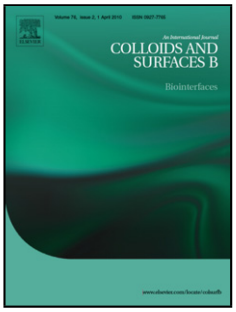

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Surfactant-free and rinsing-resistant biodegradable nanoparticles with high adsorption on natural fibers for the long-lasting release of fragrances

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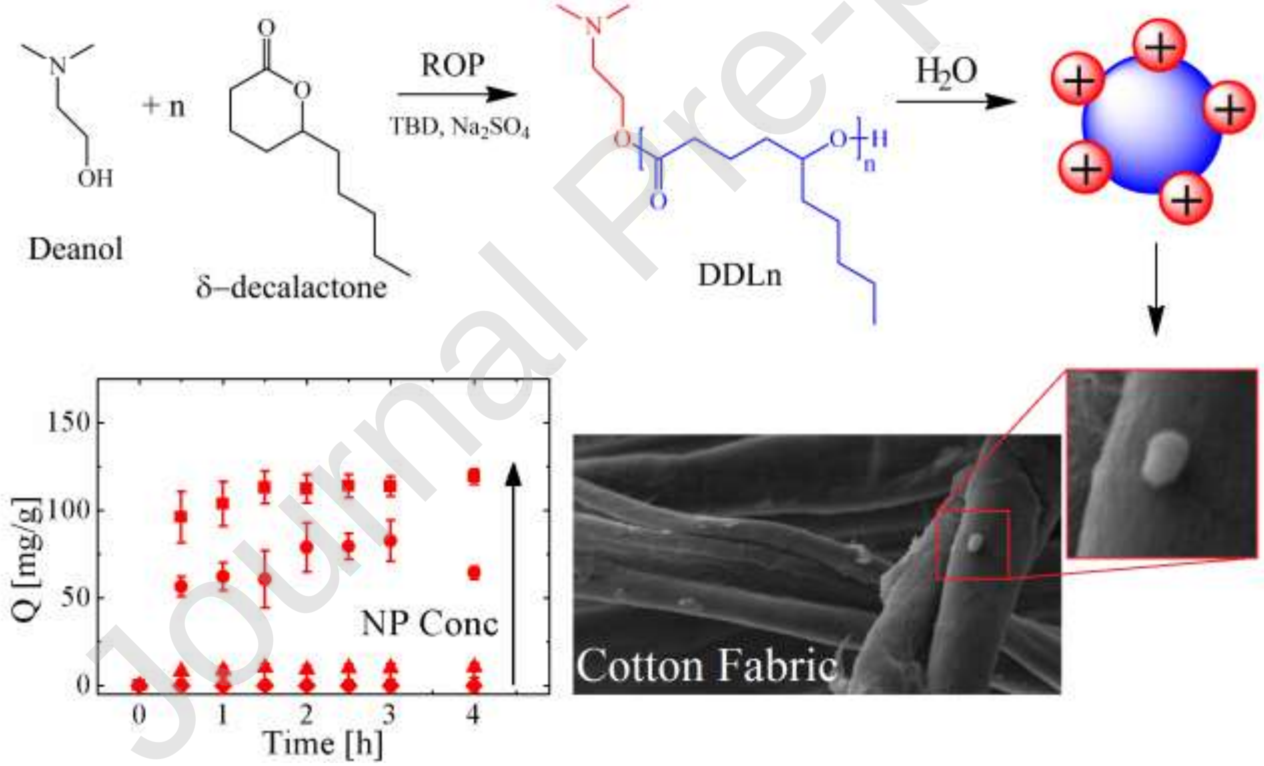

Highlights

- The available excipients for fragrance delivery suffer from poor loading and no degradability
- We synthesized biodegradable nanoparticles (NPs) with fragrance content up to 85% w/w
- The NPs show high adsorption capacity and rinsing resistance on cotton and hair
- The fragrance is slowly released leading to its perception for more than 3 weeks

Abstract: Synthetic polymers are attracting growing attention as additives for laundry and personal care products. In particular, the high volatility of many common fragrances require the development of polymeric particles for their encapsulation and controlled release. Unfortunately, the vast majority of these carriers are made from polymers that are not biodegradable. This poses severe concerns about the accumulation of nano- and microplastics. Hence, such particles are expected to be banned from the market in the coming years. Therefore, biodegradable particles enabling a long-lasting release of the fragrances are urgently needed. In this work, we produced biodegradable nanoparticles (NPs) that are structurally composed of lactones, *i.e.* well known perfumes that occur naturally and that are already considered safe by regulatory agencies. We polymerized these lactones via ring opening polymerization (ROP) using an ionizable tertiary amine as initiator to produce in a single step amphiphilic oligoesters able to directly self-assemble into NPs once nanoprecipitated in water. In this way, we can produce biodegradable NPs with a perfume loading up to 85% w/w without the need for additional surfactants. Subsequently we show that the ionizable group is able to confer a positive charge to our nanoparticles and, in turn, a high adsorption capacity on natural fibers (*i.e.* hairs and cotton fabric). Finally, we demonstrated the nanoparticle resistance to rinsing and their ability to confer a long-lasting fragrance perception to treated hair swatches for at least 3 weeks.

Keywords: lactones; ring opening polymerization; ROP; deanol; adsorption; hair product; laundry; fragrance release

1. Introduction

With a total market value of 500 billion US$ expected by 2020, the field of cosmetics and detergency is rapidly expanding with an average annual growth rate of 3.5-4.5%[1]. The market value for the ingredients is expected to increase even faster and, among these ingredients, a role of growing importance is played by functional polymers. The reason for such success is mainly related to the unique and manifold properties that polymers can impart to the final formulation. Polymers can in fact be used as thickeners, structuring agents, macromolecular surfactants, wetting agents and delivery systems[2].

