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aminoacid-based low molecular weight organogelators
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1 **Nano- and microparticles of gelled oil combining aminoacid-based low molecular weight**
2 **organogelators and nonionic amphiphilic polysaccharides**

3

4 Carlos VARGAS-GUTIERREZ^{1,2}, Freha HANSALI³, Guillaume PICKAERT^{1,2},
5 Brigitte JAMART-GREGOIRE^{1,2}, Alain DURAND^{1,2}, Michèle LEONARD^{1,2*}

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7 ¹CNRS, LCPM, UMR 7375, Nancy, F-54001, France

8 ²Université de Lorraine, LCPM, UMR 7375, Nancy, F-54001, France

9 ³Université d'Oran Es-sénia, Oran 31000, Algeria

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23 *Corresponding Author: Michèle Léonard,

24 Tel: + 33 (0)3 83 17 52 76, Fax: + 33 (0)3 83 37 99 77,

25 Email: Michele.Leonard@univ-lorraine.fr

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Abstract

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Nano- and microparticles of gelled oils were prepared using an aminoacid-based low molecular weight organogelator and amphiphilic nonionic polysaccharides as stabilizers. The investigated oils were Tetralin, M810N and M829. The preparation procedure involved organogelator dissolution in hot solvent (150-190 °C) followed by oil-in-water emulsification at 70-80 °C in liquid state and final cooling step to room temperature to obtain gelled oil particles. The range of particle diameters (sub-micrometric or micrometric) could be adjusted by selecting the emulsification process, sonication or vortex mixing. Using sonication, organogel particles could be also prepared at room temperature with the oil phase in the gel form. The suspensions of gelled oil particles could be centrifuged and fully redispersed by vortex mixing with an increase of particle diameters whose extent depended on the nature of the oil.

Keywords: Organogel, Nanoparticles, Microparticles, Dextran, Aminoacid

43 1. INTRODUCTION

44 Low-molecular weight organogelators (LMWO) were defined as small organic molecules
45 (molar mass lower than 3,000 g/mol) with the ability to self-organize in certain organic
46 solvents, giving rise to the formation of fibrous networks that dramatically modify the flow
47 properties of the medium [1]. Self-organization of gelator molecules occurred through the
48 establishment of low energy interactions (for instance hydrogen bonds, ionic interactions, π -
49 stacking, dipole-dipole, solvophobic effects or van der Waals interactions). Among the
50 properties of organogels, two common characteristics were of particular importance. First, the
51 critical gelation concentration (CGC), i.e. the concentration above which gelation was
52 observed at a given temperature. According to the chemical structure of the organogelator,
53 CGC could be reduced down to values well below 0.5 wt%. This was a very interesting point
54 for formulation applications. Second, organogels exhibited thermo-reversibility so that they
55 recovered a liquid-like behavior when temperature exceeded a critical value (which depended
56 on the concentration of organogelator). This property could be used to facilitate the flow of
57 the mixture through pipes or to trigger drug release via viscosity variation for instance.
58 Several studies have been reported about the formation and the mechanical properties of bulk
59 organogels as well as about the links between molecular structure and macroscopic properties
60 [2-7]. Nevertheless, there were much less reports about the use of organogelators in the
61 formulation of disperse systems. Schematically, two types of colloidal dispersions have been
62 reported involving organogels, according to the nature of the gelled phase. On the one hand,
63 water-in-oil emulsions have been prepared in which the oil phase was gelled [8-15]. Gelling
64 continuous oil phase prevented water droplets motion as well as coalescence and thus
65 improved the colloidal stability of the dispersions. On the other hand, the preparation of
66 aqueous suspensions of gelled oil particles has also been reported [16-25]. In that case, gelling
67 disperse phase was closely related to specific applications. Researchers explored different

68 ways of controlling the morphology of oil particles on the basis of the properties of the
69 gelator. For instance by inducing an accumulation of the gelator at oil/water interface,
70 capsules were obtained [16]. In another work, the gelator itself was designed so as to serve as
71 chiral template [22]. In most of these formulations, the gelator was 12-hydroxystearic acid
72 (HSA) with minimal concentrations of 0.5 wt% in the oil.

73 The design of new LMWO appeared as a promising track in formulation. Indeed innovation in
74 the chemical structure of gelators would be a great opportunity to obtain dispersions with
75 targeted end-use properties like polarity of gelled oil particles, size distribution, colloidal
76 stability in various conditions, temperature reversibility... Some guidelines already existed to
77 relate oil nature and required chemical characteristics of potential gelator candidates using
78 Hansen and Hildebrand solubility parameters [26-32]. Nevertheless there were only a few
79 studies in which colloidal properties of gelled oil dispersions were studied and all of them
80 used HSA as the gelator [17,20].

81 Some of us reported the design and synthesis of a family of strong LMWO based on
82 aminoacid derivatives [33,34]. Gelation of organic solvents was attributed to the formation of
83 an entangled fibrillar network through hydrogen bonds and π - π stacking interactions [35,36].

84 A detailed analysis of oscillatory rheological properties of these organogels revealed that the
85 macroscopic gel formation resulted from a jamming-induced gelation [37]. When cooling
86 down the organic solution from the liquid state, organogelator molecules formed clusters
87 below a certain temperature. These clusters started crowding when temperature further
88 decreased. When temperature became lower than a critical value called gelation temperature
89 ($T_{\text{ORGANOGELE}}$), the mechanical behavior of the system changed from liquid to solid-like.
90 Below $T_{\text{ORGANOGELE}}$ the rheological behavior of the solution was that of a soft solid, with
91 elastic modulus (G') higher than the loss modulus (G'').

