Micro/Nano Structured Materials

Continuous Production Technologies

Microencapsulation

KEYWORDS: Microcapsules/ Continuous Production/ NETmix technology / Textile application

The production of microparticles for textile applications was developed by adapting the NETmix technology for the steps more commonly made in batch processes. Melamine-formaldehyde, MF, microcapsules were obtained through a polycondensation process; different temperatures and recirculation times were tested in the curing step. Microcapsules presented diameters around 20 µm and were successfully impregnated on cotton fabrics by padding. Cellulose acetate, CA, microspheres were produced through a solvent evaporation method. Emulsions were produced at Reynolds numbers (Re) ranging from 200 to 1200 to evaluate its effect on the resulting microspheres' size, all characterised by a well-defined spherical shape with a rough and porous shell. The NETmix reactor can reduce the cure time relative to traditional batch processes, producing microcapsules with similar characteristics in a continuous process.

Introduction

Microencapsulation processes consist of coating an active ingredient by a membrane of another material, thus protecting the active principle, the functional material, from the surrounding environment. The active ingredient is referred as the core, and the surrounding material forms the shell. The textile industry is an important area of interest for microencapsulation since functionalised textiles with microcapsules can promote comfort and protection. Carrier oils such as triglycerides are non-irritating skin emollients, encapsulated due to their hydrating properties and good skin absorption. Melamine resin was used in this work as the shell material due to its good resistance against water and heat, mechanical robustness, and surface smoothness, an advantage for textile applications. Cellulose acetate is a biodegradable thermoplastic polymer and the most abundant natural polysaccharide. It is widely used in pharmaceutical formulations for sustained-release, tastes masking products and in the manufacture of various commercial products such as fabrics, plastics,

Emulsification, with the formation of a stable emulsion, is the crucial step in microencapsulation since the oily droplets' diameters define the microcapsules' diameter. Droplet size control is challenging when the emulsification process is scaled from laboratory to industrial scale, commonly resulting in polydisperse emulsions. Furthermore, in batch processes, care must be taken to obtain a homogeneous and stable emulsion in order to produce microcapsules with similar properties [8]. Various types of stirring systems can be used to get a suitable emulsion, and it must be ensured that conditions such as the power of the stirrer promote good mixing through the whole volume of the vessel.

The NETmix static mixer is a patented technology developed at LSRE-LCM/FEUP, and it consists of a network of interconnected chambers and channels where chambers operate as mixing zones and channels behave as plug flow. Above a critical Reynolds number of ca. 150, this system evolves to a self-sustained oscillatory laminar flow regime inducing local strong laminar mixing. Two different set-ups were used in this work. LabNETmix has a capacity of 23 mL and presents cylindrical chambers with a diameter of 6.5 mm and depth of 3 mm, and rectangular cross-section channels with a width of 1 mm and length of 2 mm. With smaller dimensions, MicroNETmix has a total volume of 1 ml and chambers with a diameter of 3 mm and 0.5 mm of depth and channels with 0.5 mm of width and 2 mm of length.

The production of microparticles (MF and CA) for textile applications was developed by adapting the NETmix technology for the steps more commonly made by batch processes.

For the MF microcapsules, carrier oil is used as the core material and melamine resin is used as the shell material. The goal was to produce a stable oil-in-water emulsion and to cure the shell of microcapsules by polycondensation in a continuous process, using the two NETmix devices described above. The resulting microcapsules were impregnated into cotton fabrics by padding to obtain functionalised textiles. Fig.1 shows a schematic illustration of the emulsification and cure steps in the NETmix reactor.

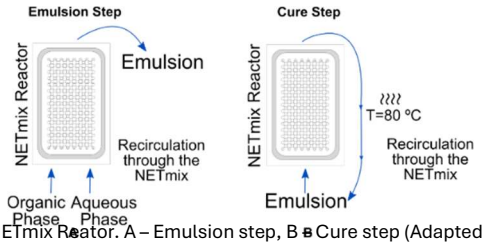

Fig 1. NETmix Reator. A – Emulsion step, B – Cure step (Adapted from Moreira et al.)