In particular, the long-lasting release of fragrances is highly desirable for many household products such as detergents and deodorants as well as for personal care products, such as shampoos, conditioners, and moisturizers. However, the high volatility of many common fragrances prevents them from being released slowly over time and causes the active component to be dispersed during the product formulation and storage, both leading to a limited duration of the fragrance perception[3-5]. This is the reason why polymer particles are increasingly employed as carriers for the controlled release of fragrances[6-11]. The incorporation of the fragrance in polymer matrixes can be obtained either physically by exploiting specific polymer-fragrance interactions, such as hydrophobic or electrostatic interactions[12, 13], or by chemically linking the active molecule to a specific functional group on the polymer chain[14-17]. In the former case, the fragrance release is driven by its diffusion through the polymer matrix. However, the process usually suffers from poor encapsulation efficiencies and loading capacities. In the case of a chemical linkage, the release rate is dictated by the kinetic of rupture of the specific fragrance-polymer bond. However, the production of such covalently linked perfumes usually consists of several complex chemical reactions and it results in low yields and high costs.

A common drawback to both the physical and chemical loading strategies is related to the environmental impact of the polymer carrier. Many of the polymers used in cosmetics and laundry are not biodegradable and accumulate in the environment, raising urgent ethical and sustainability questions[18]. In particular, regulatory agencies are expected to completely ban the use of such materials in cosmetic products in the near future[19]. For this reason, there is an urgent need for more environmentally friendly fragrance delivery systems.

Biodegradable particles are starting to appear in literature as a possible solution to these problems[20-23]. As an example, biodegradable polymer nanoparticles (NPs) can be conveniently obtained from polyesters, whose ester bonds are cleaved in aqueous media, leaving behind water-soluble degradation products[24-27]. This is an important feature to avoid the accumulation of micro- and nanoplastics in the environment. Industrially, polyesters are mainly produced *via* the ring opening polymerization (ROP) of cyclic ester monomers or lactones, to overcome the thermodynamic limitations associated with the polycondensation of the corresponding hydroxycarboxylic acids[28, 29].

Lactones in particular are known for their perfume and are largely employed as fragrances. In fact, lactones and their corresponding hydroxycarboxylic acids are approved as food additives for human consumption by the American Food and Drug Administration (FDA)[30]. Remarkable examples are γ-decalactone, which is particularly known for its peach perfume, and δ-decalactone, having a characteristic coconut perfume. However, an extremely large variety of perfumes can be accessed with lactones with different structures, ranging from fruity to floral and creamy perfumes[31-33]. A list of available lactones with the corresponding perfume can be found in ref. [34]. Therefore, a proper selection of the lactone enables to provide the formulation with the desired perfume.

However, lactones are small lipophilic molecules and, for this reason, they need to be loaded in a carrier or transformed into their corresponding hydroxyacids to be formulated in the common aqueous laundry and detergency products. In addition, the diffusivity of such small molecules is high and their long-lasting release is often challenging.

In this work, we take advantage of the possibility of polymerizing these odorous lactones *via* ROP to produce biodegradable oligoesters. In this way, we can slow down and control the release of the perfume by modulating the degradation time of the polymer. In addition, we circumvented the problem of dispersing these highly hydrophobic oligoesters in water-based products by introducing an ionizable group at the end of the polymer chain in order to induce their self-assembly in water. In this way, we are able to directly generate biodegradable NPs with high fragrance loading and without the need for surfactants. More in details, this ionizable group can be introduced in the hydroxyl initiator that is generally required to start the ROP of lactones. This strategy enables to produce the desired polyesters in a single and easily scalable reaction step and with a process that is already well established in the industry. To demonstrate the feasibility of this approach, here we synthesized different ionizable polyesters *via* the ROP of δ-decalactone, known for its coconut perfume. In particular, we synthesized amino-polyesters (APEs) by initiating the ROP with a tertiary amino-alcohol, *i.e.* 2-dimethylaminoethanol (deanol). The tertiary amine of deanol is protonated at neutral pH, leading to a positively-charged ammonium group (pKa = 9.23[35]). We proved the possibility of creating biodegradable NPs by directly dispersing these ionizable polyesters in water. Finally, we showed that our NPs could be adsorbed in high amount on natural fibers (*i.e.* hairs and cotton fabric) with a strong resistance to rinsing and, in turn, that they can assure a long-lasting fragrance release.

2. Materials and Methods

2.1 Materials

2-Dimethylaminoethanol (deanol, MW=89.14, Sigma Aldrich), δ-decalactone (DL, ≥ 98%, MW=170.25, Sigma Aldrich), 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD, 98%, MW=139.2, Sigma Aldrich), sodium sulfate (Na_2SO_4, ≥ 99%, MW=142.04, Sigma Aldrich), benzoic acid (BAc, ≥ 99.5% MW = 122.12, Sigma Aldrich), succinic anhydride (99%, MW=100.07 g/mol, Sigma Aldrich), 4-(dimethylamino)pyridine (DMAP, ≥ 99%, MW=122.17 g/mol, Sigma Aldrich), deuterochloroform ($CDCl_3$, 99.98%, MW=120.38, Sigma Aldrich), sodium hydroxide (NaOH, 0.1 M, MW=40.00, Fisher Chemical), hydrochloric acid (HCl, 1M, MW=36.46, Fisher Chemical) were used without further processing except when specifically noted. All the solvents were of analytical grade purity and used as received. Virgin Caucasian Hair were purchased from Kerling GmbH.

2.2 ROP of DL

The poly(DL)s with controllable degree of polymerization (DP) were synthesized via ROP catalyzed by TBD. Two different initiators were used, deanol and ethanol. For each of them, four target DPs, namely 3, 5, 7 and 9 were selected. For the deanol-DL3 sample (where the number refers to the DP, hereinafter DDL3) for example, 4.26 g of DL (25 mmol) were weighted together with 0.74 g of deanol (8.3 mmol, *i.e.* DL/deanol = 3 mol/mol) in a borosilicate round-bottomed flask equipped with a magnetic stirrer. 170 mg of Na_2SO_4 were added to keep the system anhydrous. The mixture was equilibrated at 25 °C in a water bath. Then, 170 mg of Na_2SO_4 and 0.35 g of TBD (2.5 mmol, *i.e.* DL/TBD = 10 mol/mol) were mixed and added to the flask to initiate the ROP.

