Ultra-dispersed particles of water-soluble and water-insoluble substances formed from gas-droplet flows

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Abstract. The work is devoted to the experimental study of the ultra dispersed particles formation process, which is essentially a fundamental problem of heat and mass transfer in gas-droplet flows under phase transformation conditions. Various methods of generating and controlling the gas-droplet flow parameters are considered. The description of the created equipment and diagnostic methods for studying gas-droplet flows is given. The particle size distribution functions are obtained using an aerosol particle spectrometer. The possibility of controlling the parameters of ultrafine particles of water-soluble and water-insoluble substances (medications) formed under evaporation of microdroplets of solutions and suspensions is shown experimentally. An attempt to reconstruct the distribution functions of microdroplets and their average dimension from measurements of the parameters of ultrafine particles formed after complete evaporation of the droplets is made.

1. Introduction
Currently, gas-droplet flows are widely used in various heat and mass transfer apparatus and devices. This includes problems such as fuel atomization, cooling of heat-stressed structures, and various metallurgical processes. It is shown that the addition of even a small amount of a droplet phase to the cooling flow significantly increases the cooling efficiency due to the use of the phase-transition heat at droplet evaporation. The study of gas-droplet flows is of great importance in space applications. Such flows arise, for example, during the operation of spacecraft orientation thrusters and purging of space station refueling lines with propellants. In this case, it is important not only to study the structure of the gas-droplet flow but also the evaporation dynamics of droplets with different dimensions and compositions.

The analysis of scientific papers shows that studies of gas-droplet flows are carried out in a wide range of operating parameters, such as temperature, pressure, composition, Reynolds, Weber, Mach, etc. numbers [1-3]. At the same time, it can be affirmed that the range of scientific and practical applications of gas-droplet flows is continuously expanding. Among the possible applications of gas-droplet flows in general, and micro-droplet flows in particular, is the production of ultrafine particles of various substances, including therapeutically unstable medications, for example, for inhalation therapy [4]. Moreover, the substances themselves can be both water-soluble and water-insoluble. In the case of using water-soluble medications, the main idea of forming particles is to obtain droplets of a solution with the required dimension (ideally, with a mono-droplet particle size distribution function) and their subsequent evaporation in a carrier gas flow. Then it is quite enough to control the size of the initially formed droplets (at a specific initial concentration of the solution) to obtain the desired dispersion of
the substance. To obtain ultrafine particles of water-insoluble medications, a method is used in which the powdered substance is mixed with water, and to obtain the required dispersion of the substance, the suspension is exposed to ultrasound affection. After spraying the resulting suspension into the working chamber and evaporation of water from droplets, dry ultrafine particles of a water-insoluble substance are formed.

2. Experimental setup and measurement technique

To carry out the research we developed and manufactured the experimental setup (figure 1).

![Experimental setup diagram](image_url)

Figure 1. Experimental setup. 1 – box, 2 – drain connection, 3 – filter, 4 – air fan, 5 – power supply, 6 – spraying device, 7 – gas flow meter, 8 – air compressor, 9 – particles spectrometer, 10 – attenuator, 11 – humidity and temperature meter, 12 – laser.

The setup was a 22 l box made of plexiglass, in which the sprayer (source) of the gas-droplet flow, the humidity and temperature meter, as well as the air fan, were installed. The diagnosis of the formed droplets was carried out by Mie scattering with laser. To register formed nanoparticles, the diffusion spectrometer of aerosol particles DSA was used, which allowed measuring the particle dimensions within the ranges from 3 to 1200 nm with concentration up to $5 \times 10^5$ particles/cm$^3$. For high particle concentrations (close to $5 \times 10^5$ particles/cm$^3$), the attenuator was used to ensure the performance of the spectrometer.

