Features of photoluminescence of biologically active drugs excited by ultraviolet laser radiation

Vladimir Semenovich Gorelik[1], Maksudjon Fayzuloevich Umarov[2], Anton Alexandrovich Sinitsyn[2]

[1]P.N. Lebedev Physical Institute of the Russian Academy of Sciences, Leninsky Ave., 53, Moscow, GSP-1, 119991, Russia
[2]Vologda State University, Lenin str., 15, Vologda, 160000, Russia

Abstract. A method of identifying biologically active drugs by manufacturers has been developed on the example of aspirin, citramonum, analgin, paracetamol and caffeine. The method is based on fiber-optical detection of the photoluminescence spectra using optical channels - photon traps, compact spectrometer and a data processing system that makes it possible to compare analyzed spectrum with the spectrum of reference substance. Difference has been established between photoluminescence spectra of aqueous solutions of pharmaceutical drugs and their pill form. With that, transition effect has been observed in the spectra from the mode of spontaneous photoluminescence to the superluminescence mode. It has been found that the nature of superluminescence is similar to the well-known mechanism in dye lasers. Based on the established superluminescence effect, it is possible to create new types of lasers with tunable frequency of generation in the ultraviolet region of the spectrum.
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Introduction

Functioning of an organism is ensured by two processes - assimilation and dissimilation - which are based on the metabolic process between the internal (body cells) and the external environment. Normal metabolic processes are ensured by maintaining constant chemical composition and physico-chemical properties of the internal environment (homeostasis). [1] It depends on certain factors, among which an important role is played by Biologically Active Drugs (BAD) [2] coming with food (vitamins, enzymes, mineral salts, trace nutrients, etc.) and ensuring harmonical interaction and interdependence of all physiological and biochemical processes in the organism. By normalizing and adjusting all vital functions, biologically active drugs also have effective therapeutic action.

BAD physiological activity can be regarded both in terms of their possible medical use and in terms of maintaining normal functioning of human organism, or giving special properties to a group of organisms [3]. Besides, BAD have pronounced pharmacological activity, so they are also called acting drugs.

Thus, BAD include a large class of substances that at the molecular level have strong influence on biological structures and living organisms. These include, in particular, various pharmaceutical objects, stimulants of life processes, amino acids, toxic substances, etc. For efficient use of BAD it is necessary to ensure compliance of their molecular structure and composition to nominal drugs whose effects on biological structures and living organisms is well established.

In this respect, there is the problem of establishing at the quantitative level the extent of compliance between molecular structure and composition of real samples used in medicine, food industry, agriculture and other areas, and nominal BAD with characteristics known and populated into the database. To solve such a problem, spectroscopic methods may be used, including fluorescence spectroscopy [4], the Raman scattering method [5], methods of optic analysis [6], etc.

In this work we consider features of the photoluminescence spectra in BADs on the example of commercially available pharmaceutical drugs from various manufacturers in solid and liquid state.

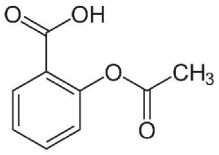
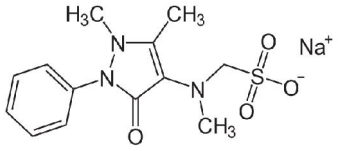
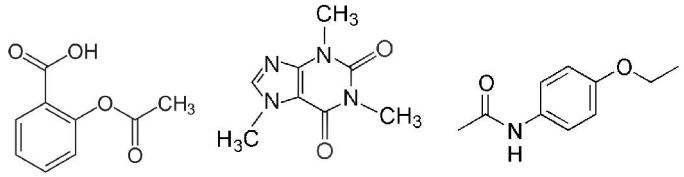
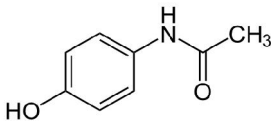
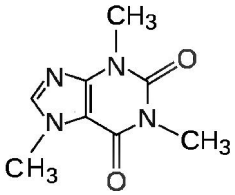
Experiment method

The subjects of study were typical pharmaceutical drugs (citramonum, analgin, aspirin and paracetamol) from various manufacturers. Each of them was studied in form of pills and in form of aqueous solution. Table 1 shows chemical and structural formula of the studied pharmaceutical drugs. As it can be seen from this table, the structure of all investigated substances includes benzene rings, which fact leads to fundamental electronic absorption in the middle UV band.