In the case of ethanol-DL3, hereinafter EtDL3, 4.26 g of DL (25 mmol) were weighted together with 0.65 g of ethanol (8.3 mmol, *i.e.* DL/ethanol = 3 mol/mol) and 170 mg of Na_2SO_4 in a borosilicate round-bottomed flask equipped with a magnetic stirrer. The mixture was equilibrated at 25 °C in a water bath. Then, 170 mg of Na_2SO_4 and 0.35 g of TBD (2.5 mmol, *i.e.* DL/TBD = 10 mol/mol) were mixed and added to the flask to initiate the ROP.

For both initiators, the reaction was carried out for 24 hours under stirring at 200 rpm and then quenched by adding an excess of a 1 M solution of benzoic acid in chloroform. The oligomer was precipitated twice in a 10-fold excess of cyclohexane to remove the unreacted monomer and catalyst, and finally dried in a vacuum oven at 35 °C overnight.

To produce the succinylated-poly(DL)s, hereinafter SADLn, the EtDLn samples were further reacted with succinic anhydride. More specifically, to obtain SADL3, 3 g of EtDL3 (5 mmol) were dissolved in 50 ml of anhydrous DCM (0.1 M solution) in a borosilicate round-bottomed flask. 0.6 g of succinic anhydride (6 mmol, 1.1 equivalents with respect to EtDL3) and 0.13 g of DMAP (0.11 mmol, 0.22 equivalents with respect to EtDL3) dissolved in 60 ml of anhydrous DCM were added to the flask and the reaction let to occur at room temperature overnight. The product was then washed three times with 150 ml of a 0.1 M HCl solution, concentrated under reduced pressure and finally dried at 35 °C in a vacuum oven overnight.

All of the synthesized oligomers were analyzed via proton-nuclear magnetic resonance (^1H NMR) operated on a Bruker Ultrashield 400 MHz spectrometer in $CDCl_3$ to assess the DP and the monomer conversion (analysis was performed before and after purification). The molecular weight distributions (MWDs) of the oligomers were measured via gel permeation chromatography (GPC). The separation was performed at 1 ml/min and at 35 °C using tetrahydrofuran (THF) as mobile phase. The instrument (Jasco series) is equipped with three styrene/divinyl benzene columns (Polymer Standards Service) in series each with particle size of 5 μm and pore size of 1000, 10^5 and 10^6 Å, respectively (length 300 mm and internal diameter 8 mm) as well as a pre-column (8x50 mm). The sample was dissolved in THF at a concentration of 5 mg/ml and filtered using a 0.45 µm pore-size polytetrafluoroethylene membrane before injection of 30 µl. Polystyrene standards were used to calibrate the system.

2.3 Nanoparticle self-assembly and adsorption study

The polymer NPs were self-assembled from the corresponding bulk oligoester by nanoprecipitation. 200 mg of oligomer were dissolved in 2 ml of dimethyl sulfoxide (DMSO) and added with a flow rate of 2 ml/h using a syringe pump (New Era Pump Systems, NE-300) to 100 mL of deionized (DI) water kept under stirring at 500 rpm. The NP suspension was then dialyzed against 1 L of DI water for 48 h with frequent water changes. The particle size distribution was assessed via dynamic light scattering (DLS), performed on a Zetasizer Nano ZS (Malvern Instruments).

Adsorption and desorption studies were then conducted on either virgin Caucasian hair swatches or fabric with composition 77% cotton, 21% polyamide, 2% elastane to determine the NP interaction with different surfaces. In the former case, before the loading test, the hair swatches were soaked in a 10% w/w sodium dodecyl sulphate (SDS) solution for 10 minutes and massaged for 30 seconds. Then, the swatches were rinsed in tap water, squeezing them along the full length between two fingers, until the surfactant is removed. The hairs were left overnight in an ethanol-water solution 50% v/v and rinsed again with water, to eliminate all the ethanol, and finally dried. On the other hand, fabric was used as received.

Samples of 0.4 g of either hair or fabric were weighted in a glass beaker and soaked in 30 ml of NP suspension at different concentrations, namely 20, 200, 1000 and 2000 ppm. Aliquots were withdrawn periodically and the light absorbance of the sample was measured at 500 nm on a Jasco V-630 UV/Vis spectrometer. The NP concentration in the liquid was related to its absorbance after calibration with samples at known concentration. The amount of adsorbed NPs normalized with respect to the amount of substrate (Q) was calculated according to Equation 1[36].

$$Q(t) = \frac{V[C_0 - C(t)]}{m_h} \tag{1}$$

Here, V is the volume of the liquid, C_0 the initial NP concentration, C(t) the NP concentration measured at time t and m_h the mass of substrate in the experiment. The NP stability during the experiment was assessed by monitoring their size via DLS. Almost constant sizes confirmed the validity of the calibration curve for the duration of the experiment.

A similar procedure was adopted to measure the NP desorption from the substrate. In this case, the pre-loaded substrates (*i.e.* textile or hair previously treated with the 2000 ppm NP suspension for 5 h) were soaked in DI water and the NP concentration in the liquid monitored by UV-Vis adsorption over time.

All of the experiments were conducted in triplicate.

After the loading experiment, the hair swatches or fabric sample were dried at 45 °C under a flow of air for 1 h. Scanning electron microscopy (SEM) was conducted to visualize the NPs adsorbed on the substrate. Micrographs were taken at an electron high tension (EHT) of 10.00 kV on a Zeiss EVO 50 XVP microscope at a magnification of 2.5kX.

2.4 Perception test

The hair swatches loaded with DDL3, DDL5 and SADL5 NPs, after drying for 1 h under a flow of air at 45 °C, were used for a perception test on a group of 50 volunteers as evaluators, following the principles of the dynamic olfactometry. The evaluators were asked to rate the odor intensity of the sample according to the odor intensity scale reported in **Table 1**[37].

Table 1. Odor intensity scale used to evaluate the coconut perfume released from the oligoester NPs adsorbed on hair over time. Adapted from [37].