92 We already reported the preparation of nanometric and micrometric oil-in-water emulsions
93 stabilized by amphiphilic polymers derived from polysaccharides (particularly from dextran, a
94 nonionic bacterial polysaccharide) [38,39]. The presence of a dense and thick superficial layer
95 of hydrophilic loops at the surface of oil droplets provided good colloidal stability and offered
96 the possibility of further chemical functionalization thanks to the reactive hydroxyl groups
97 present at the surface. In addition, polysaccharide-covered oil droplets were used as templates
98 for the preparation of polyester nanoparticles via emulsion-solvent evaporation procedure
99 [40].

100 In that work, we investigated the use of aminoacid-derived gelator molecules for the
101 formulation of gelled oil particle suspensions stabilized by amphiphilic polymers derived
102 from dextran. We particularly focused on the links between the formulation or process
103 variables and the particle size distribution as well as colloidal stability of the suspensions. For
104 the preparation of the particles, we selected three oils comprising two triglycerides currently
105 used in pharmaceutical formulations. The targeted application of the particles was
106 encapsulation of hydrophobic active substances. The presence of dextran chains at the surface
107 of particles was intended for providing colloidal stability as well as opportunity to attach
108 functional groups.

109

110 **2. EXPERIMENTAL**

111

112 2.1 Materials

113 All chemicals were purchased from Sigma-Aldrich[®] and used as received. The native dextran,
114 T40[®] sample, had a weight-average molar mass close to 40,000 g/mol according to the
115 provider. MilliQ[®] water was employed for preparing aqueous solutions. The hydrophobically
116 modified dextrans used in that work were synthesized following a previously reported

117 procedure [41]. Briefly, dextran T40[®] (10 g) was dissolved in 100 mL DMSO at room
118 temperature. After 1 h, the required amounts of tetrabutyl ammonium hydroxide (TBAOH)
119 and 1-2 epoxyoctane or 1-2 epoxydodecane were added to the solution. The reaction medium
120 was stirred over 48 h at room temperature. The crude mixture was dialyzed against a 1:1 (v:v)
121 mixture of deionized water and ethanol, followed by deionized water. The modified dextran
122 was recovered by freeze drying and analyzed by ¹H NMR in DMSO d₆ in which a few drops
123 of D₂O were added. The degree of substitution τ (%) was defined as the molar ratio
124 (expressed in percents) of attached hydrocarbon groups to the number of glucose repeat units
125 ($\tau = 100 \cdot y / (x + y)$) see **Figure 1**). Polymers were named DexC₆- τ and DexC₁₀- τ where C₆ and
126 C₁₀ referred to the nature of hydrocarbon group. Hydrocarbon groups were assumed to be
127 statistically distributed along polysaccharide backbone.

128

129 2.2 Synthesis and structure of aminoacid-based organogelator.

130 We used L-aminoacid-type gelators with carboxybenzyl (Z) as the amine-protecting group
131 and a naphthalimide moiety (**Figure 2**). As in previous studies, this molecule was named (L)-
132 Phe. The synthesis, characterization and gelation properties of (L)-Phe have been described
133 previously [32,33,35]. Briefly, commercial Z-Phe-OH was methylated using SOCl₂ and
134 MeOH in THF. Z-phe-OMe was then reacted with hydrazine in methanol and finally with
135 naphthalic anhydride in toluene.

136

137 2.3 Emulsion formulation and preparation

138 Two procedures were designed for preparing suspensions of gelled oil particles (**Figure 3**).
139 The first procedure (P1) consisted in dissolving (L)-Phe during 1 h in the solvent at 150 – 190
140 °C and performing emulsification immediately after by sonication or vortex mixing at 70 – 80
141 °C, so as to keep the oil phase in a liquid state. Then, oil-in-water emulsion was cooled down

142 to room temperature before characterizations. The second procedure (P2) comprised the same
143 operations but, after dissolving (L)-Phe at 150 – 190 °C in the solvent, the oil phase was
144 cooled down to room temperature, thus taking the form of a gel. Emulsification was then
145 carried out by sonication at room temperature after mixing the liquid aqueous phase with the
146 gelled oil phase. The chemical stability of oils and (L)-Phe during the heating step was
147 checked by comparing ¹H NMR spectra before and after the procedure. No difference could
148 be detected for all compounds. Sonication (pulsed mode) was carried out using a Vibracell
149 model 600W (Sonics & Materials Inc, Danbury, CT). For most experiments hydrophobically
150 modified dextran derivatives, DexC_n-τ, were used as stabilizers during emulsification step.
151 For comparison, some experiments were carried out where DexC_n-τ was replaced by an
152 anionic surfactant, sodium dodecyl sulfate.

153

154 2.4 Determination of average droplet diameter and droplet diameter distribution

155 Average hydrodynamic droplet diameters were measured by dynamic light scattering (DLS)
156 at low concentration using a HPPS[®] from Malvern. Dilution of emulsion samples was carried
157 out with MilliQ water. It was checked that the extent of the dilution did not change
158 significantly the results. The diameter obtained was an average value based on three
159 consecutive measurements for each sample and calculated from the analysis of the
160 autocorrelation function. Taking into account the observed variations between two
161 consecutive measurements, we considered that the obtained average values were known
162 within an interval of ± 5 nm. The “polydispersity index” (PDI) provided by HPPS was a
163 reasonable way to appreciate whether the sample size distribution could be considered as
164 monomodal. The PDI was calculated by the software and its value relied on the comparison
165 between the fitted and experimental autocorrelation functions. All samples reported in that
166 work had PDI values lower than 0.35, which could be considered as characteristic of a

167 reasonable agreement of monomodal model with real droplet size distributions of the samples,
168 even if a PDI of 0.35 indicated a rather broad size distribution.

