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Application of ultrasonic inhalers and spray heads structure and principles of operation for insulin delivery

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Abstract

The paper presents comparative analysis of several types of ultrasonic spray devices of liquid (their structure and operating principles) in order to create our own ultrasonic nebulizer of liquid in particular ultrasonic nebulizer of insulin as well as conditions of its exploiting by people suffering from diabetes.

The development of ultrasonic nebulizer of insulin is aimed at eliminating a number of problems connected with regular insulin taking (injections). They are increasing the effectiveness of treatment for patients with diabetes (possibly accelerating treatment), replacing the painful way of insulin delivering (via injections) with the device through which the medicine will be delivered and reducing the consumption of an active drug based on insulin.

Nowadays insulin ultrasonic nebulizer is one of the new ideas in the field of medical technologies. There are some experiments on the insulin inhalator implementation. However, tests have been conducted for a long time but there still hasn't been wide application. Operating principle of the ultrasonic nebulizer of insulin is fundamentally different from possible analogues, which are very few.

Keywords: Insulin, nozzle tip, insulin nebulizer, cavitation, fluid atomization, droplets size, health improvement;

1. Introduction

Ultrasonic nozzle tips systems have replaced conventional sprays, inhalers, etc. in many industries and research applications making many spraying processes possible including medicine (improvement of drug spraying). Environmental concern, unacceptable quantities of industrial waste as well as the side effects of using various medicines forced manufacturers to use systems with an ultrasonic nozzle tips as a technology that is more accurate, controllable, environmentally friendly and harmless for patients. Ultrasonic nozzle tips are non-clogging, self-cleaning devices that atomize a liquid using high-frequency sound waves (beyond human hearing) rather than pushing a liquid through a small hole with force using high pressure, which opens up a wide range of applications.

Every person with type 1 diabetes is forced to make subcutaneous injections of insulin intramuscularly leading to soft tissue damage and pain for a long time. Besides the injection procedure itself is rather painful. Therefore, development of an alternative way of drug delivery using ultrasonic nozzle tips will significantly contribute to the improvement of patients' quality of life.

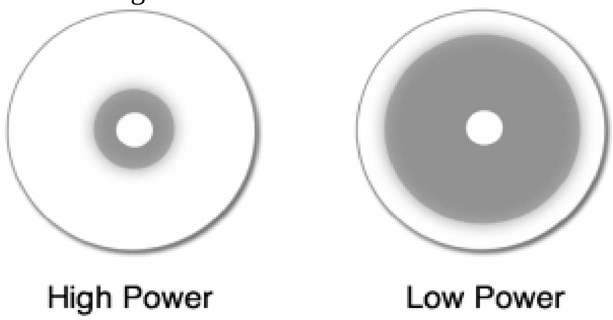
The main task associated with the research objectives is: identifying features of the spraying process using an ultrasound nozzle tip to determine the parameters of the device being developed to reduce the amount of sprayed medication [1].

2. Methodology

Ultrasonic Cavitation

Ultrasonic atomization occurs at the tip of the ultrasonic spray head due to its rapid mechanical movement up and down, which causes the liquid film to form stationary capillary waves. When the amplitude of the capillary wave, which is a function of the amount of power consumed (usually in the range from 1 to 20 W), reaches a peak required for the stability of the system the liquid at the peak of its power comes off in the form of drops. Cavitation will occur if the level of such energy is excessive. Excessive energy will cause the liquid to emerge from the nozzle for premature aerosolization (which literally means "bursting" into irregular-sized droplets) instead of forming an ideal film on the tip of the spray head. Cavitation can be seen by observing how much the liquid "moisturizes" the tip of the spray head [6].

Let us consider the "ideal" case as the first example [12]. Each image in Figure 1 is a nozzle tip view that looks straight ahead. The centre circle represents a fluid orifice from which fluid leaks out onto the tip of the spray head. The inner gray circle is a liquid film. Let us assume that the fluid and flow rate are the same for both images and, therefore, the only difference is the power level. As you can see in image (Fig. 1, b) most of the spray head surface has a liquid film but you should pay attention to the fact that the film does not extend to the edges, which means that part of the liquid is cavitating or detached from the nozzle tip before it can properly atomize. In addition, ultrasonic cavitation produces droplets of various sizes while ultrasonic spraying creates more uniform droplet size since they are formed by a more controlled mechanical process opposed to force. Therefore, the best way to set the optimum power level for a given frequency of the spray head as well as the flow rate and type of material is to set the power about one watt above the point of droplets "bursting".