Odor Intensity	Rate
Not perceptible	0
Weak	1
Distinct	2
Strong	3
Intolerable	4

After the evaluation, the hair swatches were soaked in 30 mL of water with 2% w/w of SDS, massaged for 30 seconds, rinsed with DI water, dried for 1 h under a flow of air and stored for the successive evaluation, carried out after one week. The test was kept blind in order to avoid any bias on the judgment process.

As a control, we performed the same test also on hair washed with a solution of the hydroxycarboxylic acid of δ-decalactone (DL-HCA). To obtain DL-Ctrl, 1 g of DL was dissolved in 20 mL of a 1 M NaOH solution and left under magnetic stirring (300 rpm) at 50 °C overnight. The pH of the solution was lowered to 3 by adding a 5 M HCl solution and the product extracted twice in 20 mL of DCM. Finally, the organic solvent was evaporated under vacuum and the product dried in a vacuum oven at 35 °C overnight. Hairs were then loaded with DL-Ctrl as reported in Section 2.3 and subjected to the perception test.

2.5 Degradation study

The degradation of the oligoester-based NPs was studied under accelerated degradation conditions (1 M HCl solution) by tracking the relative scattering intensity during time at the DLS. The samples were incubated at 37 °C and DLS measurements were taken every 15 minutes. The half-life for the NPs was assumed as the time leading to the 50% of the scattering intensity compared to the value measured at time zero.

3. Results and Discussion

3.1 Synthesis of surfactant-free biodegradable NPs with high fragrance loading.

First, we aimed at synthesizing biodegradable oligoesters structurally composed of a fragrance. With this goal in mind, we performed the ROP of the δ-decalactone, which is a well-known perfume. We used deanol as initiator to include in the final oligomer an ionizable functional group that could induce its direct self-assembly into NPs once dissolved in water (**Figure 1a**).

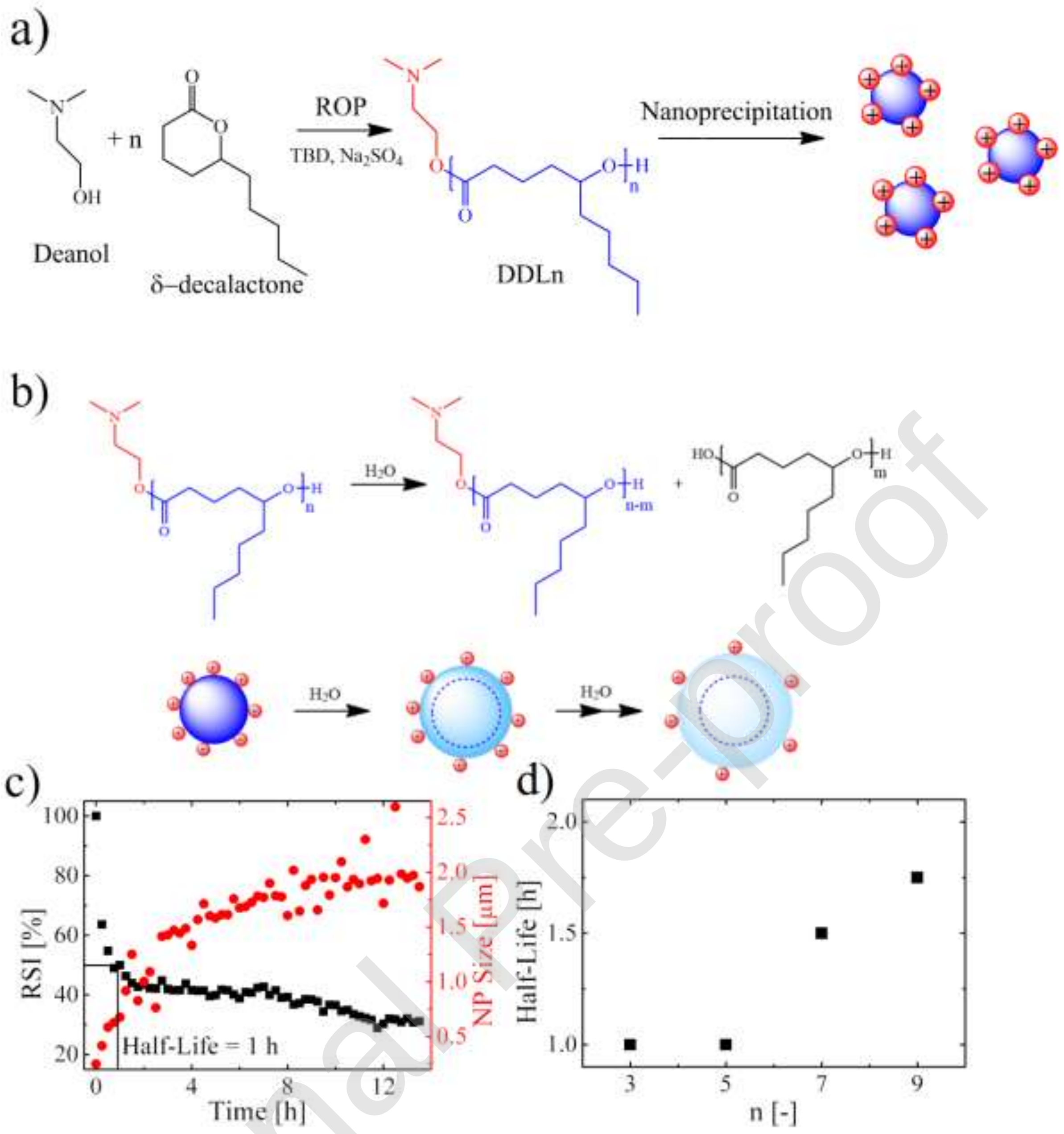

Figure 1. (a) Schematic representation of the synthesis of biodegradable DDLn functionalized with an ionizable group enabling their self-assembly in water. (b) Sketch of the degradation process of DDLn, with the hydrolysis of the ester bonds that is accompanied by the NP swelling in water and ultimately by disappearance. (b) Accelerated degradation monitored via DLS by tracking the NP size (●) and scattering intensity normalized with respect to the initial value (RSI) (■) for the DDL5 NPs as an example. (c) Half-life as a function of the number of monomer units (n). This parameter was calculated as the time leading to the 50% of the relative scattering intensity.

