ABSTRACT

Controlled-release packaging (CRP) is a rising technology by which actives such as antioxidants and/or antimicrobials can be released in controlled and desirable fashion from the packaging material over a long period of time to prolong the shelf-life of packaged food. Most of the CRP systems developed so far are based on either packaging film or packaged microparticles comprised of actives entrapped in polymeric materials. We were particularly interested in developing particle based systems because of their ease of handling and operations without losing the activity of packaging actives encapsulated in them. To the best of my knowledge, all such microparticles are mostly composed of single polymer and hence, can be useful to deliver single active. In order to release multiple actives (e.g. antibacterial and antioxidant) at desirable rates without having active-active interactions, multilayered particles entrapping different actives in various layers can be quite useful.

In order to achieve the goal, biodegradable multi-layered Poly(lactic-co-glycolic acid)(PLGA)/Poly(l-lactic acid)(PLLA) based dual actives loaded polymeric particles were fabricated and their applications as dual actives (antioxidant and antibacterial) delivery vehicles were explored in Chapter-2. Briefly, 2 kinds of microparticles (bi- and trilayered) made up of PLLA and PLGA with varying viscosity (intrinsic viscosity (I.V.)) were developed using one step emulsion solvent evaporation method. Release study demonstrated that release rate of dual actives(antimicrobial: benzoic acid and antioxidant: tocopherol) was significantly accelerated from tri-layered particles in comparison to bi-layered one. Both sets of particles exhibited long-term antibacterial activity against both *Escherichia coli(E. coli)* and *Staphylococcus aureus (S. aureus)* bacteria (residual bacterial concentration: 0-2 log(Colony forming unit(CFU)/mL)) as well as antioxidant activity (radical scavenging efficiency: 80-90%) over a period of 60 days. The results show for the first time the

feasibility of using multilayered microparticles to prolong the food shelf-life by simultaneous release of dual actives.

To achieve excellent bacterial killing efficiency, instead of using sole benzoic acid (as used in Chapter-2), a minute quantity of mustard oil as second antibacterial was incorporated into PLGA based single phase particles. Surprisingly, PLGA based porous particles were resulted in and these were found to exhibit unusually high antibacterial activity for prolonged period of time. Hence, in Chapter-3, we have focussed on the use of mustard oil in monophasic as well as multi-phasic (multilayered) microparticles to come up with a system having strong antibacterial (not achieved in Chapter-2) as well as antioxidant efficiency. This chapter has been divided into two parts. Part A describes the fabrication of porous PLGA microparticles using water/oil/water (W/O/W) double emulsion technique in presences of a minute quantity of mustard oil. The release of benzoic acid from the porous particles were found to be well-controlled in nature and influenced by surface porosity of the particles that can be manipulated by varying the amount of mustard oil. Strikingly, in liquid medium, porous particles were found completely suppressing the growth of bacteria (100% inhibition) for a prolonged period of 60 days. In a food model system, the shelf life of the watermelon juice was also found to be enhanced by suppressing the growth of the natural microbes in comparison to control. The addition of mustard oil was then extended to multi-layered system. Hence, part B of Chapter-3 focuses on the fabrication of hierarchically porous biodegradable microparticles of various architectures (Janus and core-shell configuration) by adding mustard oil into PLGA/PLLA based multilayered system and evaluation of their applications in prolonging food shelf-life. Synthesis, characterization, and mechanism of formation of various kinds of architecture obtained by varying the mustard oil content in multilayered particles, have been explored in detail. Apart from these, performance of these dual actives (antibacterial and antioxidant) loaded Janus and multi-layered particles in active

packaging area were also evaluated for prolonged period of time. Bacterial growth reductions of 2-6 log(CFU/mL) and radical scavenging efficiency of 70-90% were observed to be maintained for 60 days especially for Janus particles.

In order to develop a triggered release system along with CRP, we have focussed in designing and fabrication of dual actives loaded pH responsive systemin Chapter-4. Bi-layered particles with desirable layer compositions (core/shell and vice-versa) were achieved by using acetalated-dextran and PLGA at a mass ratio of 2:1 or 1:2. pH responsiveness was validated by monitoring hydrolytic degradation of these bilayered microparticles in two different pHs(7.4 and 5) by Scanning electron microscope (SEM) and NMR study. A faster release of benzoic acid present in outer layer (acetalated-dextran) was observed in pH 5 for theacetalated-dextran/PLGA (shell/core) system compared to the PLGA/acetalated-dextran (shell/core) system. However, both systems release benzoic acid at similar rates at pH 7.4 but lower than that at pH 5. Similar observations were also found for tocopherol release. The tunable pH responsive behaviour of these microparticles can be potentially utilized for controllable and programmable active delivery not only in acidic food protection but also in drug delivery. Finally, Chapter-5 summarises the investigations and states how these CRP systems can be potentially exploited for prolonging the shelf-life of food.