169 Particle size distributions were also characterized by laser light scattering (Mastersizer 2000[®]
170 Malvern Instruments-Cellule: Hydro 2000 μ p). The width of the distribution was quantified by
171 the mean range of particle size named Span (**Equation (1)**).

$$172 \quad \text{Span} = \frac{d(0.9) - d(0.1)}{d(0.5)} \quad (1)$$

173 In **Equation (1)**, $d(0.9)$, $d(0.5)$, and $d(0.1)$ were the diameters at 90%, 50% and 10%
174 cumulative volumes, respectively.

175 A direct comparison of the measurements made by both techniques (light scattering and DLS)
176 with a suspension of gelled olive oil particles stabilized by DexC₁₀₋₁₂ led to the following
177 results: average diameter equal to 171 nm and PDI equal to 0.24 by DLS,
178 $d(0.5)$ equal to 177 nm and Span equal to 2.2 by laser light scattering.

179 These results showed the consistency of results obtained by both techniques.

180

181 2.5 Spectroscopic techniques for the study of chemical structure and hydrogen bond formation
182 Organogels were analysed by Fourier Transform Infra Red spectroscopy to detect the
183 formation of hydrogen bonds between NH and CO groups by examination of the variation of
184 the stretching bands i.e. 3500-3200 cm^{-1} for NH and 1800-1600 cm^{-1} for CO.

185 ¹H NMR spectra were recorded using a Bruker Avance 300 MHz spectrometer at 25 °C.

186

187 2.6 Rheological measurements

188 Oscillatory experiments were performed at imposed shear stress (1 Pa) and 1 Hz frequency
189 using a parallel plate geometry (25 mm diameter) within the linear viscoelastic domain where
190 storage G' and loss G'' moduli were independent of the stress (Advance Rheometer AR 2000,
191 TA instrument). Then the temperature was increased (1°C/min) to determine $T_{\text{ORGANOGELE}}$.

192

193 2.7 Surface tension measurements

194 Surface tension measurements were carried out at 25 °C using a K20 surface tensiometer
195 (Krüss easyDyne). Surface tensions were measured using the Lecomte du Noüy ring method.
196 All samples were equilibrated for a sufficient time (15 min to 1 h) to reach constant readings.

197

198 3. RESULTS AND DISCUSSION

199 3.1 Formulation of oil phase

200 The selected oils were one aromatic hydrocarbon (Tetralin) and two aliphatic triglycerides
201 (Miglyol 810N[®], M810N, and Miglyol 829[®], M829). For all oils, 1 wt % of (L)-Phe was
202 enough to obtain a gelled oil phase at room temperature (**Table 1**).

203 A series of experiments was carried out with the aim to roughly evaluate the characteristic
204 times of gelation according to (L)-Phe concentration and nature of the oil. After complete
205 dissolution of (L)-Phe in the oil (at 100 or 150 °C), the oil phase was taken out of the heating
206 bath and let cooling. The physical state of the oil phase was visually inspected at regular time
207 intervals turning upside down the vial to evaluate flowing ability. Whatever the solvent used,
208 oil phases containing 2 wt % (L)-Phe exhibited almost instantaneous gelation after starting the
209 cooling step. For Tetralin and M810N oils, 1 wt % solutions also exhibited very fast gelation
210 after the beginning of the cooling step (**Table 1**).

211 The agreement between qualitative visual observations and quantitative rheological
212 measurements was checked with formulations containing M810N. Oscillatory experiments
213 carried out at 20 °C with 1 wt % (L)-Phe dissolved in M810N confirmed the formation of a
214 strong gel (**Figure 4a**, $G' > G''$ and very few variation with frequency). Furthermore,
215 temperature variation from 20 °C to 150 °C revealed a sharp decrease of both moduli at
216 $T_{\text{ORGANOGE}} = 85$ °C accompanied by a crossover point above which $G' < G''$ (**Figure 4b**).

217 Finally, after reaching 150 °C, the gel sample was let cooling down and both moduli were
218 continuously measured. Storage and loss modulus recovered their maximal respective values
219 after 25 min and G' became higher than G'' after about 15 min (**Figure 4c**).

220

221 3.2 Preparation of gelled oil suspensions

222 Suspensions of micrometric or sub-micrometric particles of gelled oil were prepared
223 following two procedures (P1 and P2). Previous data (see section 3.1) about kinetics of
224 gelation upon cooling were used to set experimental conditions.

225 For stabilizing oil-in-water emulsions, amphiphilic derivatives of dextran were used (**Figure**
226 **1**). Surface activity and emulsifying properties of these polymers have been reported
227 previously in detail, for the preparation of both micrometric and sub-micrometric emulsions
228 [42-44]. Measurements of the surface tension of solutions of (L)-Phe in Tetralin with
229 concentrations between $2 \cdot 10^{-4}$ and $2 \cdot 10^{-1}$ wt % at 20 °C revealed no significant difference with
230 that found with Tetralin alone. Thus, we considered that (L)-Phe exhibited no detectable
231 surface active properties and that interfacial tension was controlled by amphiphilic
232 polysaccharides.