Fiber-optical method was used for excitation and recording fluorescence spectra [7]. Schematic diagram of the experimental setup is shown in Figure 1. The source of exciting ultraviolet radiation was the fourth harmonic (266 nm) of the YAG laser that

generated pulse-periodic radiation with 1064 nm wavelength. A small amount of the substance to be analyzed (12, Fig. 1) in the form of a tablet was placed in a cuvet (13, Figure 1).

Table 1. Chemical and structural formula of the studied pharmaceutical drugs

Pharmaceutical Drug	Chemical formula	Structural formula
Aspirin	$C_9H_8O_4$	
Analgin	$C_{13}H_{16}N_3NaO_4S$	
Citramonum (aspirin, caffeine, phenacetin)	$C_9H_8O_4$ + $C_8H_{10}N_4O_2$ + $C_{10}H_{13}NO_2$	
Paracetamol	$C_8H_9NO_2$	
Caffeine	$C_8H_{10}N_4O_2$	

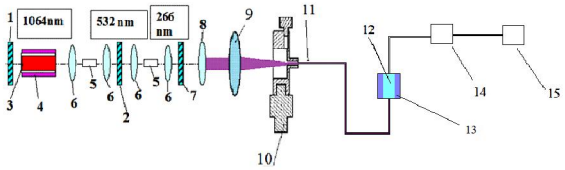


Fig.1. Experimental setup layout for recording photoluminescence spectra: 1, 2, 7-mirrors; 3 - active element; 4 - "pumping" LEDs; 5 - non-linear crystal; 6, 8, 9 - lenses; 10 - lightguide holder; 11 - lightguide; 12 - tested substance; 13 - 1 mm diameter cylindrical cuvet; 14 - miniature spectrometer FSD-8; 15 - computer.

Quartz lightguide (11, Figure 1) was used for guiding ultraviolet radiation to the substance and for diverting fluorescence emission occurring in the sample to the FSD 8 miniature spectrograph (14, Figure 1). From the FSD-8 miniature spectrometer digital information about radiation photoluminescence spectra was transmitted to the computer.

Main part

Photoluminescence spectra have been recorded following pharmaceutical drugs: citramonum, analgin, aspirin, paracetamol and caffeine. Authors [8, 9] studied the ultraviolet and infrared spectra of these drugs. After computer processing, normalized photoluminescence spectra of studied aromatic compounds were built. Fig. 2((a)-(d)) shows normalized photoluminescence spectra of citramonum in the form of pills obtained from four manufacturers. Fig. 2 ((a)-(d)) shows that in photoluminescence spectra of citramonum there was slight difference between 300-500 nm and 600-700 nm.