(a) (b)

Figure 1. View of the nebulizer nozzle tip at high (a) and low (b) cavitation power [12]

Let us consider an example with the spraying power of 3 W when liquid atomizes and does not cavitate. The film on the nozzle tip looks like something between images of high and low power (Fig. 1). Applying gradual power decrease of the device it is necessary to achieve the moment when the nozzle detachment occurs, for example at the power of 1 watt. Detachment occurs when a large drop forms on the nozzle tip and atomization stops. We add another 1 watt to the obtained value (1 watt) setting our ideal power level to 2 watts. Now if the tip of the nozzle looks something like an example with low energy consumption (Fig. 1, b), this can mean a good setting of the device power.

In addition, the film should not be too close to the edge due to the possible risk of film wrapping the tip of the spray head which will cause unwanted spraying on the sides because the liquid atomizes away from the tip.

Differences between an ultrasonic inhaler and ultrasonic spray head

Ultrasonic inhalers and ultrasonic spray head use piezoelectric transducers to generate atomized particles. Both systems apply voltage to piezoelectric transducers that will vibrate at high frequency in up and down movement. The ultrasonic nebulizer uses the surface of a piezoelectric disc as the surface of atomization while the ultrasonic spray head uses a piezoelectric transducer to vibrate the metal (for example, titanium) at a resonant frequency. The vibration of this titanium transducer is similar to the concept of a vibrating plug (Fig. 2). The same up and down movement of the piezoelectric transducer is transmitted to the ultrasonic tip of the spray head, which will also vibrate in the same direction (up and down) [5].

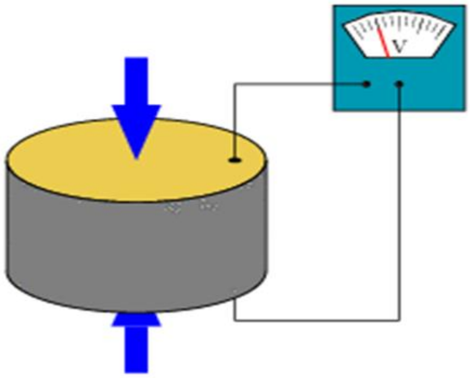


Figure 2. The concept of a piezoelectric transducer [5]

Unlike the ultrasonic inhaler that directly uses the surfaces of a piezoelectric disc the liquid is atomized from the surface of the spray head. However, both systems are called ultrasonic as they operate in the ultrasonic range which starts at 20 kilohertz [2].

Features of ultrasonic inhalers

Ultrasonic inhalers used in industry to create atomized sprays operate mostly at a frequency of 1-2 MHz. The power source is often in the range of 12-15 watts. Frequency determines the droplets size. It is said that the 2.4 MHz system, for example, will generate an average particle size of 1-2 μm, compared to a system of 1.65 MHz that generates an average particle size in the range of 5-7 μm [3].

Solid particles may accumulate on the piezoelectric transducer due to the direct contact of

the fluid which will affect its performance. This makes maintenance of many industrial inhalers difficult. Ultrasonic inhalers are popular in spray pyrolysis applications.

Features of ultrasonic spray heads

Ultrasonic spray heads operate at a much lower frequency than ultrasonic inhalers and have physical limitations in their operating range. Imagine an organ pipe. The larger the pipe, the lower the sound, and consequently, the lower the frequency. Small organ pipes make higher sounds, but they vibrate more vigorously than larger ones. This important concept is implemented in the ultrasonic design of the spray head. The operating range of the ultrasonic spray head was between 25 and 250 kHz for several decades [11]. The new material science and manufacturing practices have pushed this range slightly higher but not by much for the past few years. The main barrier is higher stress and heat in the system caused by the power generated by spray heads as they are constructed at high frequency, very small but contain a lot of power. Why then try to build high frequency spray heads [4]?