233 For all experiments, the stabilizer was dissolved in the aqueous phase before contacting it
234 with the oil phase. We intended to prepare suspensions of gelled oil particles containing about
235 9 % v/v of disperse phase. In previous work we showed that to obtain nanoparticles, a
236 minimum of 5 wt % (relative to oil phase) of amphiphilic dextran derivative should be loaded
237 in the aqueous phase [42]. Thus we chose to fix the concentration of amphiphilic dextran at 5
238 g/L in the aqueous phase.

239 Comparative experiments were carried out with a widely used anionic surfactant, sodium
240 dodecyl sulfate (SDS). The concentration of SDS was, for the sake of comparison, set to
241 identical value.

242

243 3.3 Characterization of particle size distribution of suspensions of gelled particles

244 Suspensions were characterized either by determining average droplet diameter by dynamic
245 light scattering or by using laser granulometry to obtain the full droplet diameter distributions.
246 Gelled Tetralin particle suspensions were first prepared following both P1 and P2 procedures
247 (**Figure 3**). In case of Tetralin, with or without dissolved (L)-Phe, it was not possible to obtain
248 stable particles with diameters well below 1 μm (data not shown). This was attributed to very
249 fast Ostwald ripening [45]. Because of the significant solubility of Tetralin in water (higher
250 than 30 mg/L at 20 °C), stable emulsions with droplet diameters below 1 μm were impossible
251 to obtain during a significant time interval. Consequently, we added an ultra hydrophobe oil
252 (hexadecane) in Tetralin, which was a well-known way of slowing down Ostwald ripening
253 [38]. When 5 % v/v hexadecane was added into Tetralin, nanoemulsions with average oil
254 diameters around 150 nm were obtained, either in the absence or in the presence of dissolved
255 (L)-Phe. This demonstrated that despite its insolubility in water (L)-Phe did not allow slowing
256 down of Ostwald ripening contrary to hexadecane. This result was consistent with previous
257 NMR study which showed, in case of a gel formed by (L)-Phe in toluene, that there were no
258 measurable interactions between the supramolecular network and solvent molecules which
259 filled free space within the structure [36]. Regarding the gelation properties, the presence of
260 hexadecane in Tetralin did not prevent the formation of a gel in the same experimental
261 conditions.

262 When comparing suspensions of gelled particles prepared by procedure P1 with sonication
263 and procedure P2, we found that average particle diameters were similar. Thus the physical
264 state of the oil phase, liquid or gel, during the emulsification step, had no significant effect on
265 the average particle diameter provided that sonication was used. This result was explained by
266 the high energy provided to the biphasic mixture during the sonication step. Indeed, the

267 minimal droplet diameter that could be reached was still below that obtained in the
268 dispersions. Thus the viscosity of the oil phase was not the limiting parameter for these
269 experiments. Additionally, a part of this energy was lost in heat, which could even liquefy the
270 oil phase during sonication, but we had no direct proof of this assumption. Similarly,
271 increasing the concentration of (L)-Phe in Tetralin from 0.3 to 0.7 wt % did not induce any
272 significant variation in the average particle diameter. When the amount of oil phase was
273 varied between 4.5 and 16 % v/v, average particle size remained around 150 nm. These
274 results showed that it was possible to vary the amount and the mechanical strength of
275 prepared gelled oil particles while keeping similar particle size distributions (**Table 2**).

276 Using either SDS or DexC₁₀₋₁₂ as the stabilizer, in the presence or in the absence of (L)-Phe
277 in the oil phase, led to similar results (**Figure 5**). The maximum difference observed in
278 particle/droplet diameter was ca. 40 nm lower in the case of organogel nanoparticles
279 stabilized by SDS as compared to those stabilized by DexC₁₀₋₁₂. Thus, the use of
280 polysaccharide-based stabilizer did not limit the final particle diameter as compared to
281 molecular surfactant.

282 Because of the formation of hydrogen bonds in the gel state, characteristic FT-IR signals from
283 NH and CO groups were evidenced [35]. FT-IR spectra of gels formed from 4 wt % (L)-Phe
284 solution in Tetralin before and after emulsification in 5 g/L DexC₁₀₋₁₂ aqueous solution and
285 centrifugation were compared (**Figure 6**). Signals from NH and CO were very similar, for
286 both the gel formed by cooling the bulk solution in Tetralin and the gel formed by cooling the
287 oil phase centrifuged from O/W emulsions. This experiment confirmed that the gelation
288 phenomenon in Tetralin was similar in bulk and in emulsified state.

289 The procedure P1 involving emulsification at 70 – 80 °C (**Figure 3**) was followed in the rest
290 of this work.

291 Sub-micrometric particles of gelled oil were obtained using either M810N or M829 and (L)-
292 Phe concentrations between 0.5 and 2.0 wt % in the oil (**Table 3**). Increasing sonication
293 power and duration allowed displacing particle diameter distribution towards lower diameter
294 and Span values. Particle diameter distributions were similar for both oils. When replacing
295 sonication step by vortex mixing, a much less energetic operation, micrometric suspensions of
296 particles, with high size polydispersity, were obtained with both oils (**Table 3**). Thus
297 microparticles could be produced with M810N or M829 by adjusting the operating variables
298 of the emulsification step.

299 As a conclusion, these experiments demonstrated that it was possible to prepare sub-
300 micrometric and micrometric suspensions of (L)-Phe gelled oil particles covered by dextran
301 chains. By varying (L)-Phe concentration in the oil phase, the mechanical behavior of the
302 gelled core could be modified while maintaining rather unchanged particle diameter
303 distributions.

