate), 2 signals at 42.9 and 31.7 ppm (aliphatic chain of the bis-carbamate). The absence of the isocyanate (N=C=O) signal at 120 ppm also confirms the complete reaction.

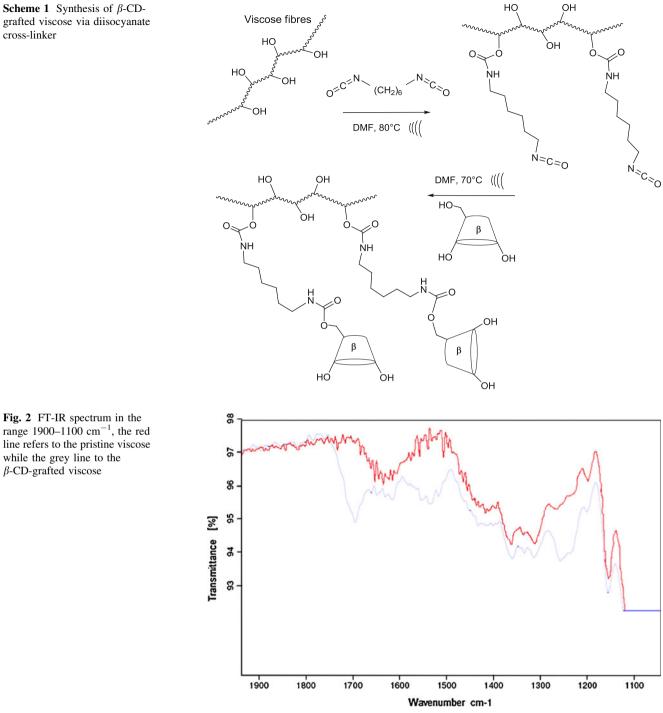


Fig. 2 FT-IR spectrum in the range 1900–1100 cm^{-1} , the red line refers to the pristine viscose while the grey line to the β -CD-grafted viscose

3.2 Studies on cosmetic preparations

3.2.1 Preparation of β -CD/aescin complex

As regards the cosmetic preparation, we prepared the inclusion complexes of β -CD with aescin in order to give the active principle optimal mobility between the emulsion, the fabric and the skin. In accordance with the literature, the formation of the β -CD/aescin complex was confirmed by

¹H-NMR, showing the typical broadened signals which are ascribable to the decrease in the molecular re-orientation time of aescin in the supramolecular adduct. Figure 4 shows 4 DCS thermograms which correspond to the β -CD/aescin complex, their physical mixture and the 2 pure compounds. The thermogram of pure aescin displayed 1 endothermic peak around 225°C while the complex $\operatorname{aescin}/\beta$ -CD did not show any peak. The disappearance of the melting peak in the thermogram of the complex indicated the presence of an

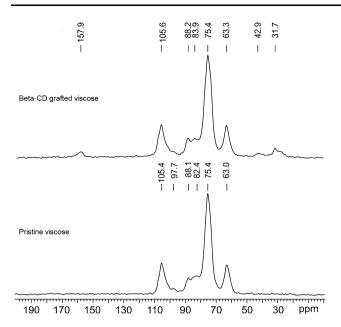


Fig. 3 CP-MAS spectra of β -CD-grafted viscose and pristine viscose

interaction between the 2 species. In the thermogram of the $\operatorname{aescin}/\beta$ -CD physical mixture, the shape and the shift of the peak indicated the existence of a new solid phase in which aescin was dispersed with a lower crystallinity than pure aescin.

Besides aescin, the complete formula emulsion also contained menthol, *C. asiatica* and *G. biloba* extracts as active principles. Due to the fact that aescin can be monitored by HPLC, we focused our investigation on the diffusion of this target molecule through a membrane and permeation through porcine ear skin. A calibration curve was obtained with an aescin standard solution (98 μ g/ml in EtOH/H₂O 4:6) with a series of dilutions 1:2,1:5,1:10.

3.2.2 Test of aescin diffusion through a membrane

The diffusion test showed the effective release of aescin from the different formulations containing the β -CD/aescin complex. As indicated in the experimental section (2.5) the 4 donor phases tested were: emulsion with $aescin/\beta$ -CD complex 2% (1), emulsion with $aescin/\beta$ -CD complex 4% (2), emulsion with free aescin 2% (4), complete formula emulsion ($aescin/\beta$ -CD complex 1%) (5).

