IMMUNOCHROMATOGRAPHY-BASED PORTABLE EQUIPMENT FOR INDICATION OF PATHOGENIC MICROORGANISMS AND TOXINS

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This review looks at analytical capabilities and composition of portable equipment based on lateral flow immunoassay for rapid indication of human pathogenic bacteria, viruses and toxins which was developed by the State Research Institute of Biological Instrumentation under the auspices of the Federal Medical and Biological Agency of Russia. The review presents technical characteristics and composition of portable test kits UIHE-1 designed for taking monoanalytical and multi-analytical lateral flow immunoassay on pathogenic microorganisms and toxins in washes from environmental objects surfaces and in culture media; it also describes kits EkB and EkB-01 for analysis of biological aerosol samplers contents. Information is given on the analytical properties of luminescence lateral flow immunoassay kit ULI-1, an on the experimental prototype of fluorimeter-reflectometer "Zondazh". The technical characteristics of indication kits were compared with those of foreign origin, areas for improvement of portable equipment based on lateral flow immunoassay were indicated.

Keywords: pathogenic bacteria, viruses, toxins, immunochromatography, identification, sets and kits

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ТЕХНИЧЕСКИЕ СРЕДСТВА НА ОСНОВЕ ИММУНОХРОМАТОГРАФИИ ДЛЯ ИНДИКАЦИИ ПАТОГЕННЫХ МИКРООРГАНИЗМОВ И ТОКСИНОВ

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В обзоре рассмотрены аналитические возможности и состав технических средств на основе иммунохроматографии для экспрессной индикации патогенных для человека бактерий, вирусов и токсинов, разработанных в Государственном научно-исследовательском институте биологического приборостроения ФМБА России. Рассмотрены технические характеристики и состав серийных укладок УИХЭ-1, предназначенных для осуществления моноаналитного и мультианалитного иммунохроматографического анализа патогенных микроорганизмов и токсинов в смывах с поверхностей объектов окружающей среды, в культуральных средах, комплектов ЭкБ и ЭкБ-01 для анализа содержимого пробоотборников биологического аэрозоля. Приведены сведения об аналитических свойствах укладки для люминесцентного иммунохроматографического анализа УЛИ-1, экспериментальном образце флуориметра-рефлектометра «Зондаж». Проведено сравнение технических характеристик индикационных укладок и комплектов с зарубежными аналогами, указаны направления совершенствования технических средств на основе иммунохроматографии.

Ключевые слова: патогенные бактерии, вирусы, токсины, иммунохроматография, идентификация, укладки и комплекты

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Immunochemical analysis in which liquid immunochromatography processes are based on specific (immune) interactions between an analyte and specific receptor molecules deposited on a porous thin membrane is called lateral flow immunoassay, or LFIA. The history of the method began in the 1980s with the development of urine chorionic gonadotropin test strips, which allowed the detection of pregnancy outside the laboratory (1). A schematic of a test strip for the sandwich version of the LFIA is shown in Fig. 1.

Typically, an lateral flow immunoassay uses a multi-membrane composite consisting of several membranes of different chemical structure and porosity, fixed to a substrate that provides structural rigidity and housed in a polymeric frame.

The principle of the sandwich version of LFIA has been described many times in the literature [2–4]. A liquid sample, potentially containing analyte antigens, is placed on a substrate for the sample to be applied. Capillary forces move the liquid through the multi-membrane composite. First the colloidal gold nanoparticles (CGN) conjugate with specific antibodies is solubilized. The CGN conjugate is cherry colored and its movement along the membrane can be observed visually. When a detectable antigen is present in the sample, an antigenic immune complex is formed, which starts to move along the analytical membrane with an excess of conjugate with the flow of liquid. The immune complex is then immobilized on the analytical membrane by specific antibodies in the

analytical region (AR), forming a 'sandwich', while unbound conjugate antibodies are immobilized by antibodies located in the control region (CR) of the test strip resulting in two colored lines. In the absence of antigen in the sample, no antigenic immune complex is formed, so a single visible line is formed by the binding of the conjugate antibody and the CR antibody (antispecific to the conjugate antibody) only in the CR.

