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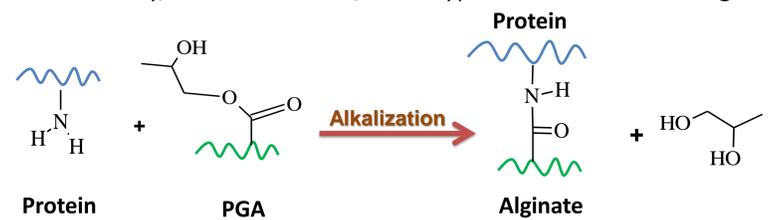
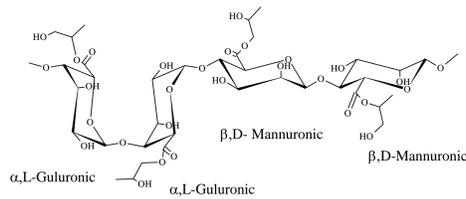
Human Serum Albumin-Alginate Esters Microparticles

Prepared by Transacylation: Effect of Ester Group

Imane HADEF (a, b); Mehdi OMRI (a, b); Christophe BLIARD (b); Barbara ROGE (b); Florence EDWARDS-LEVY (a)

1. Introduction

Microencapsulation using the transacylation reaction in a W/O emulsion is based on the creation of amide bonds between free amine functions of a protein and polysaccharide ester groups in the aqueous phase after alkalization. Several proteins have been implicated in this process, whereas commercial propylene glycol alginate (PGA) has been the only modified polysaccharide used up to now (1,2). The intrinsic properties of PGA such as viscosity, molecular mass, ester type and substitution degree limit its use in microcapsule preparation hence the need to study other potential polysaccharide esters.

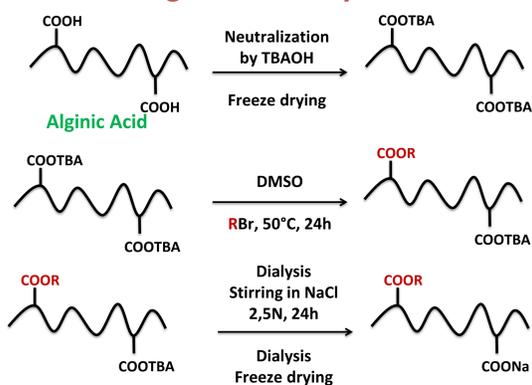


2. Purpose

Study the effect of the alginate polysaccharide ester structure and properties on the transacylation reaction and on microcapsule characteristics.

3. Methods

3.1. Alginate ester synthesis (3)

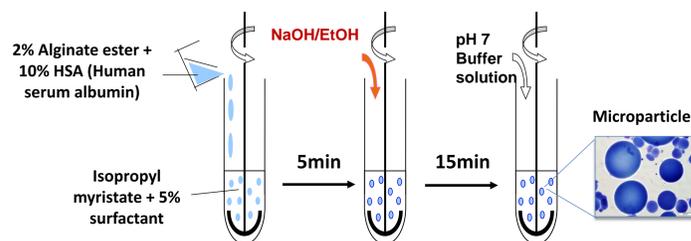


R = CH₃CH₂-, OHCH₂CH₂-, CH₃CH₂CH₂-, CH₃CHOHCH₂- or OHCH₂CH₂CH₂-

3.2. Alginate ester characterization

- The degree of esterification (DE) by ¹H-NMR and titrimetry;
- Viscosity measurement of 2% ester aqueous solution (w/w);
- Critical aggregation concentration (CAC) via Coomassie blue test(4).

3.3. Microcapsule preparation



1 - Emulsification 2 - Alkalization 3 - Neutralization

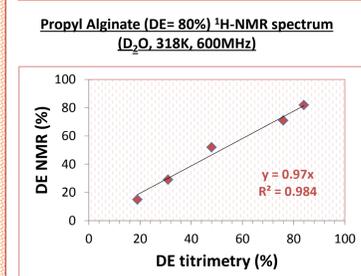
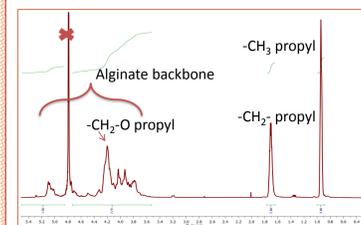
Microparticles are stable, biocompatible and biodegradable

3.4. Microcapsule characterization

- Size distribution by laser diffraction granulometry;
- Morphology by optical microscopy;
- Inner structure after microcapsule cross-section.