For the CA microspheres, eugenol (EG), the major component of clove essential oil, was used as core material; the emulsion step was transposed to continuous mode using the LabNETmix technology, and the influence of the Reynolds number was studied. Selected microspheres were impregnated by padding to obtain functionalised textiles. Treated textiles were observed with Scanning Electron Microscopy, and release studies of EG to the air were evaluated.

The functionalisation of cotton fabrics was made through padding (Fig. 2), a traditional process of textile impregnation.

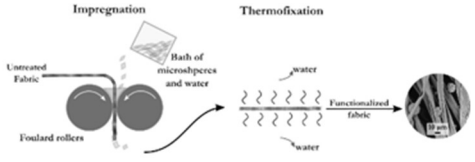

Fig 2. Foulard technique used for the impregnation of microspheres.

Current Development

For MF microcapsules produced in LabNetmix, the emulsions were obtained with either a single pass or by recirculating the mixture through the NETmix, whereby it was shown that recirculation promotes a decrease of the diameter of the oily droplets to circa 25 µm. These microcapsules were then cured and formed. After coating and stabilising steps, microcapsules present a mean diameter of 30 µm, remain stable, do not disintegrate, and show a smooth surface with no membrane fragments (Fig.3A). In MicroNETmix, emulsion with recirculation promoted a mean droplet diameter of 9 µm. After the curing step at 80 ºC, microcapsules showed a slight increase of diameter, 13 µm, which remains after coating and stabilising steps. In MicroNETmix, Re>350 ensures small diameters avoiding the breakage of microcapsules. Microcapsules are spherical, with a smooth surface, and no rupture is observed (Fig.3C). Microcapsules produced in both reactors show mean diameters within the range is 10-40 µm, the preferred size for textile application (Fig. 3B/D). Noteworthy is that, either in LabNETmix or in MicroNETmix, the curing step is reduced from 150 minutes, typically observed in the batch process, to 30 minutes.

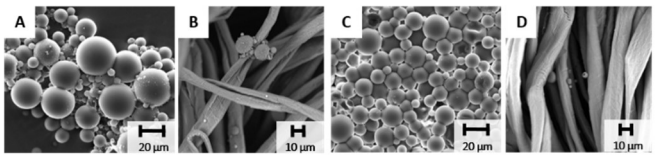

Fig 3. SEM images of melamine-based microcapsules: A and B - produced in LabNETmix and its impregnation in cotton fabrics, respectively. C and D - produced in MicroNETmix and its impregnation in cotton fabrics. respectively. A, C- resolution of 2000x; B, D– resolution of 2500x.

For the CA microspheres, the morphology of the particles is independent of the Reynolds number. Fig. 4 shows high-resolution SEM images for larger diameter CA microspheres (CA200 to CA400).

All microspheres present a well-defined spherical shape, with a porous and rough shell contrasting with the smooth surface microspheres produced in batch conditions. This porosity and roughness of the shell are likely due to the low CA concentration used and to the solvent evaporation step. With low CA concentration, less mass of CA is available to cover the DP droplets, thus explaining the porosity. This is augmented during solvent evaporation since the solvent, which is firstly entrapped into the DP matrix, is then evaporated, going through the polymer shell that is being formed, destroying it in the process. In some cases, microspheres appear to be broken or hollowed (black holes), mostly for higher Reynold numbers. The continuous mode enables the production of microspheres with a specific range of diameters by changing Reynolds number.

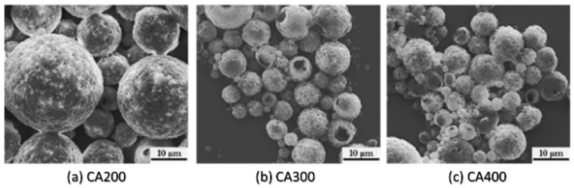

Fig 4. High-resolution SEM images of (a) CA200, (b) CA300 and (c) CA400. Resolutions of 5000x.