Depending on the task at hand, additional reagents can be added to the test strip and some membranes can be added, combined or eliminated. However, the general design and principle of analytical interactions during the movement of reagents along the membranes is retained. Simplification of the assay with respect to the Enzime Linked Immunosorbent Assay (ELISA) can be achieved by avoiding additional treatments, washes, signal-enhancing incubations, and visual assessment of the results. Typical LFIA times are 10–25 min, sensitivity for bacterial suspensions is 10^5–10^6 CFU/ml, for viral suspensions 10^4–10^6 PFU/ml; for protein toxins, sensitivity ranges from 1–100 ng/ml, depending on toxin type. Since immunochemical interactions at the membrane are in non-equilibrium mode, LFIA is considered to be inferior to ELISA in sensitivity. At the same time, there are techniques and methods to increase the sensitivity of LFIA to protein antigens to 0.1 ng/ml and to 103 cells/ml, but this requires either additional reagents or instrumental registration and significantly increases assay time.

The focus on the LFIA method has emerged against a backdrop of external global events affecting the interests of the world's major economic powers and global public health. Four waves of interest in LFIA methods can be distinguished, related to the mass use of human pathogenic bacteria, toxins and the emergence of new viral infectious diseases.

1. For the US Army's Operation Desert Storm in January-February 1991 immunofiltration personalized anthrax detection devices were created that were included in military equipment. In the event of use of anthrax spores by the Iraqi army, rapid detection was expected to reduce personnel casualties.

2. Acts of individual bioterrorism, such as mailing envelopes to US government agencies containing anthrax spores in August-October 2001. Several firms in the US have produced LFIA sandwich test strips to detect anthrax spores and other dangerous pathogens (plague, tularemia, brucellosis).

3. The US Iraq War 2003-2011. There has been an expansion in the nomenclature of tests for the detection of pathogens in environmental media.

4. COVID-19 pandemic from late 2020 — up to the present. Rapid LFIA tests have become available to detect the nucleocapsid antigen of SARS-CoV-2 coronavirus and antibodies to it in exposed individuals in nasopharyngeal wipes and serum. Production of immunochromatographic test strips has reached hundreds of millions worldwide.

Biosecurity is extremely important in modern society. Information on the presence of pathogens and toxins in environmental media should preferably be obtained immediately and directly at the sampling site. In addition to the biological threats posed by individual bioterrorism, there are concerns about the presence of biological laboratories working with highly dangerous pathogens, funded by unfriendly states, in CIS countries. The activities of these biolaboratories are not transparent and are not monitored by the local administration.

The application of LFIA in sanitation and hygiene is driven not only by biosafety issues, but also by the need for rapid information on commodities of mass consumption, e.g. the quality of agricultural raw materials entering the plant and finished food products destined for the retail chain [5]. The last decade has seen an increase in the development of modifications to the LFIA that allow for highly sensitive analysis while retaining the key strengths of speed of execution, ease of implementation and interpretation of results [6–8].

The above makes the development and serial production of domestic technical means of rapid indication of pathogenic microorganisms and toxins, suitable both for medical needs and for the control of environmental objects urgent.

Federal State Unitary Enterprise "State Scientific Research Institute of Biological Engineering" FMBA of Russia (FSUE “SSRIBE”) is the only agency in the country which is actively involved in development and massive production of portable equipment for indicating pathogens in environmental objects, based on LFIA principle.

This overview is to present the characteristics of domestic LFIA-based means for indication of pathogenic microorganisms and toxins in environmental objects (wipes from surfaces, liquids, contents of biological aerosol samplers) developed by FSUE "SSRIBE" and to compare with similar items of foreign origin.

