On the diagnostic features of the gas-discharge visualization for the assessment of medicines

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Abstract. The therapeutic efficiency of medicines containing the same active ingredient depends on the production technology, as well as the excipients included in the tablet and the type of shell. In this work, we consider some of the possibilities of using the gas-discharge visualization method based on the phenomenon of channeling electrons through a liquid medium to study aqueous solutions of medicines. The study was carried out on the example of the passage of kilovolt electrons through drops of solutions of the beta-blocker bisoprolol, produced by various pharmacological companies. We studied bisoprolol preparations without excipients and bisoprolol preparations with excipients. The obtained differences in the characteristics of the gas-discharge luminescence for the studied medicines open up prospects for assessing the quality and pharmacological efficiency of medicines, and, subsequently, for the individualization of medicines therapy.

1. Introduction
As clinical practice shows, medicine drugs with different trade names, including those based on the same active ingredient, can differ significantly in their therapeutic efficiency [1, 2]. The reactivity, and, therefore, the pharmacological effectiveness of medicine drugs are determined not only by their chemical composition and the composition of excipients, but also by the structural features of their aqueous solutions: by short-range order in the arrangement of molecular complexes, by the peculiarities of the interaction between them and water molecules, by electrochemical parameters (by transfer of energy charges) and features of magnetospin (magneto-sensitive) regions of the system.

As our studies have shown, one of the most sensitive and promising methods for assessment the pharmacological effectiveness of medicine can be used the so-called gas-discharge visualization (GDV) [3, 4]. Pictures of the angular distribution of electrons that have passed through the water medium and released into the air can be studied using the sliding gas discharge they create. This
approach provides a gas-discharge image of the internal structure of an aqueous solution. In this case, GDV images are a set of maxima corresponding to the directions (channels) of facilitated electron motion in water solutions. We have previously studied the orientational effects observed during the passage of kilovolt electrons (9 keV) in liquid media: in an isotropic micellar solution of a surfactant, cetyltrimethylammonium bromide [5-7], as well as in blood and its components before and after oxidation [8]. In this work, we consider some of the possibilities of using GDV in medicine drugs diagnostics.

2. Methodology of the investigations

For the study, we used aqueous solutions of bisoprolol \(C_{18}H_{31}NO_4\) preparations (concentration 0.05 wt%) in bidistilled water. Aqueous solutions were obtained from tablet forms by dissolving, infusing for 24 hours until sorption equilibrium is established and subsequent centrifugation and filtration.

Note that the research results largely depended on the water environment in which the substances under study were dissolved.

GDV was used to study characteristics of electron emission solutions with a GDV chamber industrial analyzer [3, 4]. Block diagram of the gas-discharge visualization device "GDV-camera" is shown in figure 1.

![Block diagram of the gas-discharge visualization device "GDV-camera"](image)

**Figure 1.** Block diagram of the gas-discharge visualization device "GDV-camera": 1 – liquid meniscus, 2 – quartz electrode with a conductive coating, 3 – voltage pulse generator, 4 – optical system, 5 – metal electrode [3, 4].

The emission of electrons from a drop of liquid with volume about \(8 \times 10^{-9} \text{ m}^3\) (liquid meniscus 1) was stimulated by electric pulses, applied between metal electrode 5 (and liquid meniscus 1) and quartz electrode with a conductive coating 2. The amplitude of pulses was 9 kV, duration of the pulse was 3 \(\mu\text{s}\), and the frequency of the pulses was 1.024 kHz. Electrons emitted from the surface and volume of the drop were accelerated by an electromagnetic field that produced electron avalanches. After exiting into the air, the electrons ionized the air molecules, and the luminescent radiation arising after the radiative recombination of the excited molecules was recorded by the GDV camera. The recorded luminescent radiation was digitized by a video converter system and visualized on a computer screen in the form of a stereographic image of a gas discharge, which showed a spatially distributed group of air luminosity areas with different brightness, wavelength, and frequency.

Gas-discharge images of double-distilled water were used to calibrate the instrument. All angular dependences of the GDV for each sample were recorded 10 times, after which the measurement results...
were averaged and displayed for a qualitative studies in the form shown in figure 2, and for quantitative estimates in the form shown in figure 3.

3. Results of the investigations
The angular dependences of the distributions of electrons passed through droplets of double-distilled water (figure 2) and droplets of double-distilled water bisoprolol solutions without excipients and bisoprolol preparations with excipients produced by different companies using two different technologies (I and II) were studied. Some quantitative results of such studies are presented in figure 3. The measurements were done in angles with a range from 0 to 360 degrees on the X-axis on a linear scale. The ordinate shows the luminescence intensity in absolute units on a linear scale too.

![Figure 3. Angular dependences of the distribution of gas-discharge luminescence for bisoprolol solutions with a concentration of 0.05%: a – without excipients, b – with excipients (technology I), c – with excipients (technology II).](image)

The data obtained by channeling emission electrons during GDV analysis show that aqueous solutions of the investigated medical drugs are complex systems of molecular assemblies that form structural elements with different spatial arrangements. In contrast to bidistilled water (figure 2), the angular dependences of bisoprolol solutions contain 6-8 streamer maxima (figure 3), which makes it possible to clearly distinguish the objects under study and consider gas-discharge visualization as a new quantitative method for evaluating medicines.
The peculiarities of such a relatively large number of GDV maxima of bisoprolol solutions are associated with the specificity of the cooperative interaction of molecular complexes of water with molecules of bisoprolol medicine drugs and excipients that determine the structural organization of solutions at micro- and nanoscale. As a result of comparing the GDV parameters of medicine drugs solutions, it can be concluded that the key factor in their difference is the energy of interaction of medicine drugs molecules with molecules of excipient and water. As a result of these interactions, associates are formed in solution, the order of arrangement of the ensembles and the sizes of which depend on the concentration and type of excipients. Despite the fact that the delicate mechanism of hydration in such complex aqueous systems is not fully understood and requires additional research, the experimental results obtained indicate a high diagnostic potential of gas-discharge imaging as applied to medicine drugs, including when assessing their pharmacological efficacy.

4. Conclusions
The use of channeling of kilovolt electrons in aqueous solutions of medicine in the method of gas-discharge imaging opens up prospects for assessing the quality and pharmacological efficacy of medicine, and, consequently, for the subsequent individualization of medical drug therapy.

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