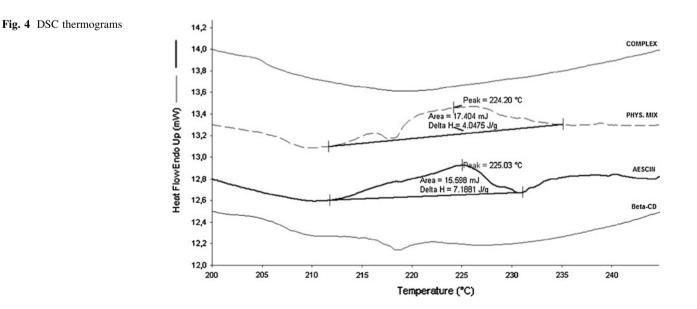
Figures 5 and 6 show gradual aescin diffusion through the membrane after a lag-time of about 90 min. The release is a function of the concentration of the aescin in the donor cell.

In Fig. 6 both emulsions have a lag time of about 90 min, though a more regular release over time can be seen for the emulsion containing $\operatorname{aescin}/\beta$ -CD complex.

3.2.3 Permeation test and uptake on porcine ear skin

This in vitro test was planned to evaluate the cutaneous permeation and the uptake of aescin emulsions, in its free or complexed form, on porcine skin. The previously described emulsions 1–5 [aescin/ β -CD complex 2% (1), aescin/ β -CD complex 4% (2), free aescin 1% (3), free aescin 2% (4), complete formula aescin/ β -CD complex 1% (5)] were tested. To facilitate the HPLC analysis, all tests and measurements were carried out with the emulsions containing aescin as the sole active principle. The values of cutaneous permeation are expressed in $\mu g/cm^2$ and are based on the receiving phase volume and the contact skin surface (Figs. 7, 8).

Only emulsion 4 (free aescin 2%) had permeated the skin 6 h after application: $21.16 \ \mu g/cm^2$ after 4 h and $42.02 \ \mu g/cm^2$ after 6 h (Fig. 7). The highest permeation after 24 h was shown by the emulsions with free aescin (3)



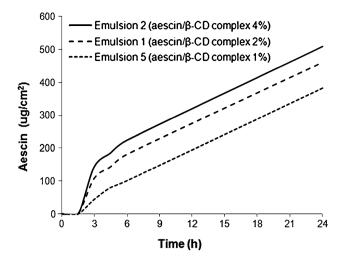


Fig. 5 Test of aescin (β -CD complex) diffusion through membrane

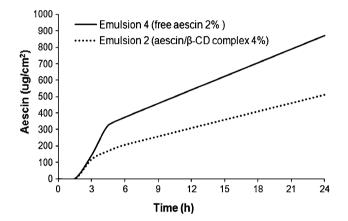
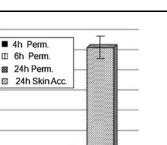


Fig. 6 Test of aescin diffusion through membrane, comparison between free aescin and $aescin/\beta$ -CD complex

and 4) which show roughly double the permeation of the emulsions with the $\operatorname{aescin}/\beta$ -CD complex. This lower permeation corresponds to a higher rate of skin uptake; in fact



50 0 **Emulsion 5** (aescin/β-CD complex 1%)

Fig. 8 Permeation test (4, 6, 24 h) and accumulation (Acc. 24 h) of aescin [complete formula aescin/ β -CD complex 1% (5)] on porcine ear skin

400

350

300

250

200

150 100

AescIn (ug/cm²)

Ш

Ø

the emulsions containing the $\operatorname{aescin}/\beta$ -CD complex (1 and 2) gave higher skin accumulation.

Figure 8 reports the permeation and skin uptake data measured with complete formula $\operatorname{aescin}/\beta$ -CD complex 1% (5). During the first 6 h no permeation was observed, after 24 h the aescin content in the receiving phase was 107.16 μ g/cm² with a skin uptake of 366.29 μ g/cm². This was in accordance with the lower permeation and a higher uptake of the aescin/ β -CD complex observed in Fig. 7. We can conclude that dermatological applications of the complete formula emulsion, can gradually release the aescin with a prolonged effect.