304

305 3.4 Shelf life of suspensions of gelled oil particles and their stability to centrifugation

306 Average particle diameter of Tetralin organogels was monitored over 100 h and no significant
307 variation could be detected (**Figure 5**). The same result was obtained with or without (L)-Phe
308 in the oil phase and using SDS or DexC₁₀₋₁₂ as the stabilizer. Thus suspensions of gelled oil
309 particles exhibited good shelf life.

310 In the case of suspensions stabilized by DexC₆₋₁₅, the ability to redisperse in water upon
311 vortex agitation after centrifugation was examined. Whatever the solvent used (Tetralin,
312 M810N and M829) centrifuged particle suspensions could be fully redispersed by vortex
313 agitation. This ability to redisperse after centrifugation was due to efficient stabilization by
314 adsorbed dextran chains which produced steric repulsions between particles. Such

315 redispersion ability has been already demonstrated in the case of oil-in-water emulsions
316 stabilized by amphiphilic dextran derivatives [38,43].
317 Nevertheless, regarding the preservation of the initial particle diameter distribution, we
318 observed rather different results according to the oil used (**Table 4**). With Tetralin and M829
319 a limited increase of $d(0.5)$ was observed. Nevertheless, aggregates were formed (with sizes
320 lower than 100 μm) which led to a significant increase of Span values. In the case of M810N
321 $d(0.5)$ was increased dramatically and aggregates with diameters above 100 μm were formed
322 (Span values increased in most cases). These results showed that despite steric repulsions
323 originating from adsorbed macromolecules, when particles were forced to pack together
324 during centrifugation step, aggregation of particles was limited but not completely avoided, as
325 it had been shown in the case of oil-in-water emulsions and polymeric nanoparticles. The
326 degree of substitution of the dextran derivative was a relevant structural parameter for
327 reducing the extent of aggregation during centrifugation. Previous results had shown that
328 degrees of substitution equal to 15 % for C_6 groups and 7 % for C_{10} groups were sufficient to
329 obtain complete redispersion after lyophilization.[40]

330

331 **4. CONCLUSION**

332 The preparation of nano- and micrometric dextran-covered gelled oil particles was described
333 for the first time. Several oils (Tetralin, M810N and M829) were gelled by an aminoacid
334 derivative. Two procedures for suspensions preparation were designed both involving
335 dissolution of (L)-Phe in oil at 150-190 $^{\circ}\text{C}$ but differing by the dispersion step. In one
336 procedure, dispersion was prepared by emulsification of hot liquid phases (70-80 $^{\circ}\text{C}$) while in
337 the other procedure, gelled oil was used and dispersed at room temperature in aqueous phase.
338 The influence of several process parameters and formulation variables was investigated. The
339 use of dextran-based stabilizers led to gelled oil particles with size distributions comparable to

340 those produced using a common anionic surfactant, SDS. The mechanical strength of the
341 gelled oil core was varied by modifying the concentration of the gelator, which could be done
342 without significant changes in the particle size distribution. Conversely, changing the
343 emulsification step (replacing sonication by vortex mixing) allowed displacing particle
344 diameter distribution from sub-micrometric to micrometric domain. The properties of the
345 gelled oil particles could be adjusted by taking the opportunity of available chemical
346 functionalities: within the gelator molecules and at the surface of the particles with the
347 hydroxyl groups of dextran chains.

348 Current work explores the use of these gelled oil particles for encapsulation and controlled
349 release of active molecules. More specifically, the effect of including another ingredient (the
350 active molecule) in the formulation and in the preparation process of gelled oil particle is
351 investigated in detail.

352

353

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475 **Table 1:** Physical state of (L)-Phe solutions in various oils after complete dissolution during 1
476 h at 100 °C (for Tetralin + 5 % v/v hexadecane) or 150 °C (for M810N and M829) and
477 beginning cooling at room temperature (initial time). Qualifications of “liquid (L)”, “gel (G)”
478 and “mixtures of liquid and gel (L+G)” were attributed on the basis of visual observations.
479

		Time after withdrawal from the heating bath (h)							
(L)-Phe (wt %)		0.25	0.5	1	2	3	4	24	
hexadecane (5 % v/v)	Tetralin +	0.3	L	L	L+G	L+G	L+G	L+G	G
		1.0	G	G	G	G	G	G	G
		2.0	G	G	G	G	G	G	G
M810N		0.5	L	L	L	L	L	L	G
		1.0	G	G	G	G	G	G	G
M829		0.5	L	L	L	L	L	L	L
		1.0	L	L	L	L	L	L	G
		2.0	L+G	G	G	G	G	G	G

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482 **Table 2:** Average particle diameter measured by dynamic light scattering for suspensions of
483 gelled Tetralin (with 5 % v/v hexadecane) prepared following procedure P1 or P2 and
484 containing various amounts of (L)-Phe in the oil phase. The stabilizer was DexC₁₀₋₁₂ at 5 g/L
485 in water and the weight fraction of dispersed phase was 9 wt %.

486

(L)-Phe (wt%)	Procedure	Average particle diameter (nm)
0.3	P1	174
0.3	P2	155
0.5	P2	148
0.7	P2	134

487

488 **Table 3:** Particle diameter distribution determined by laser granulometry for suspension of gelled oil particles prepared following procedure P1.