A kit of lateral flow immunoassay indicator elements UIHE-1

The UIHE-1 kit was developed for the detection of plague, anthrax, tularemia, glanders and botulinum toxin type A in wipes from environmental objects. The kit consists of lateral flow immunoassay indicator elements and surface sampling equipment, brushes, assay buffer container, sterile swab and assay chart, all stowed in a water and dust-proof polymer case. The kit has enough consumables for 10 tests to be carried out for five different types of pathogens. A refill set is available to quickly replace expended indicator elements and assay buffer and other disposable accessories. In the regulatory documents of FMBA of Russia the kit is recommended for use in the practical work of the centers of hygiene and sanitation acting under the auspices of FMBA of Russia. The main technical characteristics of the kit are given in Table 1.

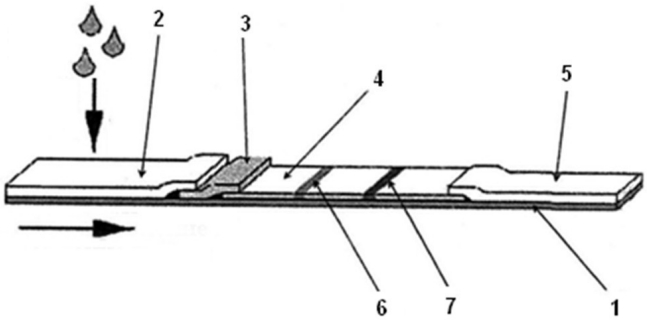

Fig. 1. Schematics of the test strip for the LFIA. 1 — rigid plastic substrate; 2 — substrate for sample application; 3 — conjugate substrate with dried conjugate of colloidal gold nanoparticles (CGN) with specific antibodies; 4 — analytical membrane with applied lines of antibody solutions; 6 — analytical zone; 7 — control zone; 5 — adsorbent substrate. The vertical arrow indicates the application of the liquid sample on the substrate, the horizontal arrow indicates the direction of flow of the test sample

Table 1. Comparative characteristics of domestic and foreign technical tools for the indication of pathogens in environmental media based on lateral flow immunoassays