In particular, we synthesized four ionizable oligomers with different molecular weights by varying the monomer to initiator mole ratio (*i.e.* DDLn with n = 3, 5, 7, and 9, see **Table 2**). We tracked the evolution of the average degree of polymerization (DP = n) and monomer conversion during the ROP of these samples *via* ^{1}H NMR (see **Figure S1**). These parameters were computed according to **Equations S1 – S2**. The reaction reached high monomer conversion (*i.e.* > 83%) and the designed DP already after 5 h (**Figure S2**), confirming the feasibility of the process on an industrial timescale. Narrow molecular weight distributions were also obtained for these oligoesters, as expected from a living polymerization (see **Table 2**). In addition, the number average molecular weight (Mn) is a linear function of the mole ratio between the monomer and the initiator adopted in the polymerization (**Figure S3**), according to **Equation 1**.

$$Mn = M_I + DP * \chi * M_M = M_I + \frac{[M]}{[I]} * \chi * M_M \tag{1}$$

Where, χ is the conversion and M_M, M_I, [M], and [I] are the molecular weights and concentrations of the monomer and the initiator, respectively.

These factors confirm the good control of the ROP, which enables to obtain well-defined oligomers with tunable molecular weight in a single reaction step. This is important in the optic of ensuring a uniform fragrance release, especially when the active molecule is the product of the degradation of the polymer chains[38].

The synthesized oligoesters were then self-assembled into NPs directly in water *via* nanoprecipitation and without the need for any surfactant. We were able to obtain narrowly dispersed NPs with an average size that increases with the DP (**Table 2** and **Figure S4**). In order to demonstrate the importance of the deanol in the dispersion of these polylactones in water, we synthesized analogue oligomers without any ionizable group, using ethanol as the initiator in the ROP (EtDLn series with n=3, 5, 7, 9 in **Table 2**, reaction scheme in **Figure S5a** and full characterization in **Figure S5b** and **Equations S3 – S4**). As expected, the EtDLn series led to stable NPs only at the smallest DPs and at high dilution, while only large aggregates were obtained at DP equal to 7 and 9. These results demonstrate that the ionizable amino group is necessary to provide stabilization to the forming NPs. In fact, the ionizable group at the chain-end of each oligoester is charged at neutral pH, as confirmed by the positive surface ζ-potential of the NPs (**Table 2**). Therefore, it is expected to be exposed to water providing electrostatic stabilization to the NPs while the hydrophobic oligoester chains are expected to be confined in the NP core.

Table 2. Characterization of the synthesized oligoester samples. Conversion after 5 h (χ_{5h}) and mean degree of polymerization after 5 h (DP_{5h}) were measured via ^1H NMR. The number average molecular weight (Mn) and dispersity (Đ) were evaluated via GPC. The NP size, polydispersity index (PDI) and surface charge (ζ-pot.) were obtained via DLS.

Sample	χ_{5h}[a] (%)	DP_{5h}[a] (-)	*Mn*[b] (Da)	*Đ*[b] (-)	*NP size*[c] *(nm)*	*PDI*[c] (-)	*ζ-pot.*[c] (mV)
DDL3	85	2.64	1000	1.3	160±4	0.15±0.01	+12±3
DDL5	87	4.83	1500	1.4	220±10	0.14±0.01	+13±5
DDL7	88	6.69	2100	1.5	250±20	0.31±0.03	+14±4
DDL9	83	8.09	2700	1.4	270±15	0.35±0.02	+13±3
EtDL3	87	3.12	1100	1.3	380±40	0.5±0.1	
EtDL5	91	4.91	1600	1.4	310±45	0.35±0.1	
EtDL7	89	6.3	2000	1.3	Large aggregates		
EtDL9	85	8.51	2300	1.2	Large aggregates		
SADL3	>99[d]	3.12	1400	1.3	170±10	0.24±0.05	-40±5
SADL5	>99[d]	4.91	1700	1.4	280±15	0.32±0.03	-53±9
SADL7	>99[d]	6.3	2000	1.4	270±30	0.35±0.1	-67±8
SADL9	>99[d]	8.51	2300	1.3	380±10	0.25±0.01	-57±7

[a] Measured from ^1H NMR using chloroform-d3 as solvent

[b] From GPC

[c] From DLS

[d] After succinylation of the corresponding EtDLn

Overall, our strategy allows producing stable NPs without the need for surfactants and with a fragrance loading higher than 85% w/w, determined as the weight of the lactone units over the weight of the oligoester chain.

In addition, the chains that compose the nanoparticles are amenable to hydrolysis in aqueous media. Therefore, we expect the NPs to be progressively degraded into water-soluble by-products, as schematically depicted in **Figure 1b**. Hence, besides enabling the controlled release of the fragrance, the degradation ultimately prevents the NP accumulation on the substrate and, in turn, in the natural environment. In particular, the degradation rate is proportional to the number of ester bonds present in the polymer chain and therefore easily controllable by manipulating the length of the polymer chain (*i.e.* the DP) during the ROP[38].

To demonstrate that we can achieve control over the NP degradation time also with our system, we studied the degradability of our NPs under accelerated degradation conditions (*i.e.* 1 M HCl) by tracking the NP size and the relative scattering intensity (RSI) over time *via* dynamic light scattering (DLS). RSI is a function of the NP size and concentration, and therefore represents a useful parameter to conclude about the NP progressive dissolution as the degradation proceeds[39-41]. As shown in **Figure 1c** for the DDL5 NPs, the NP size increases over time from 250 nm to few micrometres. This is the result of the progressive hydrolysis of the oligoester chains constituting the NP core. Consequently, its hydrophobicity is progressively reduced, thus leading to the NP swelling. On the other hand, the scattering intensity decreases rapidly over time. Since this is proportional to the sixth power of the NP size[42, 43], which is growing, the only explanation for such decrease is the NP dissolution.

