Designing Sustained Release Encapsulates loaded with Water Soluble Oxidant: Carbamide Peroxide

Fideline L. Tchuenbou-Magaia¹, James Gwyer², Nigel Young² and Zhibing Zhang¹

¹ University of Birmingham, School of Chemical Engineering, B15 2TT, UK
² Philips Research Laboratories CB4 0FY, UK

f.l.tchuenboumagaia@bham.ac.uk

ABSTRACT SUMMARY

Carbamide peroxide (CP), a hydrogen peroxide (HP) releasing agent has been encapsulated as a model active of water soluble, sensitive and reactive active. A screening of commonly used encapsulation techniques placed spray cooling of solid CP as the most promising cost effective method with paraffin wax as a carrier. The release profile of HP was temperature dependent and was tuned to achieve fast or slow release using release rate modifiers.

INTRODUCTION

Carbamide peroxide (CP) is an adduct of hydrogen peroxide and urea widely used as relatively safe, cheap and stable reagent for the replacement of hydrogen peroxide (HP) in several oxidation processes. These range from anhydrous organic synthesis to bleaching, especially tooth whitening. Teeth are generally whitened with formulations containing high concentration of CP (up to 35%) in the dentist premises (in-office bleaching) with a special care to avoid damage to soft tissue whereas consumer whitening products available today for home use such as gels, rinses, chewing gums, toothpastes, paint-on films and strips are loaded with lower concentration. However, although products of 10-15% carbamide peroxide are classified as safe by FDA, the EU legislation does not permit the use of HP concentrations greater than 0.1% (i.e. about 0.3% CP) in commercial tooth whitening or oral hygiene products.¹

It is postulated that encapsulates loaded with CP designed to release HP in a controlled and sustained manner at safe concentration would make possible a cost effective at-home whitening products with good efficacy. However, CP is soluble in water (up to 40% w/w) and when it dissociates into urea and HP, CP easily reacts with most organic matter. These properties of CP make its encapsulation very challenging.

We have extended our initial work on the encapsulation of CP ² and demonstrated that a sustained release of HP could be achieved when paraffin wax was loaded with CP via spray cooling.

EXPERIMENTAL METHODS

Solid CP was encapsulated by spray cooling in a molten paraffin wax (melting point of 53-57ºC) containing CP and processing aids/release rate modifier using syringe as a nozzle as described in the patent application WO/2013/09387 or a rotary disk to achieve micro encapsulates. Some samples were made by emulsion with shellac² or phase separation by suspending CP into Eudragit EPO dissolved in an anhydrous diethyl ether and using heptane as anti-solvent.

Encapsulates were characterized using X-ray tomography, scanning electron microscopy (SEM) and differential scanning calorimetry (DSC). HP release study was performed in Phosphate Buffered Saline (PBS), pH 7.4 or Milli-Q at 37°C or at room temperature (22 ± 2°C) and the amount of HP quantified spectrophotometrically at 351 nm.

RESULTS AND DISCUSSION

Encapsulates made via spray cooling and atomized with a syringe (Figure 1a) were formulated with Paraffin wax and polyethylene glycol (PEG) or hydrophilic particles to tailor
the release rate of HP (Figure 2a). Slower release was observed with PEG 15000 and silica nanoparticles (Aerosil) when compared to PEG 2000 and micron-size STPP, respectively indicating that the type and size of these agents may play a role in the engineering of controlled release wax based encapsulates.

CP encapsulated with only paraffin wax using an industrial spray cooling device, showed the same trend, but faster release of HP (Figure 2b) due to difference in the particle size (Figure 1b). The release of HP from the wax matrix in Milli-Q water was not significantly different from that in PBS but was affected by the temperature. Shellac encapsulates showed high burst release and degradation of HP whereas no controlled release was achieved with Eudragit EPO.

Figure 3 shows DSC curves of 9 month-old Paraffin wax based encapsulates with apparent peaks that correspond to the melting range of wax and CP for encapsulates containing silica or STPP. The melting peak of CP was absent when PEG was present in the formulation, evidencing a possible interaction between PEG and CP.

Figure 3. DSC curves of CP, paraffin wax, PEG 1500 and 9 month old encapsulates (heating rate 10°C/min in the presence of argon).

CONCLUSION

CP-loaded encapsulates with controlled and sustained release of HP have been made by spray cooling using paraffin wax as a carrier. A range of HP release profiles was achieved with PEG 1500 and 2000, silica or anhydrous STPP. However DSC results indicated long term stability only for encapsulates formulated with paraffin wax and inorganic particles.

REFERENCES

1. European Commission. 14th plenary of 18 December 2007, [Accessed 02/01/2014]