To obtain the initial dimension of the droplets, the light scattering method on droplets (Mie scattering) was employed. The method is based on the registration of the scattered laser radiation intensity. A semiconductor 50 mW laser with a wavelength $\lambda = 532$ nm was used as the light source. The intensity of the scattered light: $I_{sc} = A \cdot I_0 \cdot n \cdot \sigma$, where $A$ is the instrument constant, $I_0$ is the intensity of the probing light, $n$ is particles concentration, $\sigma$ is the scattering cross-section. The parameter $\alpha = \frac{\pi \cdot D}{\lambda}$, which characterizes the ratio of particle diameter $D$ and the wavelength of probing radiation $\lambda$ is of great importance in the scattering theory. If $\alpha \ll 1$, i.e. particles dimension is less than the wavelength of probing radiation, there is a Rayleigh scattering and the scattering diagram is isotropic. If the dimension of the particles is commensurate with the wavelength of the probing radiation, then the Mie scattering takes place, and its intensity depends on the particles' dimension and the wavelength. According to the Mie theory, the ratio of the scattered light intensities for two equal angles relative to the symmetry plane of the scattering indicatrix (scattering "forward-back") is a
function of the parameter $\alpha$ only. Thus, if we measure the intensity of the scattered light "forward" and "back" at a certain angle relative to the probing beam, then with a known wavelength $\lambda$ we can determine the average particle dimension. Since real flows always contain particles of different dimensions, then to obtain the particle size distribution functions we have to measure the scattering diagram at all angles (from 0 to 180°), followed by the solution of the inverse problem, which is not trivial.

An optical microscope and a digital camera were used to determine the number and dimension of particles in the dispersion. To process the images of the dispersion, the developed program was used. An array of data was obtained employing the program, which allowed plotting particle size distribution function.

The experiments were carried out as follows: after setting the gas and liquid flow rates (specifying the Reynolds and Weber numbers of the co-current gas flow), the source of the gas-droplet flow was switched on, and for a certain time the gas-droplet flow expired into the working chamber. The average dimension of droplets in the gas-droplet flow was measured by Mie scattering during the outflow. Then, after the source of the gas-droplet flow was turned off and the droplets were completely evaporated, samples were taken from the chamber to measure the average dimension of the formed dry particles and their size distribution function.

Air was used in the experiments as a working gas, Losartan (water-soluble substance), and Nifedipine (water-insoluble substance) were used as a substance for forming ultrafine particles. Losartan ($C_{22}H_{23}ClN_6O$) and Nifedipine ($C_{17}H_{18}N_2O_2$) are medicines widely used in medical practice to treat patients with arterial hypertension.

3. Results and discussion

3.1. Water-soluble substance. Experiments were carried out with the solution of losartan in distilled water at weight concentrations ranged from 1/200 up to 1/8000. The initial temperatures of air and solution were equal to room temperature. The distribution function of losartan particles, formed under droplets evaporation with initial substance concentration of 1/8000 (1) and 1/400 (2), is shown in figure 2.

![Figure 2. Size distribution of losartan particles. Losartan concentration in solution: 1 – 1/8000, 2 – 1/400.](image)

The average diameter of the obtained particles in the first case was about 40-50 nm, while in the second case it moved to the region of larger particles 100-120 nm. At the same time, the total number of sprayed droplets in all chosen conditions changed insignificantly. The result obtained is of fundamental importance since it experimentally confirms the assumption that it is possible to control
the particle size distribution function by changing the initial concentration of the substance in the solution.

Experimentally obtained dependence of the average dimension of particles formed under the evaporation of the droplets of losartan water solution on the initial concentration of the solution is given in figure 3. The dashed line in this figure shows the results of the calculations of the average particle dimension from the measured droplet sizes and the chosen initial concentration of the solution.

**Figure 3.** Dependence of particles dimensions on the initial concentration of the solution.

It is seen that a decrease in the initial concentration of nano-forming substances in the solution leads to the formation of smaller particles. So, when the weight concentration of a water solution of losartan changes from 1/200 up to 1/8000, the average dimension of the resulting dry particles changes from about 160 nm down to 50 nm.