Future Perspectives

The emulsion and cure steps in the production of microcapsules can be achieved using the NETmix technology. Microcapsules are stable after production and keep the spherical shape and morphology after impregnation on fabrics. The continuous process leads to microcapsules with the same characteristics as batch production, with a significative (80%) reduction of curing time when compared with the batch procedure.

With NETmix, it is possible to control the diameter by changing the Reynolds number to obtain microspheres with similar morphology and required size for textile applications.

This work provides a proof of concept for the capability of NETmix to replace batch processes for microencapsulation in industrial applications.

Related Sustainable Development Goals

Outputs

PhD Theses

[1] Ana Catarina Godinho Moreira, Continuous production of microparticles for textile applications using NETmix, a mesostructured reactor, PDEQB, FEUP, 2021.

Selected Publications

[1] A.C.G. Moreira, Y.A. Manrique, I.M. Martins, I.P. Fernandes, A.E. Rodrigues, J.C.B. Lopes, M.M. Dias, Ind Eng Chem Res, 59, 3595 (2020).
[2] A.C.G. Moreira, Y.A. Manrique, I.M. Martins, I.P. Fernandes, A.E. Rodrigues, J.C.B. Lopes, M.M. Dias. Cellulose, 29, 18510 (2022).

Team

Madalena M. Dias, Professor; **José C. B. Lopes,** Professor; **Alírio E. Rodrigues**, Professor; **Yaidelin A. Manrique**, Researcher; **Isabel M. Martins**, Researcher; **Ana Catarina Moreira,** PhD Student

Funding

TexBioPro,POCI-01-0247-FEDER-003472, 2016-2019
LSRE-LCM Base Funding, UIDB/50020/2020, 2020-2023
LSRE-LCM Programmatic Funding, UIDP/50020/2020, 2020-2023
LA LSRE-LCM Funding, UID/EQU/50020/2019, 2019
LA LSRE-LCM Funding, POCI-01-0145-FEDER-006984,2013-2018

Continuous Production Technologies

Dispersions and Pickering Emulsions

KEYWORDS: NETmix / hydroxyapatite-chitosan dispersions / Pickering emulsions

The NETmix technology was used to develop processes for the continuous production of Dispersions and Pickering Emulsions.

High-added-value hybrid materials (microparticles and scaffolds) for medical and dental applications were obtained from nano-hydroxyapatite and Chitosan, n-HAp/CS, dispersions. Stable Pickering emulsions (PEs) based on n-HAp, with potential application in the foodstuffs, were also developed.

Introduction

NETmix, a technology developed at LSRE-LCM, Faculty of Engineering University of Porto (FEUP), comprises a network of unit cells, each cell composed by one chamber and four channels (two inlet and two outlet half channels) oriented at 45° from the main flow direction. The network size is given by the number of rows (along the main flow direction) and the number of columns (perpendicular to the flow); the chambers operate as mixing zones and the channels as plug flow zones (Fig. 1). In this way, a chamber contacts with fluids from two chambers of the previous row, splitting and feeding two chambers in the following row. NETmix operation is based on this flow pattern, promoting successive contacts and separations from channels to chambers.

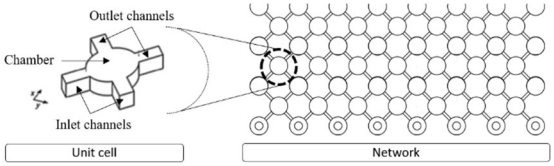

Fig 1. NETmix schematic representation: unit cell and network.