Features	Domestic kits and sets				Foreign kits and sets							
	EkB, EkB-01	UIHE-1		MID	Pro Strips™	RAID	NIDS	Toxin Screen	IMASS	RAMP**	BADD	KBTB
	376.00.00.000;	304.00.00.000	304.00.00.000-01									
1	2	3	4	5	6	7	8	9	10	11	12	13
Manufacturer	Federal State Unitary Enterprise "SSRIBE", Russia				ADVNT Biotech-nologies, USA	Alexeter Tech-nologies, USA	ANP Tech-nologies, USA	Gen Prime, USA	BBI Detection, U.K.	Responce Biome-dical Corp., Canada	Osborne Scientific, USA	CEA, France
Number of pathogens detected	17	5	10	5	6	3, 5, 2008	3, 5	3	9	5	3	6
Name of pathogens, infectious agents and toxins detected by the technical detection aid	Anthrax, plague, brucellosis, tularemia, glanders/melioidosis, botulinum toxins types A and B, ricin, SEB***, cholera exotoxin, Ebola virus, orthopoxvirus, Lassa virus/Machupo virus, virus and rickettsial growth medium based on chicken embryo	Depending on configuration: Anthrax, plague, brucellosis, tularemia, glanders/ melioidosis, legionellosis, salmonellosis, Bernet's rickettsia, orthopoxviruses, botulinum toxins types A and B, ricin, SEB, cholera exotoxin	Anthrax, plague, brucellosis, tularemia, glanders/ melioidosis, botulinum toxins types A and B, ricin, SEB, cholera exotoxin	MID bacteria: anthrax, plague, brucellosis, tularemia, glanders/ melioidosisMID toxins: botulinum toxins type A and B, ricin, SEB, cholera exotoxin	Anthrax, plague, botulinum toxins types A and B, ricin, SEB	Depending on configuration: anthrax, plague, brucellosis, tularemia, botulinum toxins, ricin, SEB, smallpox virus	Depending on configuration: anthrax, plague, brucellosis, tularemia botulinum toxins, ricin, SEB, cholera exo-toxin, smallpox virus	Botulinum toxins, ricin, SEB	Anthrax, plague, brucellosis, tularemia, glanders/ mel-iodosis, botulinum toxin, ricin, SEB	Anthrax, plague, botulinum toxins, ricin, smallpox virus	Anthrax, plague, botulinum toxins, ricin	Anthrax, plague, tularemia, botulinum toxins, ricin, SEB
Sensitivity threshold: -spore forms of bacteria, m.c./ml -vegetative forms of bacteria, m.c./ml - Viruses, PFU/mL - Bacterial and plant toxins, ng/ml	1×10^6 1×10^6 $(1…100) \times 10^5$ 30–250	1×10^6 1×10^6 1×10 PFU/mL 50–1000	1×10^6 1×10^6 Not detectable 20–500	1×10^6 1×10^6 Not detectable 20–500	$1{,}5 \times 10^4$ – $8{,}3 \times 10^4$ 1×10^6 Not detectable 10–500	1×10^6 $3{,}6 \times 10^4$ – $1{,}6 \times 10^6$ $1{,}6 \times 10^6$ 6–30	no data no data no data no data	Not detectable Not detectable Not detectable 400	5×10^6–5×10^7 1×10^6 – 1×10^8 Not detectable 10–20	$1{,}5 \times 10^4$ no data 3,8 ng/mL 19–38	1×10^6 1×10^5 Not detectable 10–500	no data no data Not detectable no data
Operating time, min	25	25–30	25–30	25–30	15	15	no data	15	no data	15	15–25	15
Number of samples to be analysed	50/5	10	4	1	1	1	10	3	10	5	5	5
Availability of sampling equipment	Sampling equipment is available											
Availability of sample preparation tools for assay	yes	yes	yes	no	yes	yes	no	yes	no	yes	yes	yes
Operating temperature range, °C	+10…+ 40	+10….+ 35			from 4	no data	no data	+20...+ 42	no data	no data	from 4	no data
Shelf life, years	2	2	2	2	2	2	2	1	no data	no data	2	2
Weight, kg	30 /0,405	5,5	2	0,03	no data	no data	4,54	no data	no data	9,08	no data	no data
Dimensions, mm	994 × 600 × 445 200 × 128 × 90	490 × 390 × 190	235 × 195 × 108	140 × 140 × 20	no data	no data	no data	no data	no data	no data	no data	no data
Method of recording the results of the analysis	Visual/ Instrumental (mains or internal battery supply)	Visual					Instrumental. Battery powered	Visual. Instrumental	Visual	Instrumental. Battery and mains powered	Visual	Visual. Instrumental
Mono/multi-analytical tests	Multi	Mono	Multi	Multi	Multi	Multi	Multi	Multi	Multi	Mono	Mono	Mono

Note: * — the decimal numbers of the design documentation are indicated; ** — lateral flow immunoassays use a fluorescent tag; *** — SEB — Staphylococcal enterotoxin type B; The table contains manufacturers' information on indication equipment such as portable kits and sets to counteract the bioterrorist threat. The list of individual lateral flow immunoassays produced in Russia and abroad for medical purposes for the diagnosis of particularly dangerous and dangerous infectious diseases is more extensive.

Table 2. Comparative characteristics of UIHE-1 kit and other methods of rapid pathogen indication [9]

Concentration mln cl./ml	PCR time (2,0 h)	IHR time (3,5 h)	ELISA time (2,0 h)	UIHE-1 time (15–20 min)
Y. pestis 0,1	+	+	+	+
Y. pestis 0,01	+	–	–	+/–
B. anthracis 1,0	+	+	+	+
B. anthracis 0,1	+	+/–	+	+/–
B. anthracis 0,01	+	–	–	–
Fr. tularensis 0,1	+	+	+	+
Fr. tularensis 0,01	+	–	–	+/–

Note: PCR — polymerase chain reaction; IHR — indirect haemoagglutination reaction; ELISA — enzyme linked immunosorbent assay.