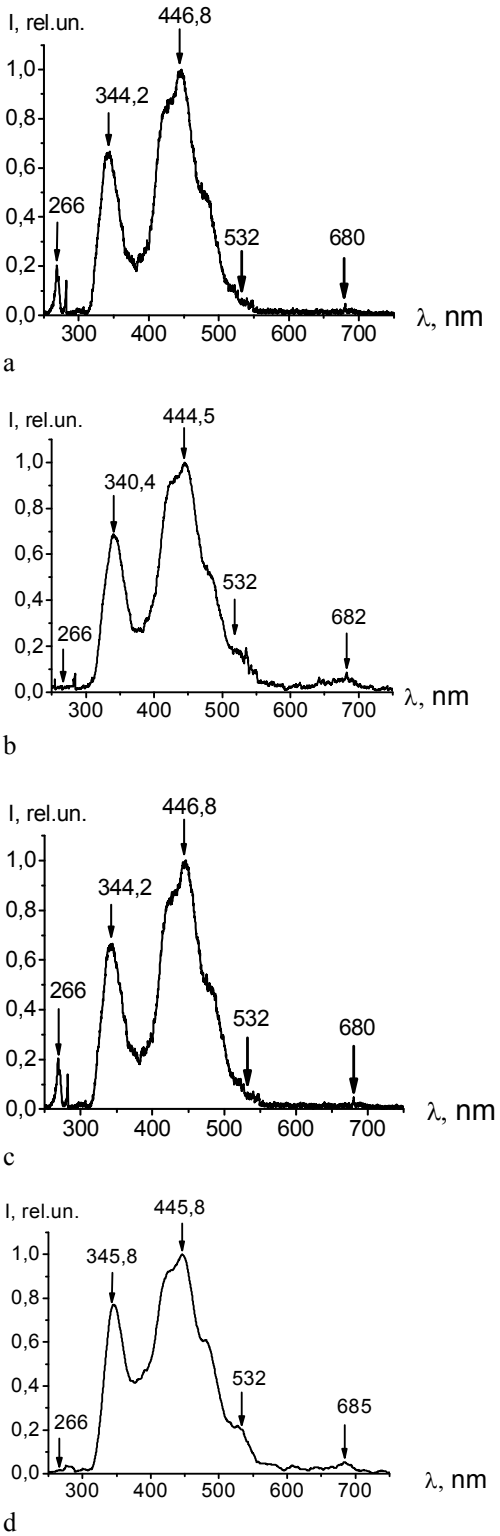


Fig. 2. Normalized photoluminescence spectra of citramonum solid phases: a - citramonum No. 1, b - citramonum No. 2, c - citramonum No. 3, d - citramonum No.4.

Similar measurements were made for other pharmaceutical drugs. Basing on the photoluminescence spectra of all the five objects structured fluorescence band in violet-red region of the spectrum was found, shape of which slightly differs. Similarity of fluorescence spectra for citramonum and aspirin is caused by the presence of the same component, and the difference is caused by the fact that citramonum also contains other components, beside aspirin (see Table 1), which generate an additional band between 400 and 550 nm. Broadening of the fluorescence band for analgin compared to paracetamol spectrum can be attributed to the more complex molecular structure of analgin [10].

For establishing quantitative differences between photoluminescence spectra obtained from various pharmaceutical drugs, correlation coefficients of analyzed drugs were calculated as compared to the reference one [10]. Reference substances were normalized photoluminescence spectra of aspirin (sample No.1), citramonum (sample No. 1), analgin (sample No. 1), paracetamol (sample No. 1) and caffeine (sample No. 1).

All calculated values of correlation coefficients in studied drugs are shown in Table 2. As can be seen from Table 2, correlation coefficients of the pharmaceutical drugs studied were different for each manufacturer. In this regard, the proposed method makes it possible to identify manufacturers of pharmaceutical drugs.

Table 2. Pharmaceutical drugs correlation coefficients

Substance Name	Sample No.	Correlation coefficient
Aspirin	1	reference
	2	0.92
	3	0.90
Citramonum	1	reference
	2	0.77
	3	0.76
	4	0.79
Paracetamol	1	reference
	2	0.58
	3	0.57
Analgin	1	reference
	2	0.51
	3	0.53
Caffeine	1	reference
	2	0.67
	3	0.65

Now let us consider the results of analyzing photoluminescence spectra of pharmaceutical drugs in aqueous solution [11].

Fig. 3 ((a) - (d)) shows photoluminescence spectra obtained from saturated aqueous solutions of the same four samples of citramonum.

From the comparison in Figure 2 ((a) - (d)) and 3 ((a) - (d)) we can see that in course of transition from solid samples to saturated aqueous solutions there is an increase in photoluminescence intensity in the short-wave area of the spectrum, and its decay in the purple-blue area. Besides, similar effect is observed, most clearly defined for samples of citramonum No. 1 and No. 3: spectra reveal an intense narrow band with maximum at 330 and 338 nm, respectively (see Fig. 3 ((a)-(d))). Similar effects were observed for other pharmaceutical drugs.

The observed effects of intensity redistribution in the photoluminescence spectra of the aromatic compounds studied can be explained by transition from the spontaneous photoluminescence mode to the superluminescence mode. This is due to effective population of excited singlet term of an aromatic molecule caused by intense pulsed ultraviolet laser radiation [11]. Boost nature in this case is similar to the well-known mechanism in dye lasers. Boost rate in this case has the form:

$$K = S \cdot (N_{s1} - N_{s0}) \approx S \cdot N_{s1}. \quad (1)$$

Provided that effective cross section $S \sim$ 10-16 cm2, and molecules concentration in aqueous solution $N_{s1} \sim 10^{17}$ - 10^{18} cm^{-3}, we find that the boost $K \sim$ 10-100 cm^{-1}. In accordance with the Bouguer law for active medium ($L \sim$ 0.1 - 1 mm), we have:

$$I(L) = I_0 \cdot e^{K \cdot L} \sim \left(10^2 \div 10^3\right) \cdot I_0 \quad (2)$$

Assessments made explain the appearance of photoluminescence spectrum in thin layers of the solid phase and in aqueous solutions of compounds tested. Characteristic of the effect observed is the effect of superluminescence in ultraviolet area of the spectrum that corresponds to the position of the first excited electronic singlet term in studies aromatic substances.