489 The stabilizer was DexC₆-15 at 5 g/L in water and the weight fraction of dispersed phase was 9 wt %.

Oil	(L)-Phe (wt %)	Emulsification	d(0.5) (μm)	Span
M810N	0.5	Sonication (power 30 W, 60 s)	0.41	30.3
	0.5	Sonication (power 60W, 120 s)	0.18	3.0
	1.0		0.19	3.8
	0.5	Vortex (5 min)	9.15	9.9
	1.0		5.37	7.0
	M829	1.0	Sonication (power 60W, 120 s)	0.21
2.0		0.22		5.0
1.0		Vortex (5 min)	5.14	23.6
2.0			0.69	6.5

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492 **Table 4:** Particle diameter distribution of gelled oil particle suspensions after preparation and after centrifugation (1,800 rpm, 45 min) and
 493 redispersion by vortex mixing. The stabilizer was DexC₆-15 at 5 g/L and the weight fraction of disperse organic phase was 9 wt %.

494

Oil	After preparation (24 h)			After centrifugation and redispersion by vortex mixing	
	(L)-Phe (wt %)	d(0.5) (μm)	Span	d(0.5) (μm)	Span
Tetralin + 5 % v/v hexadecane	1.0	0.16	5.5	0.24	12.2
	0.5	0.18	3.0	5.21	7.9
M810N	1.0	0.19	3.8	2.04	9.6
	1.0	5.37	7.0	13.31	4.9
M829	1.0	0.21	4.4	0.27	52.6
	2.0	0.22	5.0	0.27	28.9

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Figure captions

Figure 1: Chemical structure of amphiphilic dextran derivatives, DexC₆- τ and DexC₁₀- τ . The degree of substitution was defined by $\tau = 100 \times y / (x + y)$. The linear aliphatic hydrocarbon group R was -C₆H₁₃ and -C₁₀H₂₁ for C₆ and C₁₀ series, respectively.

Figure 2: Chemical structure of (L)-Phe organogelator.

Figure 3: Experimental procedures P1 and P2 followed for preparing suspensions of gelled oil particles. For details see text.

Figure 4: Rheological (oscillatory) measurements with 1 wt % (L)-Phe solution in M810N. Storage (G') and loss modulus (G'') at 20 °C as a function of frequency (a). Variation of storage and loss modulus with temperature (b). Variation of storage and loss modulus with cooling time after reaching 150 °C (c).

Figure 5: Average particle diameter determined by dynamic light scattering of 0.3 wt % (L)-Phe Tetralin organogel suspension (bold symbols) or Tetralin emulsion (open symbols) prepared by procedure P1. Tetralin contained 5 % v/v hexadecane in all cases. The weight fraction of organic disperse phase was 9 wt %. The stabilizer was SDS (circles) or DexC₁₀-12 (squares). Time = 0 h corresponded to measurements carried out immediately after preparation. Lines are guide for the eye.

521 **Figure 6:** Comparison of IR bands from NH (left) and CO (right) groups for 4 wt % gels of
522 (L)-Phe in Tetralin in bulk (red) or in particles recovered after centrifugation of an aqueous
523 suspension (blue).

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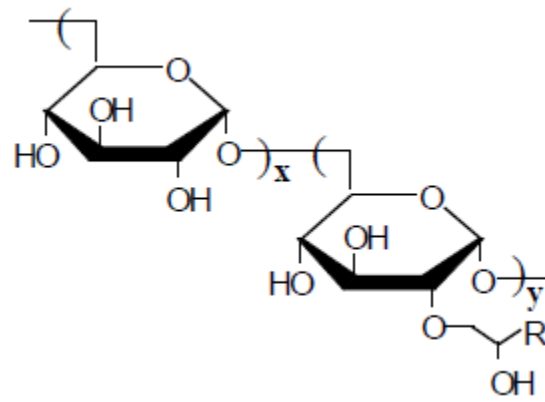
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Figure 1

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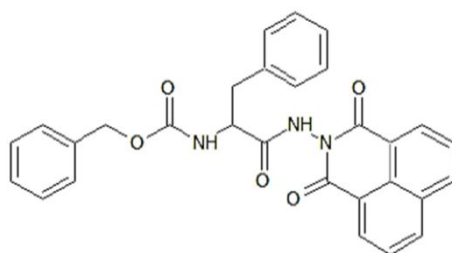
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Figure 2



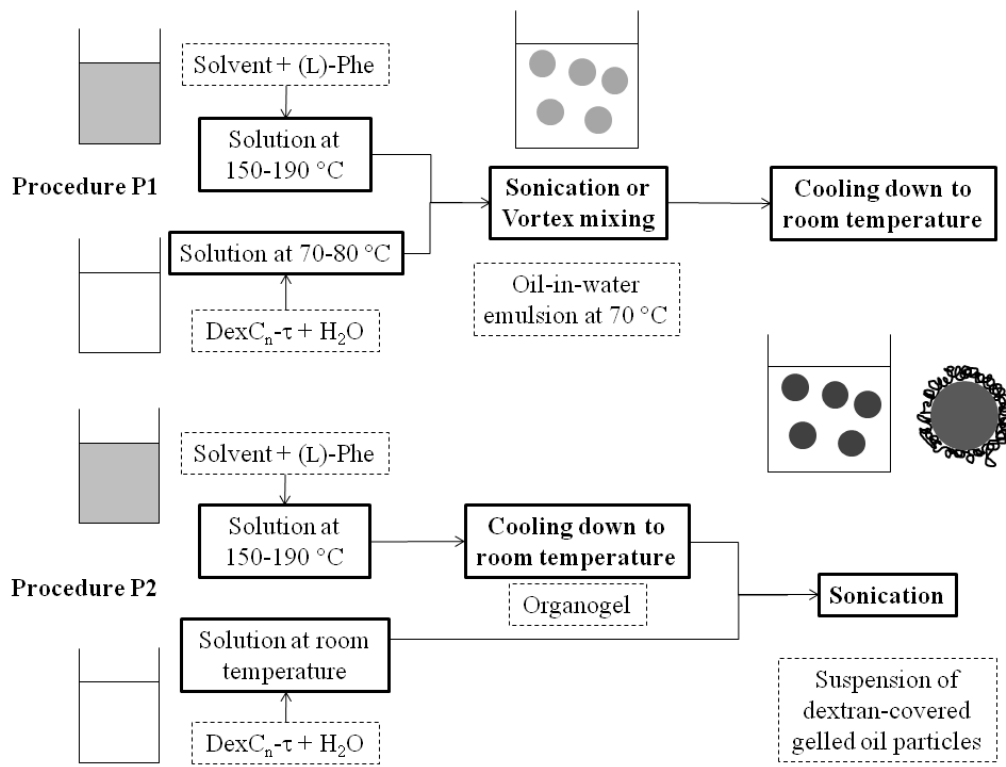
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Figure 3



