Design of Cellulose Based Micro- and Nanostructures for Encapsulation and Release of Curcumin

Francisca Casanova, Carla F. Pereira, Alessandra B. Ribeiro, Ricardo Freixo, Eduardo Costa, Manuela E. Pintado, João Fernandes & Óscar L. Ramos

Universidade Católica Portuguesa, CBQF - Centro de Biotecnologia e Química Fina – Laboratório Associado, Escola Superior de Biotecnologia, Rua Diogo Botelho 1327, 4169-005 Porto, Portugal

Introduction

Numerous liposoluble compounds, such as carotenoids, cannabinoids and phytosterols, have very interesting biological activities, but their low water solubility, stability and bioavailability restrict their applications [1]. These limitations can potentially be overcome by using enabling delivery systems, which require the use of carrier materials with desirable properties. Microcrystalline cellulose (MCC), cellulose nanocrystals (CNC) and cellulose nanofibers (CNF) are promising carriers due to their unique features, i.e. renewability, biocompatibility, high surface area and amphiphilic nature [2]. Furthermore, the surface chemical reactivity and accessible hydroxyl groups of nanocellulose provide sites for chemical modification to give additional functionalities [3]. Surface modification [4,5] or coupling with cationic polymers [6] may be necessary in order to modulate the loading and release profile of hydrophobic and lipophilic compounds from nanocellulose structures.

Objectives

- Investigate MCC, CNC and CNF as carriers for the delivery of curcumin as model liposoluble compound;
- Evaluate the impact of the addition of a surfactant (Tween 40); a cationic polymer (chitosan); nanocellulose modification with a surfactant (CTAB); and modification by TEMPO oxidation, on the encapsulation and release of curcumin;
- Assess the release profile of curcumin upon simulated gastrointestinal conditions (i.e. time, temperature, pH)

