# CHAPTER 2

# LITERATURE REVIEW

As applications of supercritical fluid could be found in various industries such as in the pharmaceutical, cosmetic and specialty chemistry industries, number of publications and patents are issued every year. This chapter presents a survey of published literature classified according to the concepts currently used in particle manufacturing. RESS refers to the 'Rapid Expansion of Supercritical Solutions' such process consists of solvating a solute in the fluid which finally undergoes rapid depressurization by flowing through an adequate nozzle, causing an extremely rapid nucleation particulate of the solute. This process is attractive due to the absence of organic solvent use. However, its application is restricted to products that present a reasonable solubility in supercritical carbon dioxide (low polarity compounds).

The production of particles upon depressurization of supercritical fluid solutions was first noted over a century ago [Hannay *et al.*, 1879]. The formation of particles during the expansion of supercritical fluid solutions through a nozzle has more recently been studied in many experiments. In 1991, Tom and Debenedetti proposed a means of identifying potential applications and suitable process conditions. Theoretical work aimed at gaining fundamental, quantitative understanding of RESS. They included an analysis of nucleation rate profiles along different expansion paths. The fundamentals, experimental methods, applications, and available results from studies of particle formation with supercritical solutions were also summarized.

In 1993, Debenedetti proposed the fundamental understanding of the various processes that occur during RESS, such as nucleation, growth, coagulation, with particular emphasis placed on relating particle size and size distribution to process conditions, such as nozzle length, geometry, upstream, downstream conditions and one-dimensional model of nucleation and particle growth during isentropic flow. He also presented how process conditions affect the size distribution of particles emerging from the nozzle. Since mathematical modeling and simulation are a handy and effective tool, the predictions of RESS process were investigated more comprehensively. He presented mathematical model of nucleation and particle growth during the partial expansion of a dilute supercritical solution in a sub-sonic converging nozzle. With basic assumption of steady one-dimensional flow, the calculations suggested that the partial expansion of supercritical solutions was an effective route to the formation of mono-disperse, and sub-micron powders.

In 1995, Tsutsumi et.al. had conducted the experiment of fluidized-bed coating process using the rapid expansion of supercritical fluid solutions (RESS). Supercritical carbon dioxide solutions of paraffin were expanded through the nozzle into the bed of the glass beads fluidized by air. The coating mass and coating rates were measured by a sampling method. A stable coating of fine particles was achieved without the formation of agglomerates at room temperature. The study examined the effects of hydrodynamics and solute concentration on coating rate and coating efficiency.

In 1996, Reverchon and Pallado proposed the hydrodynamic modeling of RESS process through an orifice which incorporated the heat transfer through the transonic shear layer and found the calculated temperature profiles to be in reasonable agreement with measurements. Moreover, Ksibi (1996) presented the numerically a two-dimensional flow field including shock waves, coupled with particle population balances but neglecting coagulation. It was based on the hyper-compressibility and the change of the solution capacity of the fluid from supercritical fluid condition in expansion to a lower pressure environment.

In 1999, Turk and co-workers modeled RESS process by considering the three parts of capillary inlet, capillary, and free jet. One-dimensional time-independent flow model for the pure solvent included heat-exchange in the capillary and the free jet, friction in the capillary and isentropic flow in the capillary inlet area. The resulting pressure and temperature changed along the expansion path were used to calculate the solute solubility in the solvent and the supersaturation of the real mixture with the Peng–Robinson equation of state. Moreover, in 2000, they had conducted the experiments which were carried out with an apparatus suitable for temperatures up to 600 K and pressures up to 60 MPa. Carbon dioxide ($CO_2$) and trifluoromethane ($CHF_3$) were used as supercritical solvents and cholesterol and benzoic acid as solutes. Besides the experimental investigations, the RESS process was modeled numerically by taking three parts of capillary inlet–capillary–microscale free jet into account. The evolution of fluid pressure and temperature along the expansion path were used to calculate the super saturation of the real mixtures and the respective nucleation rates.

In 2001, Tsutsumi et al. studied mechanism of particle coating granulation of fine particles with RESS process in a fluidized bed for pharmaceutical application. They had carried out experiments using glass beads as core particles, sand as fine particles and supercritical carbon dioxide solution of paraffin for expansion through a nozzle into a fluidized bed. According to their experiment results, achievement of stable coating granulation without significant agglomeration was verified.

In 2002, Debenedetti computed the particle size distribution accounting for nucleation, condensation, and coagulation by using a sectional method to solve the aerosol dynamic equation along an expansion device with given pressure, temperature, and density profiles.