NETmix ensures easy control of the parameters affecting mixing, providing good reproducibility between assays; it does not limit the production volume, can reduce the production time, and allows production in continuous mode. Thus, NETmix can offer several advantages for producing different products, namely n-HAp/CS dispersions and PEs with relevant industrial applications.

A great interest has been given to synthetic and stoichiometric hydroxyapatite (HAp) as a biomaterial due to its similarity with the mineral phase found in hard tissues. It possesses exceptional biocompatibility and bioactivity with respect to bone cells and surrounding tissues, which makes it a suitable material for the replacement of small parts of bone, filling cavities in dentistry, and coating metallic implants. Additionally, due to its hydrophobicity, HAp is suitable as Pickering stabilizer, i.e., to be used as an emulsion stabilizer, which makes them an interesting material for substitution of conventional emulsifiers used in the food industry. In this work, nano-crystalline hydroxyapatite produced by Fluidinova (fluidinova.com) and commercialized under the brandname NanoXIM was used.

HAp-based hybrid materials are promising not only in terms of market opportunities but also due to their contribution to regenerative medicine, such as for hard tissue regeneration. The incorporation of nano-hydroxyapatite (n-HAp) into polymeric materials, particularly natural polymers such as chitosan (CS), is recognized as one of the most viable approaches to produce materials mimicking natural bone, that can be used as devices for bone regeneration.

Pickering emulsions (PEs) arose as alternatives to traditional counterparts and are receiving high interest, both from industrial and academic levels. These emulsions are stabilized by solid particles (here n-HAp) that are able to be attached in the oil or water surface, forming a thicker barrier. The formation of the protective shell around the oil, or aqueous core, can provide encapsulation systems for drugs and bioactive compounds. The “surfactant-free” character makes PEs more suitable for various applications, particularly in the food area.

Current Development

Dispersions

A process for production of n-HAp/CS scaffolds was developed. Fig 2 shows three different studied procedures. The first step (A) is the incorporation of n-HAp particles into a CS solution at controlled pH.

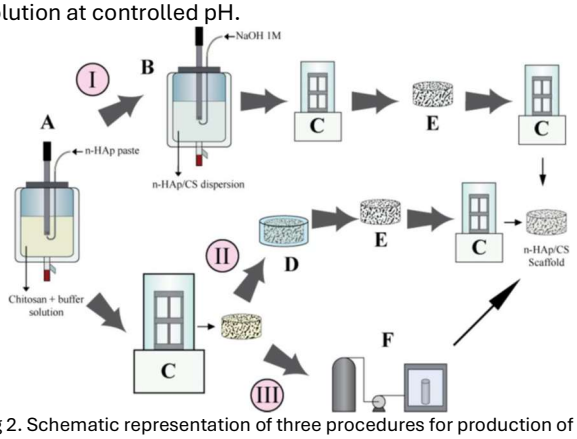

Fig 2. Schematic representation of three procedures for production of n-HAp/CS scaffolds: (a) Dispersion preparation; (b) Neutralization of acetic acid by dropwise addition of NaOH 1M; (c) Freeze drying; (d) Neutralization by immersion in NaOH/ethanol solution; (e) Washing with ultrapure water; (f) Acetic acid extraction with scCO2.

HAp/CS hybrid scaffolds are obtained by freeze-drying the dispersion (step C). The best and innovative procedure was obtained in a single purification and sterilization step based on scCO2 extraction. The conditions that best achieved an acetic acid extraction yield of 80% were two 2-h cycles in static mode at T=75°C and p=8.0 MPa. The produced scaffolds (Fig 3) mimicked bone composition and exhibited adequate porosity, interconnected porous structure, and fast swelling, highly desirable features for bone regeneration.