Materials and Methods

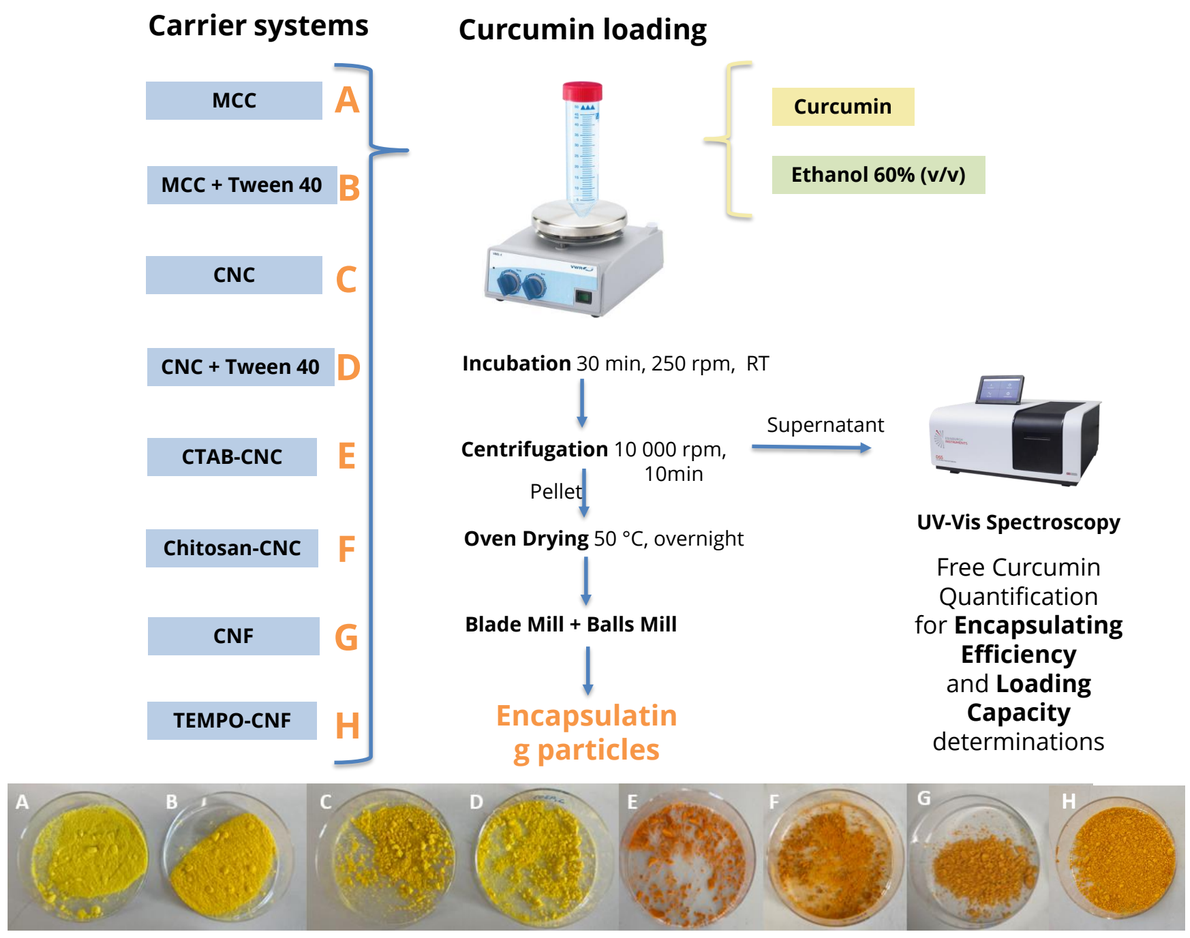

Figure 1. Photographs of the curcumin-loaded particles obtained using the different carrier systems.

Materials MCC, Tween 40, chitosan (high molecular weight) and cetrimonium bromide (CTAB) were purchased from Sigma-Aldrich. CNC was purchased from Celluforce. CNF and TEMPO-CNF (TEMPO - (2,2,6,6-tetrametil-piperidi-1-nil)oxil) were purchased from Cellulose Lab. CTAB-CNC was produced experimentally by the method described by Zainuddin et al. 2017 [4].

Carrier systems Neat MCC, CNC and CNF were tested as carriers. MCC and CNC mixed with Tween 40 and CNC mixed with chitosan were also studied. CNF functionalized by TEMPO oxidation and CNC modified with CTAB have also been tested has carriers.

Characterization The FT-IR spectra were recorded using the Frontier™ MIR/FIR spectrometer from PerkinElmer in a scanning range of 550-4000 cm^{-1} for 16 scans at a spectral resolution of 4 cm^{-1}. ● The crystallographic structure was evaluated by PXRD using a Rigaku MiniFlex 600 diffractometer with Cu kα radiation, with a voltage of 40 kV and a current of 15 mA ($3^{o} \leq 2\theta \geq 60^{o}$; step of 0.01 and speed rate of 3.0° /min). ● Zeta potential was evaluated by dynamic light scattering using a Malvern Instrument Zetasizer Nano ZSP.

Release Profile Curcumin-loaded particles were incorporated in simulated gastric fluid pH 3 at 37 °C for 2 h, followed by simulated intestinal fluid pH 6.8 at 37 °C for 6 h. Every hour a small aliquot was removed from each container, solubilized in EtOH 60% (v/v) and centrifuged. Released curcumin was quantified by UV–Vis spectroscopy at λ= 425 nm.

Results

The nanocellulose modifications with the CTAB surfactant and by TEMPO oxidation were confirmed by the functional groups and crystallographic structure analyzed by FT-IR and PXRD (Figure 2).

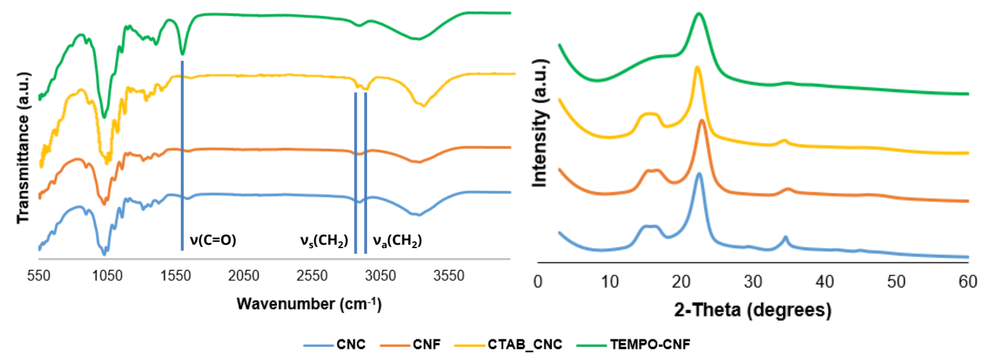

Figure 2. FT-IR spectra (a) and PXRD analysis (b) of the modified nanocellulose (CTAB-CNC and TEMPO-CNF) in comparison with plain CNC and CNF.

