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Research Article

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CFD simulation of multi-inlet jet-swirl nozzle for preparing nano-drug by SEDS process

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ABSTRACT

Based on the structure of jet-swirl nozzle, a new nozzle called multi-inlet jet-swirl nozzle (MIJSN) was designed for preparing nano-drug by SEDS process. The innovative character of the new nozzle is three same swirl vane distributed uniformly in the circumferential of swirl insert and used to introduce same solvent. MIJSN was validated by computational fluid dynamics (CFD) simulation. Volume fraction of methylene chloride and turbulent intensity were selected to act as indicators in order to compare MIJSN with jet-swirl nozzle. Results indicate that MIJSN can obtain more uniform mixing in the swirl chamber than jet-swirl nozzle and can be utilized to prepare nano-drug with sharper particle size distribution. The three swirl vanes uniformly distributed in the circumferential of MIJSN contributed a lot to the even mixing.

Key words: CFD simulation; multi-inlet jet-swirl nozzle; SEDS; nano-drug

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INTRODUCTION

The aqueous solubility of most drug candidates are poor, which has became a major challenge for the pharmaceutical scientists involved in drug development. It is an effective and versatile option for solubility improvement to reduce particle size [1, 2]. Nanocrystallization is an attractive solution to improve the bioavailability of the poorly soluble drugs, improved therapies, in *vivo* imaging, in *vitro* diagnostics and for the production of biomaterials and active implants[3]. Many methods are utilizing to prepare nano-drug, such as high-gravity anti-solvent precipitation[4], medium milling[5], crystallization by supercritical fluid technology[3, 6]. Currently, crystallization by supercritical fluid technology (CSFT) has been used more and more widely in preparing nano-drug[7]. Solution enhanced dispersion by supercritical fluid (SEDS), a method based on the principle of CSFT, is a promising method for nanoparticle preparation, especially for nano-drug preparation [8, 9]. In this process, two kinds of fluids should be introduced into the nozzle to mix completely and spray fiercely. The extent of mixing affects directly particle size distribution in nano-drug preparation. Therefore, configuration of the nozzle becomes a key factor for preparing nano-drug in SEDS process.

Much studied about configuration of the nozzle in SEDS process have been done in recently years. Reverchon E et al used capillary injection tubes to micronize some biopolymers [10]; Bałdyga Jet al prepare nano-drug by coaxial nozzles [11]; Ghaderi R et al prepare biodegradable microparticles using internal twin-fluid mixing nozzles [12], Jarmer D J et al design a jet-swirl nozzle for preparing nanoparticles in SEDS process [13], and Xiao Kefeng et al designed tangential-inlet swirl nozzle and simulated it by CFD[14]. All these configurations have merits in different aspects, while jet-swirl nozzle is one of the most effective among these nozzles. It has been tested by experiments that jet-swirl nozzle allows for the production of nanoscale particles with a smaller average particle diameter [13].

However, the particle size distribution (PSD) of nano-drug prepared by jet-swirl nozzle can be improved. Uniform conditions within the nucleating medium [15] is the necessary condition to produce sharp PSD during SEDS process and can be realized by perfect fluid mixing, resulting in a single supersaturation level and a homogeneous nucleation rate. However, the internal flow of jet-swirl nozzle is not so uniform as to form homogeneous nucleation rate. In this study, the configuration of jet-swirl nozzle was changed and a new nozzle called multi-inlet jet-swirl nozzle was designed in order to improve the mixing condition in the nozzle and make the nucleation rate more homogeneous. Computational Fluid Dynamics (CFD) has become an important approach to simulate the complex flow. Consequently, in this study, CFD Simulation was used to analyze the flow in the new nozzle for preparing nano-drug during a SEDS process.