The degradation time of the NPs composed of oligoesters with different DPs can be compared by considering their half-life, *i.e.* the time necessary to reach the 50% of the initial scattering intensity. As shown in **Figure 1d**, this parameter increases with the DP, thus confirming the possibility of controlling the degradation time by acting on the oligomer length.

3.2 NP adsorption on natural fibers and resistance to rinsing.

With biodegradable NPs structurally composed of fragrances in our hands, we proved their ability to adsorb on natural fibers (i.e. hairs and cotton fabric) and, subsequently, their ability to resist to rinsing under "washing mimic" conditions. This is pivotal in the employment of this type of formulations in common detergency and laundry products to provide long-lasting perfume.

Towards this goal, we intentionally selected a tertiary amine as ionizable functional group for the direct self-assembly of our oligoesters in water to confer an overall positive charge to the biodegradable NPs. In fact, it is widely known that natural fibers, despite their heterogeneity, exhibit globally negative surfaces. As an example, cotton fabrics exhibit a surface ζ-potential that is highly negative (*i.e.* ~ -25 mV), with an isoelectric point around 2.9[44]. This is the reason why the most common finishing products for textiles often comprise cationic surfactants and/or polymers[45-47]. For this reason, we expect a higher adsorption on these substrates with positively charged NPs. In order to prove the importance of the NP charge and validate the design of our NPs, we synthesized similar oligoesters with an ionizable carboxylic functional group (pKa = 4.3[48]). This functional group was provided by succinylation of the EtDLn series with succinic anhydride (SADLn series in **Table 2**, see reaction scheme in **Figure S6a** and a full characterization in **Figure S6b**). Similarly to the DDLn series, we nanoprecipitated these oligoesters in water to form negatively charged nanoparticles. Then, we compared the amount of adsorbed positively and negatively charged NPs on natural fibers by tracking the NP concentration in the liquid phase in contact with the substrate by UV-Vis absorbance. With this respect, a significant contribution to the measurement is given by the light scattering operated by the NPs. Hence, for a reliable analysis, it is essential that the NPs preserve the same size over the experiment. This is what we observed for the negatively charged NPs (SADLn) and the positively charged NPs composed of the oligoesters DDL3 and DDL5 (**Figure S7**). In contrast, the NPs composed of DDL7 and DDL9 showed an increasing size during the experiment, thus testifying that some destabilization occurred in contact with the natural fibers. Therefore, the adsorption in the case of both cotton fabric and hairs was studied only for the samples DDL3 and DDL5 and the corresponding SADL3 and SADL5.

We first explored the adsorption on cotton fabric by investigating the evolution of the amount of adsorbed NPs per unit mass of substrate (Q) over the first 4 hours. We observed a striking difference between the adsorption of positively charged (DDL3 and DDL5) NPs and that of negatively charged NPs (SADL3 and SADL5), as shown in **Figure S8**. While the former reach more than 120 mg/g of adsorbed NPs, the adsorption of negatively charged NPs on fabric was very poor (~ 5 mg/g). These results were in agreement with what we expected. Therefore, the functionalization of our oligoesters with a tertiary amine is crucial not only for enabling the dispersion of the oligoesters in aqueous media, but also to promote their adsorption on fabric.

Given the much higher adsorption of NPs from DDLn oligoesters, we went into more details in their study. In particular, the adsorption kinetics at different NP concentrations in the suspension are reported in terms of Q over time in **Figure 2a** for DDL3 NPs and in **Figure 2b** for DDL5 NPs. In both cases, the adsorption equilibrium is reached within the first 4 h. Such a long time can be explained with the slower diffusivity of polymer NPs compared to small molecules[36, 49]. However, it is worth mentioning that after 45 minutes, considered as a reference washing time[50], the amount of adsorbed NPs is already more than 40% of the equilibrium value for DDL3 and more than 60% for DDL5. This confirms the suitability of the synthesized NPs for application in conventional washing processes.

The amount of adsorbed NPs increases with their concentration in the liquid phase, reaching values up to 75 mg/g in the case of DDL3 and 140 mg/g for DDL5. Hence, DDL5 NPs provided enhanced adhesion to the fabric substrate, as confirmed by the adsorption isotherm reported in **Figure 2c**. It is possible to observe that the isotherm is favorable for the DDL5 NPs, with a high adsorption capacity that is not reached in the experimental concentration range investigated in this work. On the other hand, the adsorption isotherm for DDL3 NPs is unfavorable at low concentrations, with an upward concavity, while becoming favorable at approximately 0.2 mg/ml. In this case, the adsorption capacity of ~70 mg/g is reached at 0.3 mg/ml.