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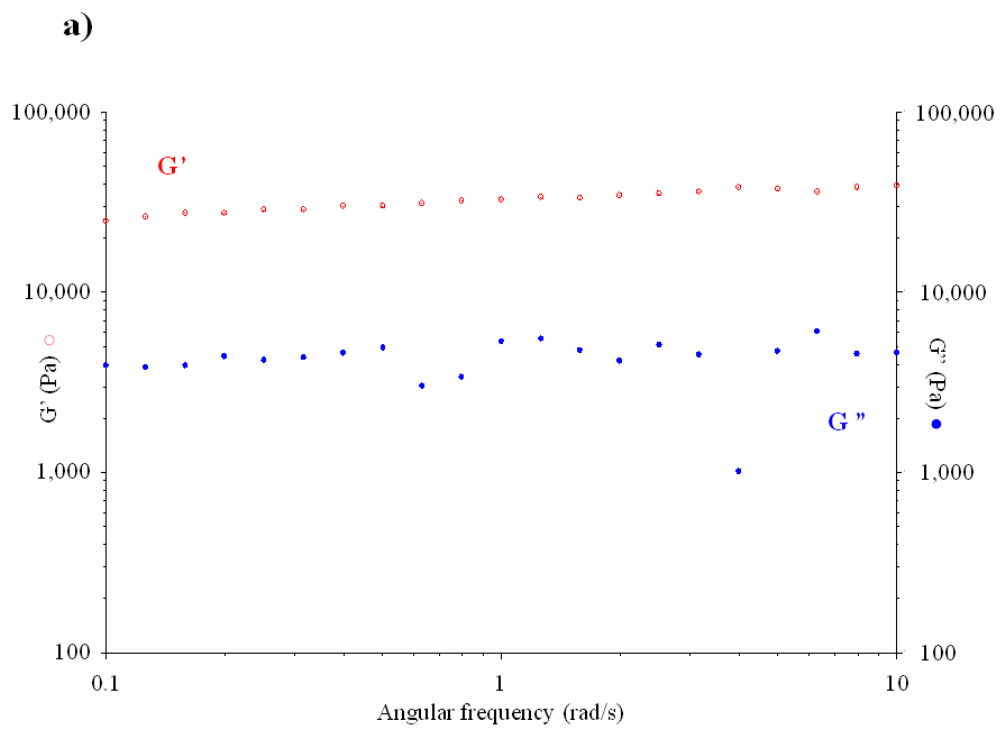
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Figure 4a

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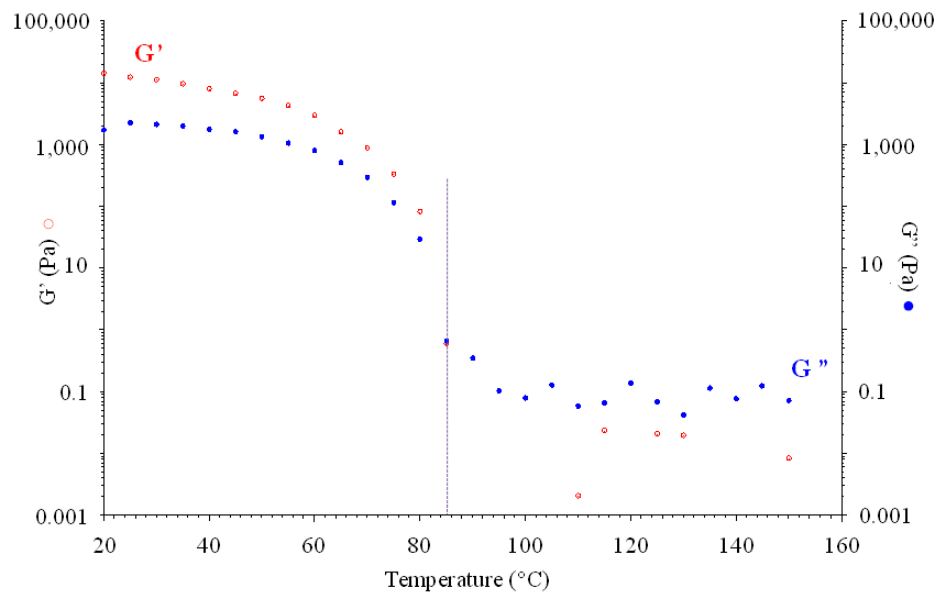
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Figure 4b