EXPERIMENTAL SECTION

Configuration design and computational domain modeling

Jet-swirl nozzle was designed by Daniel J. Jarmer et al, especially for the SEDS process. [13], as shown in Figure 1. A swirling vane designed in the swirl insert is used to optimize gaseous mixing between the solvent and antisolvent in a micro-mixing volume. This nozzle was equiped with the merits of two other nozzles, a plain orifice pressure atomizer and a pressure swirl atomizer. Supercritical CO_2 flows as a solid co-axial jet, and the solvent as a swirled annular jet that surrounds the axial jet. These jets mix in the swirl chamber, the discharge orifice, and then spray out. In order to obtain uniform condition for nucleating medium, the configuration of jet-swirl nozzle can be improved. The new nozzle in this paper was designed based on the configuration of jet-swirl nozzle. It was concluded from previous study that the reason why the condition for nucleating is not uniform is that the swirl vane deviates from the center of swirl insert. Consequently, to improve the performance of the nozzle, three swirl vanes uniformly distributed in the circumferential were designed innovatively in the swirl insert of the new nozzle, called multi-inlet jet-swirl nozzle (MIJSN). It was expected that MIJSN could achieve uniform mixing between SC-CO_2 and solvent so as to make uniform condition for nucleating medium.

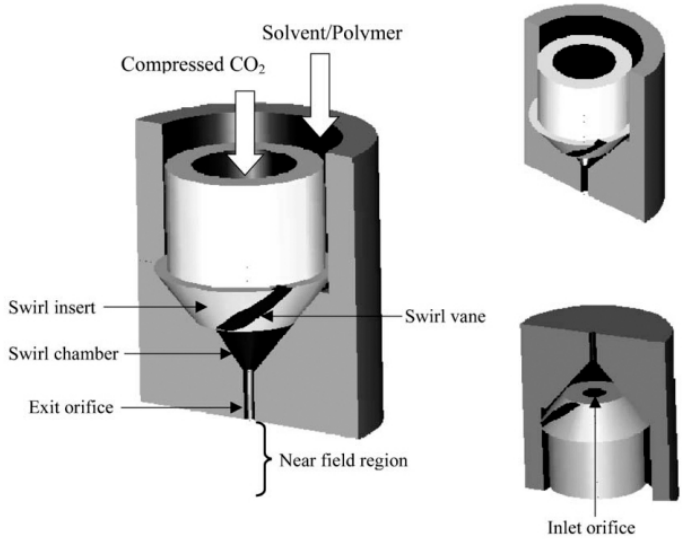

Figure 1. Schematic that illustrates the structure of the jet-swirl nozzle [13]

The 3D geometrical computational domain of MIJSN under consideration for CFD simulation is shown in Figure 2. The dimensions of the nozzle are the same as what mentioned in literature [13]. The most distinguished characteristic of the nozzle is that there are three inlets for the same solvent or polymer.

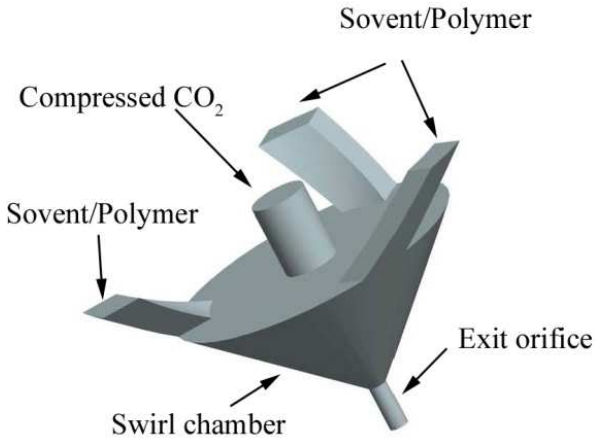

Figure 2. 3D geometrical computational domain of multi-inlet jet-swirl nozzle

Governing equations

In CFD analysis, both SCF and solution phases are treated in an Eulerian framework. The SCF phase is considered as the primary phase, whereas the solution phase is considered as secondary or dispersed phase. The solution phase is characterized by a conductivity, a viscosity, a thermal conductivity and a specific heat.

The continuity equation for phase *i* is defined as Eq. (1) [16].

$$\frac{\partial}{\partial t}(\alpha_i \rho_i) + \nabla \cdot (\alpha_i \rho_i \vec{u}_l) = \sum_{p=1}^{2} (\dot{m}_{pi} - \dot{m}_{ip}) \tag{1}$$

where $\vec{u}_l$ is the velocity of phase *i* and $\dot{m}_{ip}$ characterizes the mass transfer from the *p*th phase to *i*th phase.