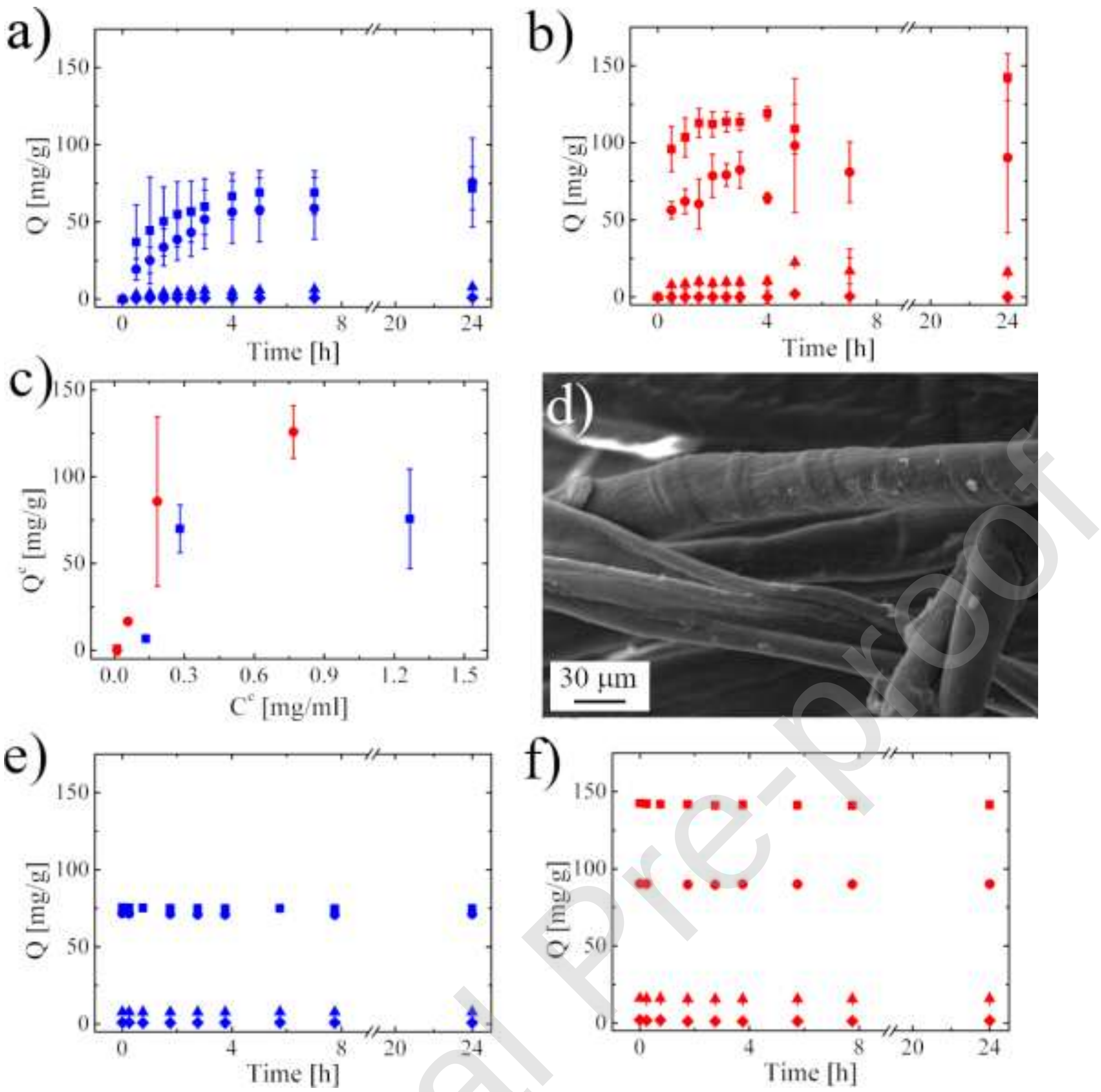

Figure 2. Specific amount of adsorbed NPs over time for DDL3 NPs (a) and DDL5 NPs (b). The measurement was performed at different NP initial concentration in the liquid phase, namely, 20 ppm (♦), 200 ppm (▲), 1000 ppm (●) and 2000 ppm (■). (c) Adsorption isotherm reporting the amount of adsorbed NPs (Q^e) in equilibrium with the liquid phase (C^e) for DDL3 (■) and DDL5 (●) NPs. (d) Micrograph of the fabric after washing for 1 h with DDL3 NPs at 1000 ppm. Desorption kinetics for DDL3 (e) and DDL5 (f) NPs. The measurement was performed with the samples loaded at 20 ppm (♦), 200 ppm (▲), 1000 ppm (●) and 2000 ppm (■).

A visualization of the adsorbed NPs on fabric is shown in the SEM micrograph reported in **Figure 2d**. This was obtained after washing the fabric with 1000 ppm of DDL3 NPs for 1 h. Spherical NPs can be observed on the fiber surface, thus confirming the physisorption of the NPs.

Finally, after loading the fabric samples with the NPs, their desorption in fresh water was studied over time (**Figure 2e, f**). Actually, a very low amount of NPs desorbed from the surface, probably due to the strong electrostatic interaction between the negative fiber surface and the positive NP surface. This resistance to rinsing is important to grant sustained fragrance release for a prolonged time.

A similar adsorption study was performed using pre-cleaned hair swatches as substrate to demonstrate that our polylactone-based formulation can be also used for the controlled fragrance release in personal care products.

As in the case of the fabric, we compared the adsorption performances of negatively charged and positively charged NPs (**Figure S9**). In agreement with what seen for the fabric, the cationic NPs were able to adsorb on the hair surface in higher amounts compared to their anionic counterparts. In fact, albeit heterogeneous and prone to modification following repeated treatments with quaternary ammonium surfactants present in the conditioners[51], the surface of hair is overall anionic[52, 53]. Therefore, the amino-oligoesters proved to be once more the top candidates among the synthesized samples for the controlled fragrance release in hair care products.

As already shown, also in the case of hair, the amount of adsorbed NPs per unit mass of substrate increases with the NP concentration in the liquid phase (**Figure 3a**). The equilibrium is reached in the first 3 h. However, also in this case, after 20 minutes the amount of adsorbed NPs is already more than 25% for DDL3 and more than 50% for DDL5 of the equilibrium value. This confirms that a suitable amount of NPs can be adsorbed on hair in typical washing conditions. In addition, in this case, the amount of adsorbed NPs is not significantly influenced by the length of the oligoester chains, with similar equilibrium capacities of 140 mg/g (**Figure S10**).

3.3 Perception test

Finally, to demonstrate the long-lasting release of perfume from the hair treated with the DDL NPs, a perception test was carried out by 50 volunteers following the principles of the dynamic olfactometry[54-56]. The volunteers were asked to evaluate the hair treated with DDL3, DDL5 and the hydroxycarboxylic acid of DL (DL-HCA) as control based on the odor intensity scale reported in **Table 1**. From **Figure 3b,** it is possible to observe that the perfume perceived from the hair treated with DL-HCA rapidly decayed to “not perceptible” after 2 weeks. On the other hand, the perfume from the hair treated with the NPs exposing the amino group on the surface (DDL NPs) was perceived for the whole duration of the experiment. In addition, this is maintained in the region of strong odor intensity (green band in **Figure 3b**) for more than two weeks. These evidences confirm that our positively charged NPs allow retaining the perfume perception even after extensive rinsing and for at least 3 weeks, with an improvement with respect to the pure perfume.

