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Lutein PGSS encapsulation at low temperature for a better controlled release

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1. Introduction

In the past decades, the pharmaceutical industry faced novel challenges linked to the increase of age-related and chronic illness due to the ageing of the population in industrialized countries. Age related macular degeneration (AMD) is one of them. Currently, due to the availability of palliative treatments only to mitigate the progression of AMD, the pharmaceutical industry brings a particular attention to the identification and development of preventing agents.

Lutein, a carotenoid with strong antioxidant properties found in the macular region was identified as a strong preventing factor of AMD. Consequently, lutein diet supplements for elderly persons were developed. Some daily recommendation intakes can be found in the literature. Some studies suggested a 4 mg per day intake to reduce risk of development of AMD. [1]Another study also investigated a 20 mg daily dose and concluded to no toxicity.[2]

Due to the lutein low water-solubility and consequently low bioavailability, as well as the low lutein chemical stability (photosensitive compound), some studies focused on lutein delivery optimization through encapsulation processes. In a recent review of Steiner *et al.*, it can be seen that mainly solvent-based methods have been used, suggesting the risk of hazardous solvent residues. [3]

To avoid such residues, supercritical carbon dioxide ($scCO_2$) technology, especially particles from gas saturated solution (PGSS) process, can be an alternative to solvent-based methods. De Paz et al., demonstrated the feasibility of lutein encapsulation in polycaprolactone (PCL) using $scCO_2$ at 70 °C under 15 MPa with moderate yields (up to 44 % collected particles).[4]

In this study, PGSS technology is investigated using pure PCL and PCL/polyethylene glycol (PEG) blend to entrap lutein. Thus, the lutein release could be modulated thanks to the hydrophilic behavior of PEG and the hydrophobic behavior of PCL. Regarding PGSS processing, moderate temperatures (38 to 45°C) are applied, demonstrating the ability to encapsulate thermolabile compounds, while optimizing the process yield.

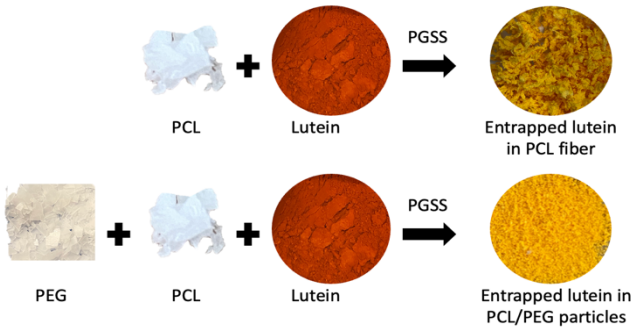

Figure 1. Graphical abstract

2. Materials and Methods

Polycaprolactone (average Mw ~ 14,000, average Mn ~ 10,000 by GPC) was purchased from Merck (Saint Quentin Fallavier, France). Poly (ethylene glycol) (average Mn ~4,000) was purchased from Sigma Aldrich (Germany) Lutein extract from marigold flowers was provided by Shaanxi Superior Bio Technology Co., (Shanxi, China). Carbon dioxide (CO_2, purity 99.7 %) was supplied by Air Liquide (France). All chemicals and solvents were used as received.

Figure 2. illustrates the process flow diagram of the PGSS set-up used for lutein encapsulation into PCL or PCL/PEG blend.

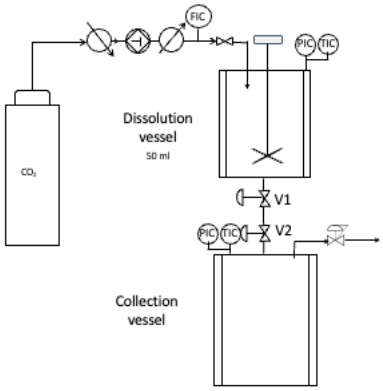

Figure 2. PGSS process flow diagram

The drug loading of the resulting powders was evaluated using UV-VIS spectroscopy, as well as NMR spectroscopy. *In-vitro* release was performed in PBS solutions. The antioxidant activity was also characterized.

3. Results and discussion

Operatory conditions of pressure and temperature were fixed basing on preliminary characterizations of the behavior of the investigated polymers in supercritical CO_2 using a high-pressure view cell.

Process yields up to 81% were obtained at 38°C.

In all the tested conditions, a pale-yellow powder was obtained indicating an entrapment of lutein within the polymer. (**Figure 1**)

The morphology of the resulting powder varies according to the operating conditions. (**Figure 3**)

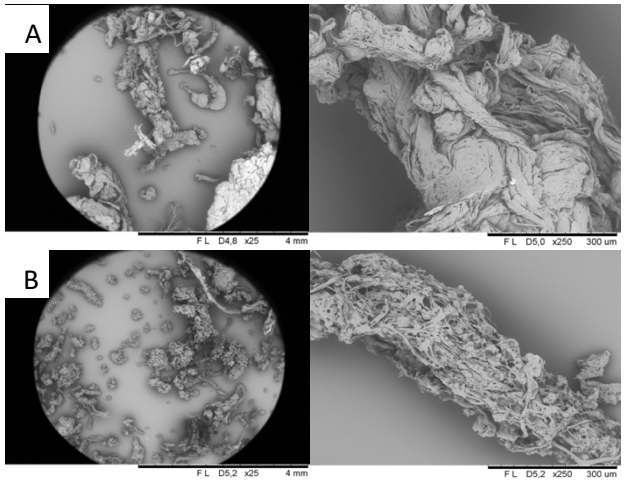

Figure 3. Scanning electron microscopy of lutein-entrapped in. A) pure PCL and B) PCL: PEG blends.

4. Conclusions

This study highlights the potentiality of applying PGSS process to encapsulate lutein in mild conditions of temperature (38°C) with good process yields (up to 80%). In addition to enhance the drug stability, the release from the polymer formulation can be modulated by adjusting the polymer blend ratio.

References

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