The momentum balance for phase *i* yields Eq. (2) [16].

$$\begin{aligned} &\frac{\partial}{\partial t}(\alpha_i \rho_i \vec{u}_l) + \nabla \cdot (\alpha_i \rho_i \vec{u}_l \vec{u}_l) = -\alpha_i \nabla P + \nabla \cdot \bar{\tau} + \alpha_i \rho_i \vec{g} \\ &+ \sum_{p=1}^{2} (\vec{R}_{pl} + \dot{m}_{pl} \vec{u}_{pl} - \dot{m}_{pl} \vec{u}_{lp}) + (\vec{F}_i + \vec{F}_{lift,i} + \vec{F}_{vm,i}) \end{aligned} \tag{2}$$

where $\bar{\tau}_i$ is the *i*th phase stress strain tensor, $\vec{F}_i$ is an external body force, $\vec{F}_{lift,i}$ is a lift force, $\vec{F}_{vm,i}$ is a virtual mass force, $\vec{R}_{pi}$ is an interaction force between phases and *P* is the pressure shared by all phases. $\vec{u}_{pl}$ is the interphase velocity. If $\dot{m}_{pi} > 0$; $\vec{u}_{pl} = \vec{u}_p$ and if $\dot{m}_{pi} < 0$; $\vec{u}_{pl} = \vec{u}_l$

Turbulent kinetic energy *k* can be calculated by Eq. (3).

$$k = \frac{3}{2}(\bar{u}_{ref} I)^2 \tag{3}$$

where $\bar{u}_{ref}$ is the mean velocity at inlet, which can be calculated by mass flow rate. *I* is the turbulent intensity of inlet, which can be calculated by Eq. (4).

$$I = 0.16(\mathrm{R}_{eDH})^{-1/8} \tag{4}$$

Turbulent dissipation rate ε was estimated by Eq. (5) and Eq. (6).

$$\varepsilon = 0.09^{3/4} \frac{k^{3/2}}{l} \quad (5)$$

$$l = 0.07L \quad (6)$$

where, k is turbulent kinetic energy, L is characteristic length, which can be calculated according to the equivalent diameter.

Model analysis

Navier–Stokes equations were solved using commercially available finite volume code software Fluent which solves the classical mass and momentum conservation equations to describe the fluid behavior and properties. According to relative literature[17], we make hypothesis that the parameters of the fluid in MIJSN are independent with time and the system was considered as incompressible in order to develop CFD simulations[16, 18]. Consequently, Fluent 3D solver was selected and pressrue-based implicit was the solve method. The turbulent flow in MIJSZ can be treated as three-dimensional and steady state flow. First order upwind discretization scheme was selected to solve the momentum, the volume fraction, the turbulence kinetic energy and turbulent dissipation rate. The phase coupled SIMPLE algorithm was utilized for pressure-velocity coupling. The under-relaxation factors were in default.

Materials and operating parameters.

In order to compare with literature [13], materials used in this simulation were same with that in literature [13]. Methylene chloride and SC-CO_2 were selected as solvent and anti-solvent respectively. Because the solute contained in the solution was relatively slight, the effect of the solutes on the property of the solution was ignored. Consequently only SC-CO_2 and methylene chloride were taken into account as fluid candidates.

SC-CO_2 was introduced from central inlet and methylene chloride was introduced from the other three inlets as shown in Figure 1. SC-CO_2 was selected as the primary phase and methylene chloride was the secondary phase. All fluid variations were treated isobaric at 8.5MPa. The physical properties of materials such as density, viscosity, thermal conductivity, standard state enthalpy, were inputted. The operating pressure was default and the gravitational acceleration was taken into account.