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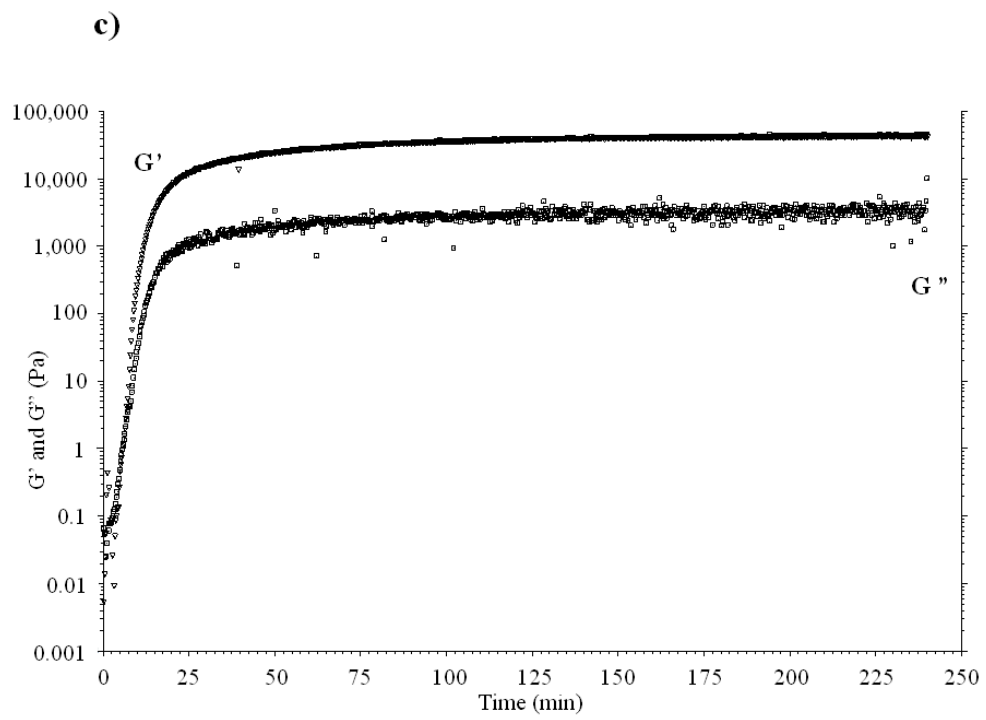
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Figure 4c

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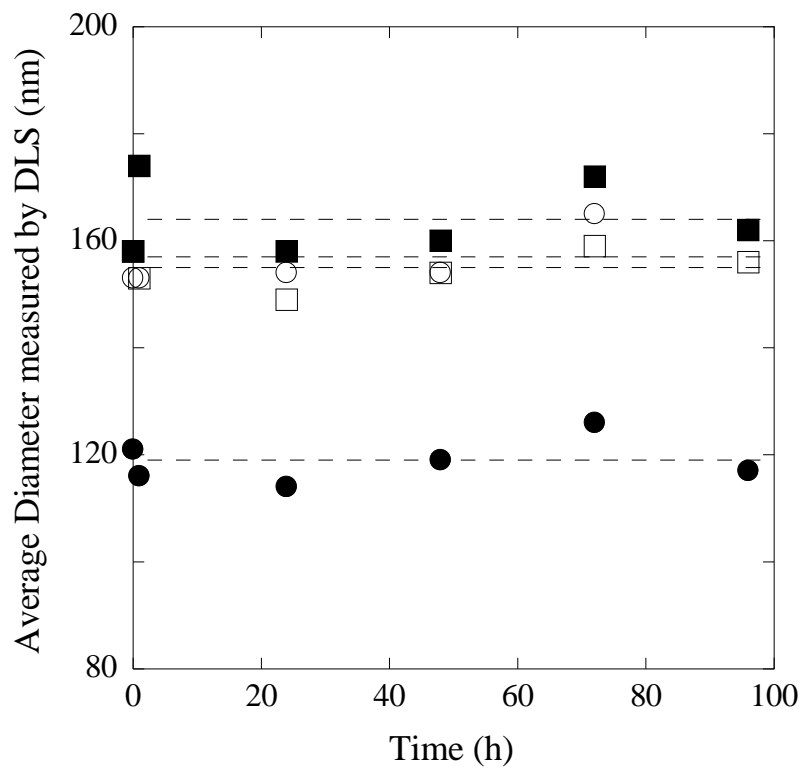
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Figure 5

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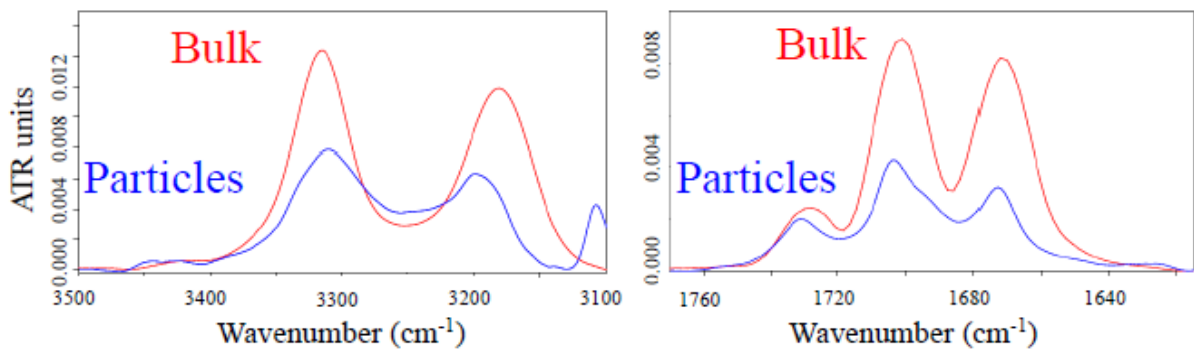
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Figure 6

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