Droplets size is the answer to this question. As the frequency increases, the ultrasound head generates smaller droplets. Droplets size is very important not only in many thin film applications but also when the spray process undergoes transformation (spray pyrolysis, etc.) [4]. Thus, it is very important to apply the correct technology and frequency of the device operation.

Sizes of sprayed drops

The frequency of the ultrasonic spray head determines the size of the droplets. The higher the frequency, the smaller the "initial" drop. Most consumers, however, are more concerned about the size of the drop that comes in contact with their component. A thin film coating on a wide substrate was considered as an example [7]. An ideal functional coating can be more not like a film but more like a spray pattern. Many factors should be analysed to get such kind of coating. One of which, of course, is the initial size of droplets generated by this ultrasonic spray head. What many consumers do not pay attention to becomes the important feature of evaporation in the final drop size that comes into contact with a component [8].

It is not uncommon for consumers to think that they need the smallest possible initial droplets (i.e. a high frequency ultrasonic spray head). But when they run their system the coating becomes dry. All solvents are evaporated before the solids in the solution have time to coat the part. In other words, they lose all the characteristics of film making and become powder coating instead (Fig.3).

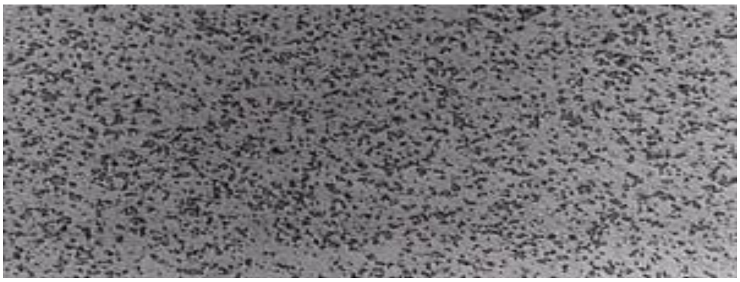


Figure 3. SEM image of powder coating [10]

The principles of spraying powder and liquids described above can be applied to the spraying of drugs under certain conditions and parameters of the device. Surface on which the spray occurs is of great importance too. These parameters and characteristics for creating an ultrasonic insulin nebulizer were experimentally determined in the course of calculating pore sizes for the sublingual and buccal mucosa of the oral cavity [9] (Table 1).

Table 1. Values for rp (in Å) and Є / L (in cm-1) for the sublingual and buccal mucous membranes [9]

	Є/L(см$^{-1}$)	r_p(Å)
Using the radius of rotational motion		
Sublingual mucosa	1.24	52
Buccal mucosa	1.42	23

The use of the radius by the Stokes-Einstein equation		
Sublingual mucosa	1.74	30
Buccal mucosa	1.94	17.5

3. Discussions

Undoubtedly, the frequency of the ultrasonic spray head is very important but the highest frequency is not always better. Consideration of drug types (with a high boiling point, compared with a low one (insulin solutions), the distance of the spray head from the base plate and the flow rate also play a role in determining the final size of the droplets and, consequently, the quality of the coating.

It is necessary to ensure control over the level of input power, which should not exceed 5 W.

The ideal calculated droplet size of the active preparation based on insulin should be in the range: 23 - 52 Å (5.2 – 2.3 nm). But it is hard to get due to power and frequency limitations. These limitations are due to the parasitic process of ultrasonic cavitation, which enhances its effect on spraying as the power level and frequency increase.

According to the conducted research, we have found “balanced” parameters of insulin nebulizer prototype:

Typical power is 1-5 W. Operating frequency range is 25-250kHz. Amplitude of oscillations on ultrasonic transducer is 3-9 microns. Presumed type of insulin used is "regular insulin" (average duration of action is 3-6 hours). To reduce the effect of ultrasonic cavitation it is necessary to install a self-cleaning, non-clogging filter head at the outlet.

4. Conclusion

The technical result of the investigation is an increase of the process productivity at high spraying frequencies and the possibility of spraying liquid drugs.

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