3.2.4 Release of aescin from the CD-grafted viscose fabric

The CD-grafted viscose fabric was charged with aescin via its immersion in a H₂O/EtOH 6:4 solution (25 ml) of known active principle concentration (4%). The ethanolwater solution was evaporated and weighed. The residual amount of aescin in the fabric was calculated by taking the

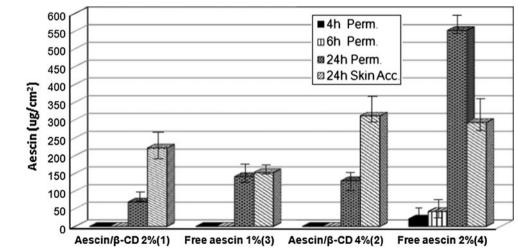


Fig. 7 Permeation test (4, 6, 24 h) and accumulation (24 h) of aescin on porcine ear skin

difference (about the 7–9% of the released aescin). As described in the experimental part (2.7) the re-extracted aescin was quantified by HPLC. The sample of dry fabric was magnetically stirred for several hours in a H₂O/EtOH 6:4 solution. The release of aescin was: 88.99 mg/g after 4 h, 98.27 mg/g after 6 h, and 105.78 after 24 h of stirring.

3.2.5 In vitro efficacy of CD-grafted fabric compared to pristine viscose

The results of the various methods of aescin permeation and accumulation on porcine skin, emulsion 2 alone, with pristine viscose fabric, or with the CD-grafted viscose derivative are reported in Fig. 9. Probably due to an occlusive effect, both fabrics increased aescin permeation through the skin, reducing the skin uptake. Aescin permeation, in the presence of CD-grafted viscose, after 4 and 6 h was lower than with pristine viscose, however after 24 h it was higher. The inclusion properties of the CD-grafted viscose prolonged the release of aescin. As regards the aescin content in the 2 fabrics after 24 h, we observed a higher amount in the CD-grafted viscose (7.9 vs 12.4 µg/cm^2).

3.2.6 In vitro efficacy of cosmeto-textile

We evaluated the cosmeto-textile's capacity to be loaded with active principles and then promote skin permeation and uptake as described in the experimental part (2.8). As shown in Fig. 9, we could reasonably demonstrate that intimate contact with the cosmeto-textile fabric favours the transcutaneous permeation of the aescin, probably due to an occlusive effect, and reduces the skin uptake. This favourable effect should enable aescin to easily reach the site of biological action, namely the blood vessels in the deeper cutis layers.

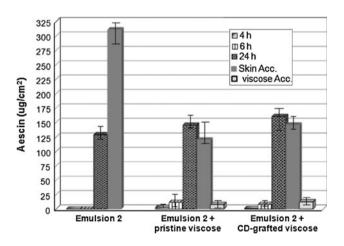


Fig. 9 Aescin (emulsion 2) permeation (4, 6, 24 h) and accumulation on porcine ear skin (Skin Acc. 24 h) and amount of aescin on fabric (Viscose Acc. 24 h)

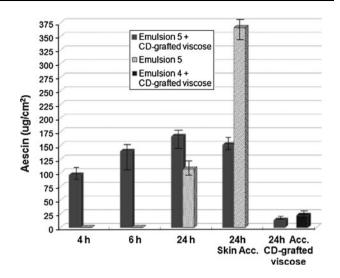


Fig. 10 Aescin (complete formula emulsion, 5) permeation (4, 6, 24 h) and accumulation (Acc.) on porcine ear skin; the *last two bars* of the histogram show fabric the recharge with free aescin released by emulsions 5 and 4 (aescin/ β -CD complex 1% and free aescin 2%, respectively)

In other words, we can speculate that the combined treatment of the CD-grafted viscose fabric and the bioactive emulsion present a synergic effect. The fabric can be considered a slow-release dispenser of flebotonic substances that can act in 2 directions: release or recharge depending on the concentration of aescin emulsion on the skin surface (Fig. 10).

4 Conclusions

In this study we have described a simple synthetic procedure to prepare β -CD-grafted viscose fabric using a diisocyanate cross-linker. As shown by the spectroscopic characterization of the products, this ultrasound-assisted grafting is fast and repeatable. We have formulated a suitable cosmetic preparation to charge the CD-grafted textile. Permeation and accumulation studies on membranes and porcine ear skin showed the advantages of this cosmeto-textile for its potential application in the treatment of venous insufficiency in legs. The low production costs, optimal application compliance and easy fabric recharging lay the foundations for future industrial production. Product compliance and observational studies with a small panel of voluntary women are in progress.

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