Boundary conditions

For the MIJSN, as shown in Figure 2, the inlet of CO_2 was inlet1, and the three inlets of solvent were inlet2, inlet3 and inlet4 respectively. For the inlet boundary condition of inlet1, a simple mass flow inlet was selected and allows specifying mass flow and temperature of SC-CO_2, turbulent kinetic energy, turbulent dissipation rate and volume fraction of methylene chloride. The mass flow SC-CO_2 was 2.460×10^{-4}kg/s. The volume fraction of ethanol is 0. Turbulent kinetic energy k and turbulent dissipation rate ε were estimated by Equation (4) and Equation (6) respectively. The inlet boundary condition of inlet2, inlet2 and inlet3 were set to be same. Velocity-inlet was selected for the three inlets and allows specifying velocity magnitude, turbulence intensity, hydraulic diameter, volume fraction of methylene chloride and so on. The velocity magnitude of the three inlets was 0.42m/s which was transferred from the volume flow 1ml/min in literature [13]. Turbulent intensity and hydraulic diameter were 1% and 0.1mm respectively. For boundary condition of the outlet, pressure-outlet was selected. The pressure of outlet was set to be 8.5Mpa. The conditions of pressure, mass flow rate and velocity magnitude, mentioned in this paper, were selected because they presented the best results regarding the morphology and the particle size distribution of the obtained particles [11, 13, 19].

RESULTS AND DISCUSSION

Analysis of CH_2Cl_2 volume fraction in the mixture

In order to validate the new nozzle, the parameters of the flow in MIJSN were compared with that in jet-swirl nozzle. The materials used in the simulation of the flow in jet-swirl nozzle were same with that in MIJSN. For the purpose of being observed clearly, the CH_2Cl_2 volume fraction in the mixture was express in three cross sections, respectively being A-A, B-B, C-C, as shown in Figure 3 for both of these two nozzles.

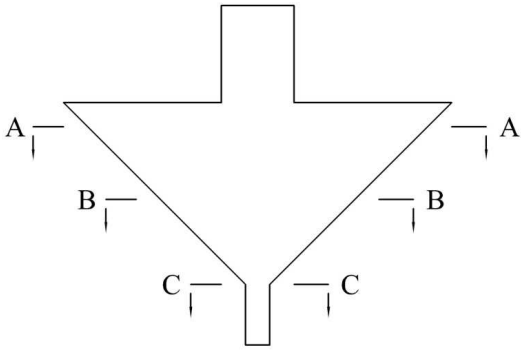

Figure 3. The schematic of cross sections for expressing CH_2Cl_2 volume fraction in the mixture

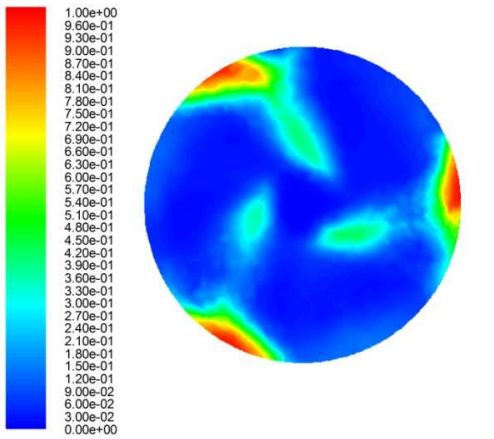

Figure 4. The contour of CH_2Cl_2 volume fraction at cross section A-A of MIJSN

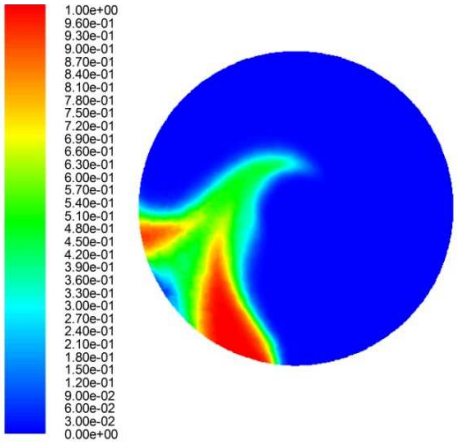

Figure 5. The contour of CH_2Cl_2 volume fraction at cross section A-A of jet-swirl nozzle