The characteristics of lateral flow immunoassay indicator elements of the kit in terms of sensitivity and speed, in comparison with other lateral flow immunoassay express methods of pathogen indication are given in Table 2. The data were obtained in the course of exercises on detection of microbial cells of vaccine strains of anthrax, plague and tularemia pathogens [9].

As can be seen from comparative tests, the LFIA method and the UIHE-1 lateral flow immunoassay indicator elements have sensitivity comparable to indirect haemagglutination reaction (IHR) and ELISA, and outperform them in terms of speed. The range of lateral flow immunoassay indicator elements that can be optionally supplied with the kit has now been extended to 15 items [10, 11]. As a further effort, a version of UIHE-1 kit was created which is complete with multi-analyte lateral flow immunoassay indicator devices (MID) designed for the detection of bacteria and toxins [12]. The test strips in the MID are arranged in separable polymeric rims of 5 pieces each, whereby the selected liquid sample has to be introduced into the sample application hole and distributed evenly over all test strips. The top cover of the polymeric MID rim has rectangular slots for visual recording of assay results and appropriate labeling. The use of the MID has made the kit more compact and increased the nomenclature of bacteria (five names) and toxins (five names) detected in a single assay cycle. The causative agents of glanders and melioidosis have no species distinction in LFIA, due to the close antigenic structure of the Burkholderia genus. Both versions of UIHE-1 kit have high resistance to mechanical and climatic factors and are used in mobile biolaboratories. The plastic kit cases are resistant to disinfectants. The small dimensions and weights of 5.5 kg and 2.0 kg make them also suitable for use as a portable specific indication.

Express Kit-Bio

The Express Kit Bio (EkB) is designed for:

– sampling and preparing samples of the contents of biological aerosol samplers, culture media after the biological enrichment stage, wipes from environmental objects;

– detection of viruses (orthopoxviruses, Lassa and Machupo haemorrhagic fevers, Dengue fever, West Nile fever, virus accumulation medium and rickettsia (antigens of growing chicken embryos), vegetative and spore forms of bacteria (plague pathogens, glanders and melioidosis, brucellosis, anthrax spores, tularemia), bacterial and plant toxins (botulinum toxin type A (BTA), botulinum toxin type B (BTB), staphylococcal enterotoxin type B (SEB), cholera exotoxin, ricin;

– recording the results of the LFIA and transmitting the results to authorities.

The kit is designed for sampling, preparation and carrying out assays of 50 samples and is operated between +10 °C and +40°C [13]. It consists of a kit of accessories for the preparation of selected samples for carrying out assays, which includes a device for elution of the sample from solid sorbent media of aerosol samplers; a set of multi-analyte lateral flow immunoassays (MLFIA). The indication capability of the kit is provided by three types of MLFIA: Bacterial MLFIA, Virus and Accumulation Medium MLFIA and Toxin MLFIA (Fig. 2).

The detection and indication of glanders and melioidosis pathogens is indistinguishable from the bacterial species.