Since the droplet evaporation process is fast (fractions of a second for micron-sized mono-liquid droplets [7] and from fractions of a second up to several seconds for multi-component liquid droplets), and the rate of gravitational sedimentation of dry ultrafine particles is small (about $10^{-4}$ cm/s for particles of 100 nm in diameter [8]), then the measured size distribution function of dry particles and chosen concentration of the solution allows obtaining the size distribution function of droplets in a gas-droplet flow. An example of the reconstructed distribution function is shown in figure 4.

**Figure 4.** Reconstructed droplet size distribution function.
From figure 4 one can see that the droplet dimensions in the gas-droplet flow are about 1-2 μm. These data are in good agreement with the data obtained from Mie scattering on the average dimension of droplets in the flow. Thus, from the measurement results on the average droplet dimension of multicomponent liquids in a gas-droplet flow it is possible to determine the average dimension of the droplets of dry ultradispersed particles formed as a result of evaporation, and, conversely, from the results of measuring the distribution function of dry ultradispersed particles, it is possible to restore the droplet distribution function in the gas-droplet flow.

3.2. Water-insoluble substance. When using water-insoluble substances, the preparation of a solution for its subsequent spraying and obtaining dry ultrafine particles is impossible. In this case, the way out is to use a dispersion (suspension of solid particles in liquid) of a water-insoluble substance. The idea of the gas-droplet method for obtaining ultradispersed particles of water-insoluble substances is to spray a dispersion of a substance using a gas-droplet flow source, followed by the formation of dry particles. In this case, it is possible to control the dimension of forming ultradispersed particles by changing the size of solid particles of a water-insoluble substance in dispersion (their micronization).

In this work, for the micronization of water-insoluble substances, a method based on the use of thermophysical and hydro-gas-dynamic effects, namely, ultrasonic cavitation (ultrasonic micronization), was used.

To obtain ultrafine particles of nifedipine, a suspension of the initial substance was prepared, and then it was processed in the ultrasonic disperser UZDN-2T with a magnetostrictive emitter (operating frequency was equal to 22 kHz, power ~ 800 W) for 3 cycles of 1.5 minutes each, with intermediate reactor cooling. The results of processing the dispersion were evaluated from photographs obtained using an optical microscope. Analysis of the results showed that the size distribution functions of nifedipine particles are close to the log-normal distribution. Particles with dimensions from 1 up to 100 μm were observed, the maximum of the distribution function was within the range of 3-4 μm.

After ultrasonic treatment, the maximum of the distribution function moved to the left (to the region of 2-3 μm), while the total number of particles increased significantly (by about one order of magnitude). At the same time, the relative number of large particles decreased significantly. Subsequently, the resulting dispersion was sprayed through the source of the gas-droplet flow into the working chamber of the experimental setup. After complete evaporation of the droplets, the concentration and distribution function of dry particles were measured using a diffusion spectrometer of aerosol particles [5]. An example of the obtained distribution functions is shown in figure 5.
Analysis of the obtained results showed that the distribution functions are close to the log-normal distribution. Particles with a dimension from 20 up to 300 nm were observed, the maximum of the distribution function was within the range of 90-100 nm. After ultrasound treatment, the maximum of the distribution function moved to the left (in the range of 70-80 nm), while the total number of particles increased, but at the same time, the number of large particles (larger than 100 nm) decreased.

4. Conclusion
The paper shows the possibility of obtaining ultrafine particles of water-soluble substances from microdroplets of solutions, as well as controlling the dimension of the forming particles by changing the initial concentration of the solution and the size of microdroplets. For water-insoluble substances, a method was developed for producing ultrafine particles by creating micro-droplet flows of dispersions and subsequent evaporation of droplets. In this case, the dimension of the formed ultrafine particles is determined by the size of the solid particles in the dispersion, and the size of the solid particles, in turn, can be controlled by changing the duration of the ultrasonic treatment of the dispersion. The most promising area for using the results obtained is a medical application, in particular, the production of nanoscale forms of medications for inhalation therapy.

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