4. Results

4.1. Alginate derivative DE



Esterification degree by ¹H-NMR vs titration

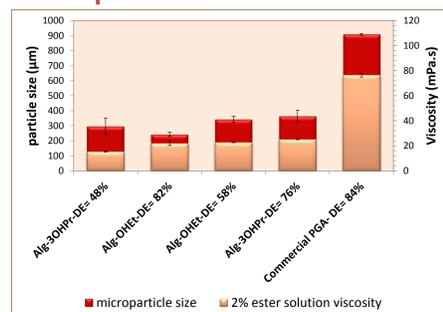
- Good agreement between ¹H-NMR and titrimetric results.
- The DE could be controlled by adjusting the quantity of bromide reagent.

R	Equivalent RBr	DE (%)
Ethyl	0.5eq	43%
	1eq	82%
2-Hydroxyethyl	0.5eq	58%
	1eq	82%
Propyl	0.3eq	25%
	1eq	90%
	2eq	80%
2-Hydroxypropyl	0.5eq	19%
	1eq	31%
3-Hydroxypropyl	0.5eq	48%
	1eq	76%

4.2. Alginate ester microparticles

R	DE (%)	Particles	Particle size (µm)	Cross-sections
2-Hydroxypropyl	Commercial PGA (84%)		908	Reference MM-1000KD
Ethyl	43%	No microparticle		
	82%	No microparticle		
2-Hydroxyethyl	58%		343	Synthetic alginate esters MM-10 KD
	82%		243	
Propyl	25%	No microparticle		
	60%	No microparticle		
	90%	No microparticle		
	80%	No microparticle		
2-Hydroxypropyl	19%	No microparticle		
	31%	No microparticle		
3-Hydroxypropyl	48%		297	Synthetic alginate esters MM-10 KD
	76%		364	

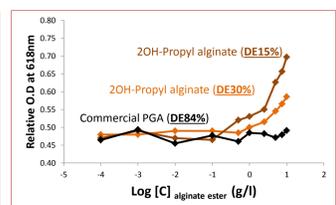
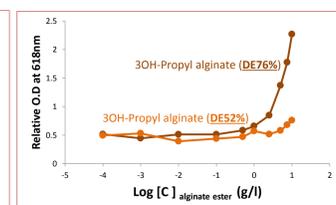
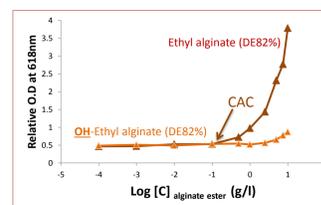
10% HSA-2% alginate ester (w/w) microparticles prepared by transacylation



- Alkyl alginate (propyl and ethyl) → no microparticle.
- Hydroxyalkyl alginate with \nearrow DE → microparticles with lacework inner structure.
- 1-Bromo-2-propanol was less reactive during esterification → 2-Hydroxypropyl alginate with \searrow DE → No microparticle.
- \searrow alginate molecular weight → \searrow aqueous solution viscosity → \searrow microparticle size.

4.3. Critical aggregation concentrations (CAC)

The spectral change of Coomassie blue was studied in the presence of alginate derivatives in water at increasing concentrations.



Absorbance change of Coomassie blue as a function of alginate ester concentration: effect of ester type and substitution degree

- For alkyl esters, hydrophobic microdomains were formed due to the association of alkyl chains at lower polymer concentrations compared to hydroxyalkyl esters.
- Increasing the esterification degree or the length of the ester chain led to the formation of hydrophobic microdomains at lower polymer concentrations, except for propylene glycol alginates (2OH-propyl alginate) for which increasing the esterification degree reduced significantly their hydrophobicity.
- The formation of hydrophobic microdomains seemed unfavorable to the reaction with HSA.

5. Conclusion

- The replacement of commercial PGA by a variety of other synthetic alginate esters in the process of microcapsule formation using the transacylation procedure was studied.
- The best candidates for the reaction with HSA were alginate esters with the highest critical aggregation concentrations observed with the hydroxyalkylated esters.
- Alkyl alginates or low DE alginate esters didn't lead to microcapsule formation under the given conditions of transacylation.
- The use of low molecular weight alginates, displaying low aqueous solution viscosity, led to the formation of smaller microparticles.

6. References

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