Figure 4 and Figure 5 show the contour of CH_2Cl_2 volume fraction at cross section A-A of MIJSN and jet-swirl nozzle respectively. The position of cross section A-A is near inlets of CH_2Cl_2 and SC-CO_2. Therefore, Figure 4 and Figure 5 show the initial state of mixing between CH_2Cl_2 and SC-CO_2. It can be seen that the regions with high volume fraction of CH_2Cl_2 in MIJSN are distributed evenly in the circumferential direction while that in jet-swirl nozzle is eccentric. That indicates that the fluids in MIJSN are more inclined to mixing completely than that in jet-swirl nozzle. The position of cross section B-B is the middle part of the swirl chamber. Therefore, Figure 6 and Figure 7 show the intermediate state of mixing between CH_2Cl_2 and SC-CO_2. One can see that CH_2Cl_2 and SC-CO_2 almost mix completely. Only in some region is there a little high volume fraction. The difference between the highest volume fraction and the lowest one in MIJSN is less than 10%, while that in jet-swirl nozzle is more than 20%. The position of cross section C-C is the orifice exit of the swirl chamber. Figure 8 and Figure 9 show the state of mixing between CH_2Cl_2 and SC-CO_2 just before spraying out. As can be seen from Figure 8, the volume fraction of CH_2Cl_2 in MIJSN has been very uniform. Whereas, that in jet-swirl nozzle is still not even, as shown in Figure 9.

From all above-mentioned analysis, it can be concluded that the fluids in MIJSN can mix more evenly than that in jet-swirl nozzle and the new configuration design is facilitated to forming uniform mixing for nucleating and obtaining sharp particle size distribution.

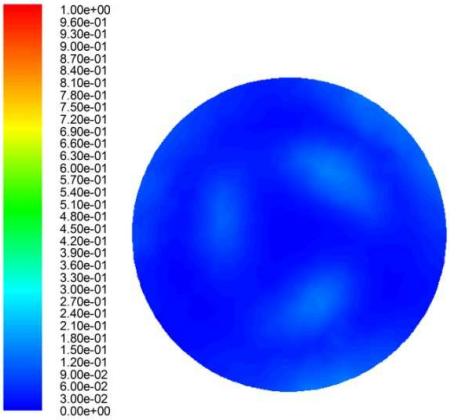

Figure 6. The contour of CH_2Cl_2 volume fraction at cross section B-B of MIJSN

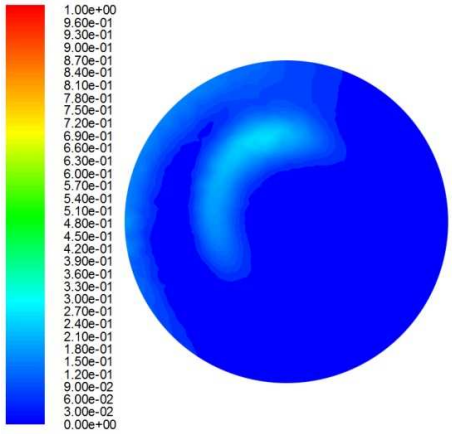

Figure 7. The contour of CH_2Cl_2 volume fraction at cross section B-B of jet-swirl nozzle

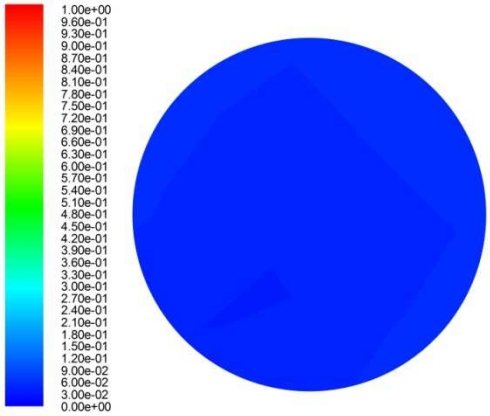

Figure 8. The contour of CH_2Cl_2 volume fraction at cross section C-C of MIJSN

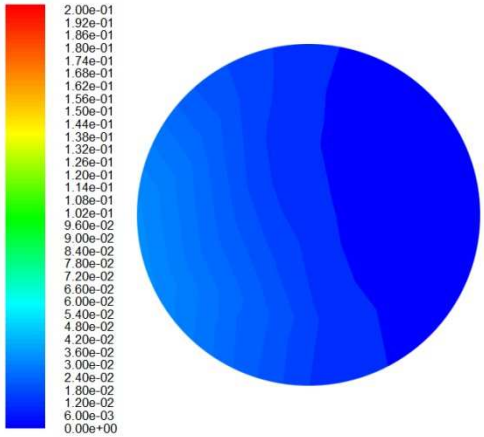

Figure 9. The contour of CH_2Cl_2 volume fraction at cross section C-C of jet-swirl nozzle