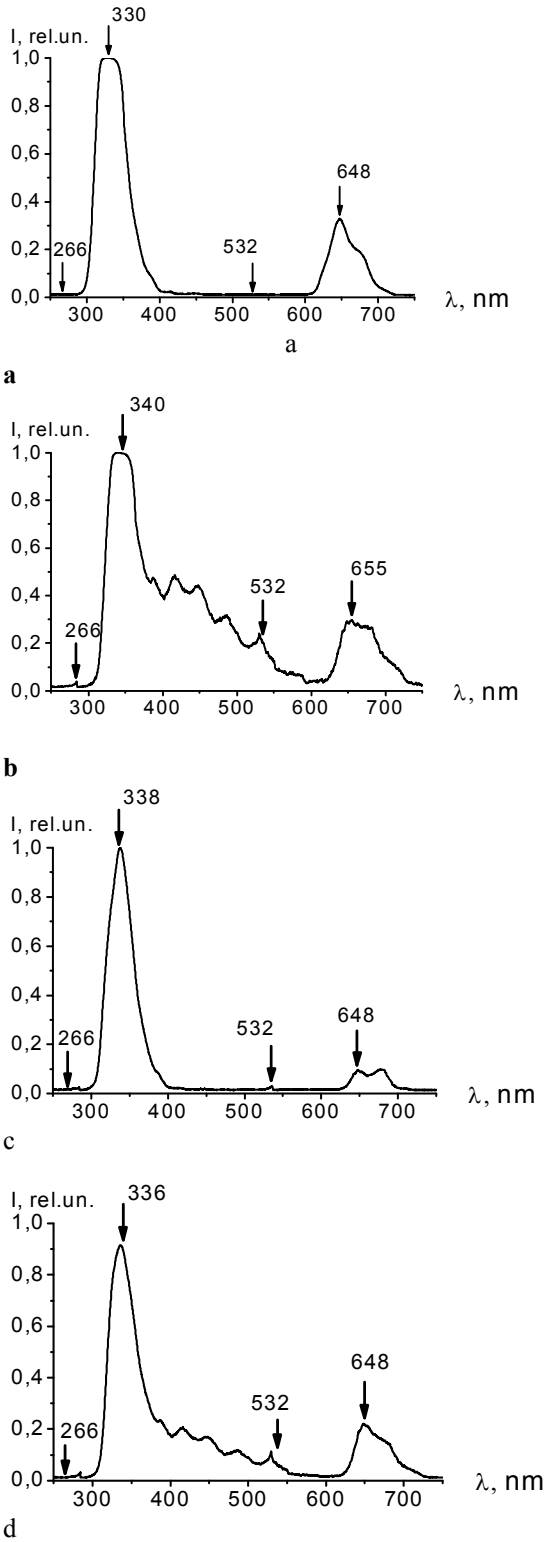


Fig. 3. Normalized photoluminescence spectra of aqueous solutions of drugs: a - citramonum No. 1, b - citramonum No. 2, c - citramonum No. 3, d - citramonum No.4

Conclusions

It has been shown that correlation coefficients of the pharmaceutical drugs studied were different for each manufacturer. In this regard, the proposed method makes it possible to identify manufacturers of pharmaceutical drugs. It has been found that in course of transition from solid samples to saturated aqueous solutions there is an increase in photoluminescence intensity in the short-wave area of the spectrum, and its decay in the purple-blue area. The observed superluminescence effect can be used for creating new types of lasers with tunable frequency of generation in the ultraviolet region of the spectrum.

Corresponding Author:
Dr.Gorelik Vladimir Semenovich
P.N. Lebedev Physical Institute of the Russian Academy of Sciences
Leninsky Ave., 53, Moscow, GSP-1, 119991, Russia

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