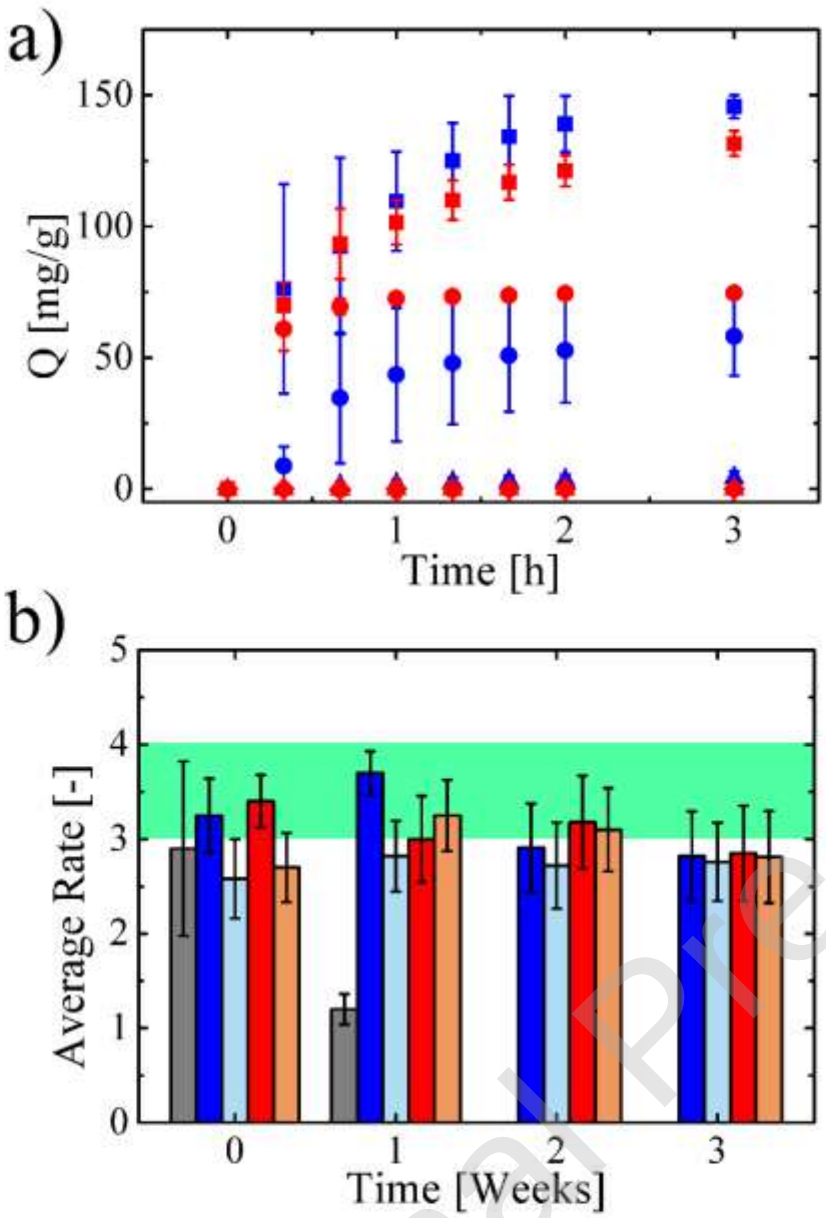

Figure 3. (a) Specific amount of adsorbed NPs over time for DDL3 NPs (blue symbols) and DDL5 NPs (red symbols) on Caucasian human hair. The measurement was performed at different NP initial concentration in the liquid phase, namely, 20 ppm (♦), 200 ppm (▲), 1000 ppm (●) and 2000 ppm (■). (b) Average odor intensity obtained in the perception test carried out by 50 evaluators. The test was performed blind in order to avoid any influence on the evaluators. The rated samples were: the hair treated with 2000 ppm of the hydroxycarboxylic acid of δ-decalactone (DL-HCA) as control (grey bars), hair treated with 2000 ppm of DDL3 (blue bars), hair treated with 1000 ppm of DDL3 (light blue bars), hair treated with 2000 ppm of DDL5 (red bars) and hair treated with 1000 ppm of DDL5 (orange bars). The green box indicate the region of strong odor intensity, according to Table 1. The error bars represent the standard deviation of the measurements.

4. Conclusions

In this work, we synthesized surfactant-free and rinsing-resistant biodegradable nanoparticles that are structurally composed of lactones, *i.e.* perfumes that occur naturally and that are already considered safe by the FDA. We took advantage of the possibility of polymerizing these lactones via

ROP using deanol as initiator to create ionizable oligoesters in a single scalable reaction step and in a reasonable timescale for industrial production. The inclusion of an ionizable group at the end of each oligomer chain allowed us to self-assemble directly these species into NPs in water via nanoprecipitation without the need for any surfactant. In this way, we can achieve a perfume loading up to 85% w/w. In addition, we demonstrated that the use of a tertiary amine as ionizable group is an effective strategy to confer an overall positive charge to our NPs and, in turn, to obtain high adsorption capacities on negatively charged natural fibers (up to 150 mg/g on cotton fabric and up to 140 mg/g on human hairs). The positively charged NPs were also resistant to rinsing, an important property in laundry and personal care products to provide a prolonged perfume perception. In the end, we proved with a perception test that our NPs confer a long-lasting fragrance perception to the treated hair swatches for at least 3 weeks compared to the pure perfume.

Supplementary Material: Electronic Supplementary Information are available online and include the ^{1}H NMR characterization of the oligoesters reported in this work, the evolution of conversion and DP over time, the dependence of the oligoester molecular weight from the conversion, and the variation of the particle size with the DP.

Credit Author Statement

- **Umberto Capasso Palmiero**: Conceptualization, Methodology;
- **Juri Ilare**: Investigation, Validation, Data Curation;
- **Carola Romani**: Validation;
- **Davide Moscatelli**: Project administration;
- **Mattia Sponchioni**: Supervision, Writing - Original Draft, Writing - Review & Editing.

Author Contribution: U. C. P. and J. I. equally contributed to the work.

Conflicts of interest: The authors declare no conflicts of interest.

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