Analysis of turbulent intensity at outlet

As an essential parameter for analyzing SEDS process, turbulent intensity can influence two key events: the rate at which supersaturation is reached and the level of supersaturation obtained. If the turbulent intensity is uniform, the level of supersaturation would be uniform and particle size distribution of nano-drug prepared would be narrow. As shown in Figure 10 and Figure 11, the turbulent intensity of the flow at the outlet of MIJSN was more even than that of jet-swirl nozzle. The biggest difference of turbulent intensity in Figure 10 is about 16%, while that in Figure 11 is about 50%, far more than the former. Figure 12 indicates that turbulent intensity in MIJSN is lower than that in jet-swirl nozzle in the same conditions, but can meet the requirements of SEDS process. The turbulent intensity in MIJSN can be enhanced by increasing input power of inlet1.

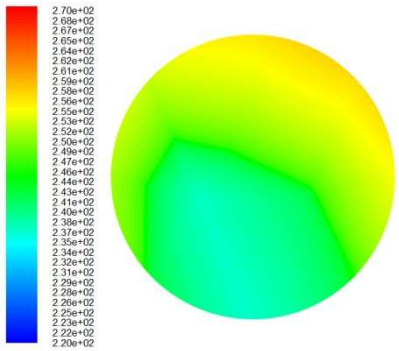

Figure 10. The contour of turbulent intensity in MIJSN

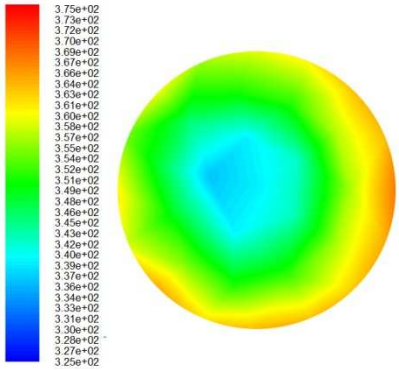

Figure 11. The contour of turbulent intensity in jet-swirl nozzle

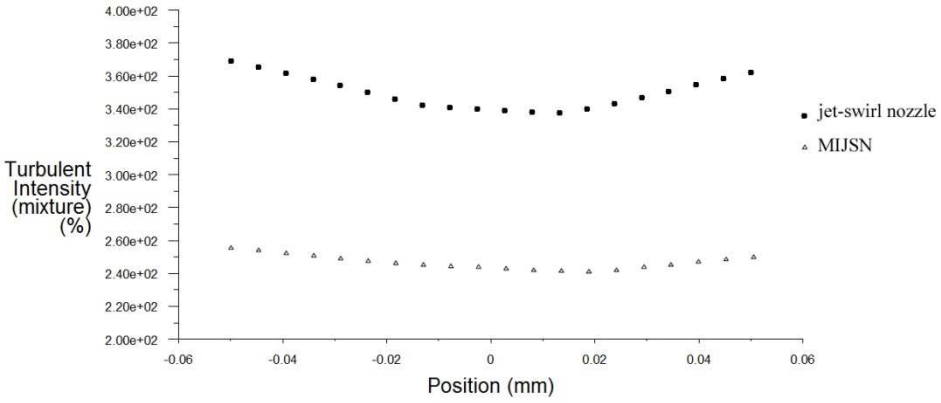

Figure 12. The distribution of turbulent intensity on the diameters of outlet for MIJSN and jet-swirl nozzle

CONCLUSION

The MIJSN newly designed for preparing nano-drug by SEDS process was validated by CFD simulation. The Results indicate that MIJSN can obtain more uniform mixing in the swirl chamber than jet-swirl nozzle and can be utilized to prepare nano-drug with sharper particle size distribution. The three swirl vanes uniformly distributed in the circumferential of MIJSN contributed a lot to the even mixing. However, according to what shown in Figure 12, there still exists an issue. Although the turbulent intensity in MIJSN is more even than that in jet-swirl nozzle, the former is lower than the latter in the same conditions. This issue can be addressed by increasing input power of inlet1.

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