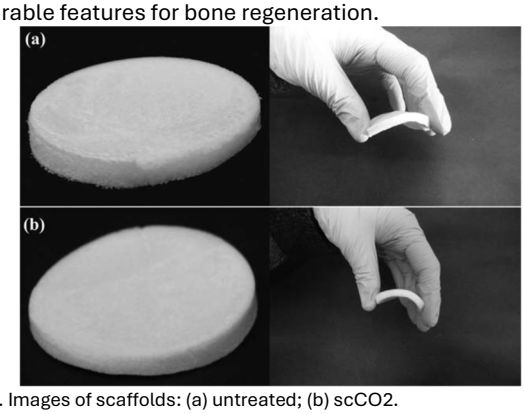

Fig 3. Images of scaffolds: (a) untreated; (b) scCO2.

Microbiological assays showed no microbial growth evidencing that scaffolds were sterile, enabling the adhesion and proliferation of osteoblastic cells, which increased gradually along the tested 21-days period, without any

disinfection or sterilization treatment, which is a quite promising result.

Based on the best conditions achieved in batch mode, n-HAp/CS composite dispersions were produced in continuous mode using NETmix. Highly homogeneous and stable n-HAp/CS composite dispersions (10 µm of size and >+30 mV of potential zeta) were produced. The process exhibited excellent reproducibility, proving the viability of NETmix to produce n-HAp/CS nanocomposite dispersions with desirable properties, process that can be easily scaled up, having in view a possible industrial scale.

Pickering Emulsions

PEs were produced considering the relevant parameters affecting their stability, such as solids content and oil-water ratio. For both batch and continuous modes, a stable emulsion was achieved with a 20-80 oil-water ratio and 5 %wt. n-HAp.

In batch mode, the mean diameter of the oil droplets ranged between 10-25 µm (Fig 4 A1), while in continuous mode (at Re~400) were droplets with 5-7 µm were obtained (Fig 4 B1). This lower size obtained in the continuous process, not possible to achieve with batch mode, was also accompanied by the narrowing of the size distribution. Cryo-SEM images (Fig 4 A2, B2) show Pickering droplets with a n-HAp layer around the oil core, and EDS analysis confirmed the presence of these materials at the oil surface. In both cases, the PEs remained stable for at least 2 months, with a higher long-term stability expected for the NETmix emulsions, due to their lower size.

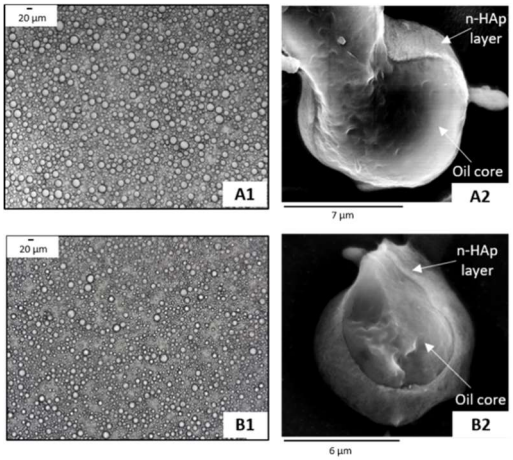

Fig 4. Optical and cryo-SEM images of the Pickering emulsions (PEs) obtained in batch (A1 and A2) and continuous (B1 and B2) modes.

Space-time yield (STY), defined as the mass flow rate per reactor volume, was used to compare the batch and continuous modes. STY was estimated in 2.4×10^5 kg/m^3/day using a rotor-stator, and at 3.0×10^7 kg/m^3/day using NETmix, that is, two orders of magnitude higher.

The stability of the produced emulsions against different environmental stresses was studied to cover a wide range of stress conditions with interest in food products production, storage and ingestion (temperature: 5, 22, 30, 50, 70 and 90 °C, pH: 2, 4, 6, 8 and 10, and ionic strength: 0, 100, 200, 300, 400 and 500 mM). In general, the n-HAp PEs were stable within the tested ionic strength range, at relatively high pH environments (6–10), and at temperatures up to 70 °C. PEs undergo complete phase separation at very low pH (2) due to n-HAp particle's disruption. A clear tendency to aggregation and coalescence was observed for high temperatures (70–90 °C).

