UNIVERSITÀ DEGLI STUDI DI SALERNO

Department of Industrial Engineering

Corso di dottorato in Scienza e tecnologie per l'industria chimica, farmaceutica e alimentare - curriculum Ingegneria Chimica (XI ciclo)

PhD thesis in "Novel technologies and process intensification in the production of micro-systems with pharmacological/nutraceutical activity"

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Purpose of the PhD thesis was to develop a novel microencapsulation process, designing and building a single-pot semi-continuous bench scale apparatus. The novel process is based on the coupling of two emerging techniques, involving ultrasound and microwave, used in atomization and heating operations, respectively. The process has been designed to respond to the needs for process intensification, i.e. improvement of process efficiency and cutting down of energy consumption. With this aim, a review of the main processes used for microencapsulation was first performed: conventional processes showed a number of drawbacks, such as high energy consumption, batch configuration, use of solvents and long times of production. On the basis of the state of the art, the idea of an intensified apparatus for particles production, exploiting alternative resources, such as ultrasound and microwave, was formulated. The apparatus was composed of three main sections: feeding, atomization, separation/stabilization. The feeding and atomization sections were built connecting a double channel ultrasonic atomizer to a system for feeding solutions in a purposely designed separation/stabilization section, thus realizing a semi-continuous apparatus. Separation section consisted of a wet-collector, i.e. a sort of hydrocyclone, which allowed a uniform distribution of the hardening solution and the consequent contact with the atomized drops, a filtering device, and a microwave oven. The wet-collector was placed into the microwave oven to obtain an "on-line" drying. Recirculation of the hardening solution, to renew contact surface between droplets and cross-linker, was guaranteed by a system of centrifugal pumps. In this configuration, when atomization occurred, drops were harvested in the wet-collector. After atomization, the obtained suspension was collected in the cross-linker tank, then the filtering device was inserted in the lower part of the wet-collector, so that hardening solution was recovered and particles settled on the filter, when the suspension was brought again to the wet-collector and after its complete emptying. An eventual following washing step can be done in a similar way to the previous hardening step. Finally, particles were stabilized by microwave drying, and then recovered.

The steps for building the microencapsulation apparatus were accurately shown. Then, criteria used for components selection, in order to obtain the best performances from the plant, were highlighted. After building the plant, the process parameters were defined. First, the research for the best combination of feeding parameters, such as type of materials, composition, concentration and feed rate, that assure the encapsulation of the core material in the shell, was carried out. Then, the parameters of the ultrasonic atomizer (atomization section), essentially power, were tuned. Finally, for stabilization/separation section, fundamental was the relevant stabilization step, where microwave power was set to avoid too high temperatures that could degrade molecules.

The ability of the novel plant to obtain micronized systems, that exhibit a behavior interesting for the pharmaceutical or nutraceutical markets, was tested. Micro-particles characterization showed that it is possible to obtain a shell-core configuration encapsulating two functional molecules, vitamin B12 and □-tocopherol. Some important results were: 1) high loading and enteric (gastro-resistant) behavior of micro-particles; 2) delayed release for shell-core micro-systems compared to matrix ones; shell-core configuration in macro-scale (beads) able to prevent degradation of □-tocopherol, instead observed in matrix beads. Moreover, microwave treatment (not harsher for the short irradiation times) caused, especially for shell-core configuration, a little delay in molecule release. Resuming, better release properties for systems produced in the novel apparatus were achieved by the coupling of ultrasonic atomization and microwave drying. Furthermore, the basic

transport phenomena occurring in the ultrasonic assisted atomization were investigated, emphasizing the role of operative parameters, and literature correlations, based on forces balance, were also applied for droplets size prediction. All these results endorses the usefulness of the novel plant, based on the combination of two powerful tools of process intensification, ultrasonic atomization and microwave drying, to obtain micro-systems, particularly interesting for specific drug delivery applications. Moreover, working at room conditions and in absence of solvents, improving the energy transfer rate (faster process times), reducing process chambers volume (low particles inertia in ultrasonic atomization, single-pot process realization), enhancing the product quality (micro-particles with tailored features), makes the apparatus more attractive in terms of improved inherent safety and reduced costs.