Cellulose micro- and nanostructures encapsulating curcumin were prepared by incubation and casting, and evaluated in terms of entrapment efficiency (EE), loading capacity (LC), yield, surface charge (zeta potential) and release profile. Results are presented in Table 1 and Figure 3.

Table 1. Yield, EE (%), LC (%) and Zeta potential of the curcumin encapsulating particles.

Sample	Yield (%)	EE (%)	LC (%)	Zeta Potential (mV)
A	73.2 ± 2.7	74.3 ± 3.2	25.0 ± 7.1	-29.87 ± 2.37
B	52.7 ± 2.9	77.7 ± 2.1	29.2 ± 1.1	-27.67 ± 1.46
C	68.0 ± 3.2	84.3 ± 3.1	31.0 ± 5.4	-49.83 ± 2.75
D	51.4 ± 4.4	85.1 ± 2.5	29.1 ± 0.9	-52.00 ± 4.69
E	90.4 ± 3.2	90.2 ± 1.6	24.8 ± 3.5	-16.37 ± 1.18
F	50.1 ± 4.1	99.6 ± 3.4	49.3 ± 2.9	-20.03 ± 1.56
G	91.2 ± 3.6	84.8 ± 4.8	24.7 ± 3.1	-19.67 ± 5.52
H	68.9 ± 2.7	85.4 ± 0.3	35.4 ± 8.7	-29.13 ± 0.90

Modification with CTAB and mixture with chitosan resulted in higher binding efficiencies (90.2-99.6%), corroborated by a more intense orange color of these particles (Figure 1). This is probably due to the hydrophobic CH_2 groups in CTAB (confirmed by FT-IR, Figure 2) and the amino groups in chitosan, which facilitate curcumin binding.

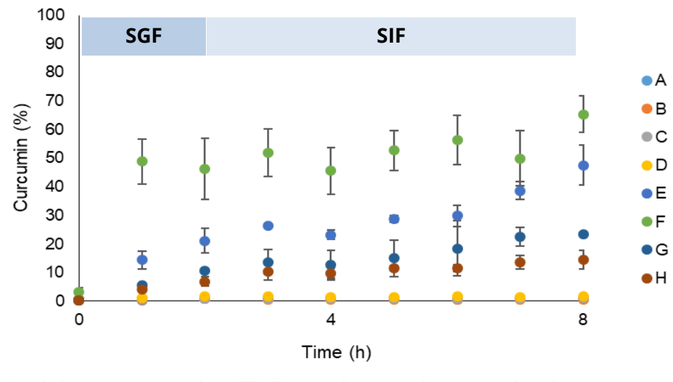

Figure 3. Curcumin release profile from the prepared encapsulating particles in conditions that mimic the gastrointestinal fluids, namely the pH, temperature and time of exposure in simulated gastric fluid (SGF, 2 h) and intestinal fluid (SIF, + 6 h)

Modification with CTAB and coupling with chitosan also allowed a faster release of curcumin (47-65% released in 8 h), while the other systems only released up to 23% within the same time period.

Conclusions

CNC and CNF were more efficient than MCC in curcumin binding. Modification with CTAB and coupling with chitosan resulted in higher curcumin binding efficiencies (90-99%). These also allowed a faster release of curcumin in simulated gastrointestinal conditions. CNC-Chitosan released ca. 50% of curcumin after 1 h in SGF, while CNC-CTAB released only ca. 20% in SGF (after 2 h), but up to 47% in SIF (after 8 h), which may be particularly interesting for intestinal delivery of bioactive compounds.

Acknowledgements

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