Results are promising and show the feasibility of using the NETmix technology to produce PEs. This fact is an advantage from an energy point of view (NETmix is a low-energy device) and allows continuous production that supports a high-volume scale compatible with industrial production, facilitating the development of end-user applications, namely food applications loaded with lipophilic vitamins.

Future Perspectives

NETmix is a valuable option for producing dispersions and PEs and represents an interesting achievement in the transition from batch to a continuous process. This approach can be applied to other PE formulations to answer the industrial needs for more reproducible and high-volume scale production. Additionally, PEs can be used as versatile vehicles for encapsulating hydrophobic compounds such as vitamins, which is technologically an important issue. This work will continue as part of the workplan of a FCT Stimulus of Scientific Employment Grant (2022.00798.CEECIND).

Currently, other types of solid particles, such as lignocellulosic biomass (LCB) from leek trimmings are being used to develop stable O/W PEs. Here, the stabilization mechanism is based on the formation of a network that traps the droplets and prevents coalescence. Results show the scale-up feasibility of the production of PEs containing LCB,

Related Sustainable Development Goals

Outputs

PhD Theses

[1] Andreia Ribeiro, Nanohydroxyapatite Pickering emulsions: From product development to functional ingredients in food applications, PDEQB, FEUP, 2021.

Master Dissertations

[1] Mariana Pereira, Development of emulsion products from natural raw materials, MIEQ, FEUP, 2022

Selected Publications

[1] G. Ruphuy, T. Weide, J.C.B. Lopes, M.M. Dias, M.F. Barreiro. Carbohydrate Polymers, 202, 20-28 (2018)

[2] G. Ruphuy, M. Souto-Lopes, D. Paiva, P. Costa, A.E. Rodrigues, F.J. Monteiro, C.L. Salgado, M.H. Fernandes, J.C. Lopes, M.M. Dias, M.F. Barreiro. Journal of Biomedical Materials Research - Part B Applied Biomaterials, 106, 965-975, (2018)

[3] A. Ribeiro, Y.A. Manrique, F. Barreiro, J.C.B. Lopes, M.M. Dias. Colloids and Surfaces A: Physicochemical and Engineering Aspects, 616, 126365 (2021)

[4] A. Ribeiro, Y.A. Manrique, I.C.F.R. Ferreira, M.F. Barreiro, J.C.B. Lopes, M.M. Dias. Journal of Dispersion Science and Technology, 43, 814-826 (2022)

[5] A. Ribeiro, Y.A. Manrique, M.F. Barreiro, J.C.B. Lopes, M.M. Dias. Biophysics, 17, 422-436 (2022)

[6] M. Souto-Lopes, L. Grenho, Y.A. Manrique, M.M. Dias, M.H. Fernandes F.J. Monteir; C.L. Salgado. Biomaterials Advances, 146, 213280 (2023)

Team

José Carlos B. Lopes Professor; Madalena M. Dias, Professor; Yaidelin Manrique, Researcher; Gabriela **Ruphuy**, PhD Student; Andreia Ribeiro, Researcher; **Eduardo Pimentel**, Project Fellowship; Mariana Pereira, Project Fellowship; Margarida Brito, Researcher.

Funding

LSRE-LCM Base Funding, UIDB/50020/2020, 2020-2023
LSRE-LCM Programmatic Funding, UIDP/50020/2020, 2020-2023
LA LSRE-LCM Funding, UID/EQU/50020/2019, 2019
LA LSRE-LCM Funding, POCI-01-0145-FEDER-006984,2013-2018
NoMIC2Bone, NORTE-01-0247-FEDER-017905, 2017-2020
PDEQB, NORTE-08-5369-FSE000028, 2016-20020
S4Hort_Soil&Food, NORTE-01-0145-FEDER-000074, 2021-2023
FCT Grant: 2022.00798.CEECIND (A. Ribeiro)