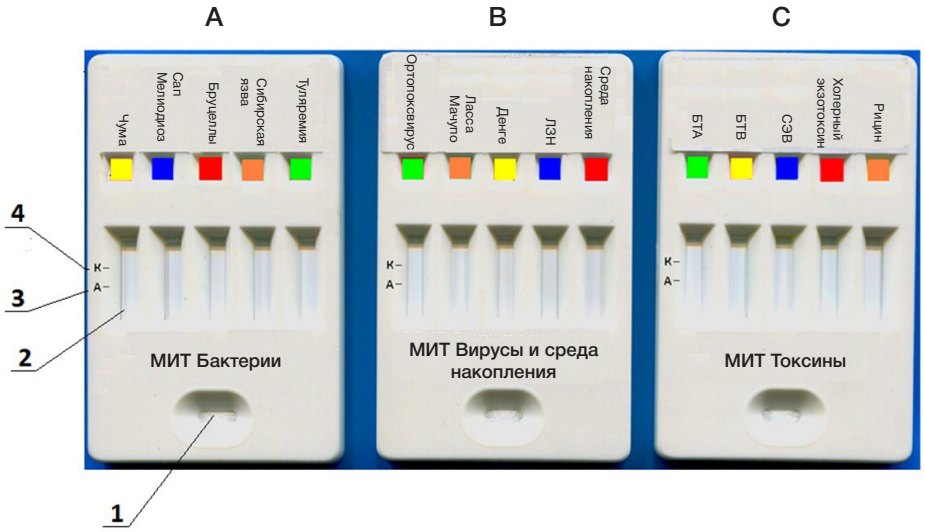

Fig. 2. Appearance of the multi-analyte lateral flow immunoassays included in the EkB and EkB-01 kits. **A**. Bacteria for multi-analyte lateral flow immunoassays. **B**. Viruses and accumulation media for multi-analyte lateral flow immunoassays. **C**. Toxins for multi-analyte lateral flow immunoassays 1 — sample put-in opening; 2 — opening for recording the test finding; 3 — analytical area; 4 — control area

In the case of orthopoxviruses, Lassa fever and Machupo fever viruses, detection and indication by LFIA is also without species distinction. This is due to a lack of antibodies capable of differentiating the antigens of these pathogens at the species level. The kit is equipped with a reflectometric device (Fig. 3) whose software allows automatic recognition of positive analysis results, setting of intensity thresholds for coloring MLFIA zones, archiving of assay data and transmission by email to higher authorities for decision-making.

The computer used in the reflectometer device is highly resistant to mechanical stress and moisture. The EkB kit is fully autonomous, has its own power supply for the reflectometer and can be deployed both in the laboratory and in the field. The kit is housed in four impact-resistant, waterproof polymer cases and contains all the necessary accessories for carrying out an assay of the contents of the aerosol sampler when sampling into liquids, filters or dense sorbent media. The kit is also equipped with a transport container, allowing it to be transported by all means of air and ground transport.

Fig. 3. Exterior view of the reflectometer device of EkB kit

Portable version of the kit "Express-kit-Bio"

A portable version of the "Express-Kit-Bio " (EkB-01), (Fig. 4) allows it to be used as a means of individual control of the biological situation. The EkB-01 kit is designed to analyze five samples for 17 types of pathogens. The device is designed for LFIA of prepared samples of the contents of aerosol samplers, immunochemical verification of microbial colonies after sample enrichment on culture media, making wipes from the surfaces of environmental objects and their analysis.

The portable version of the kit uses the same MLFIA as for the EkB, the kit casing is dustproof, made of carbon composite material, the total weight of the kit is 0.405 kg.

Development of indication tools based on luminescent tags in lateral flow immunoassay

Luminescent tag molecules have also been successfully used in LFIA, along with NCG. For example, Response Biomedical Corp. (Canada) created the RAMP analyzer for lateral flow immunoassay detection of pathogenic bacteria, orthopoxviruses, and toxins. Technical specifications are presented in Table 1.

The Federal State Unitary Enterprise "SSRIBE" under FMBA of Russia developed and tested a prototype of luminescent lateral flow immunoassay kit ULI-1 containing luminescent lateral flow immunoassay indicator elements based on latex sub-micron particles functionalized with carboxyl groups. Obtaining conjugates of antibodies with latex particles was performed by covalent binding. The ULI-1 kit also contains a battery-operated LED visualizing device that allows the operator to observe the luminescence of the analytical and test zones of the lateral flow immunoassay indicator element and perform visual registration of the assay results [14]. There is an advantage in terms of detection sensitivity when using

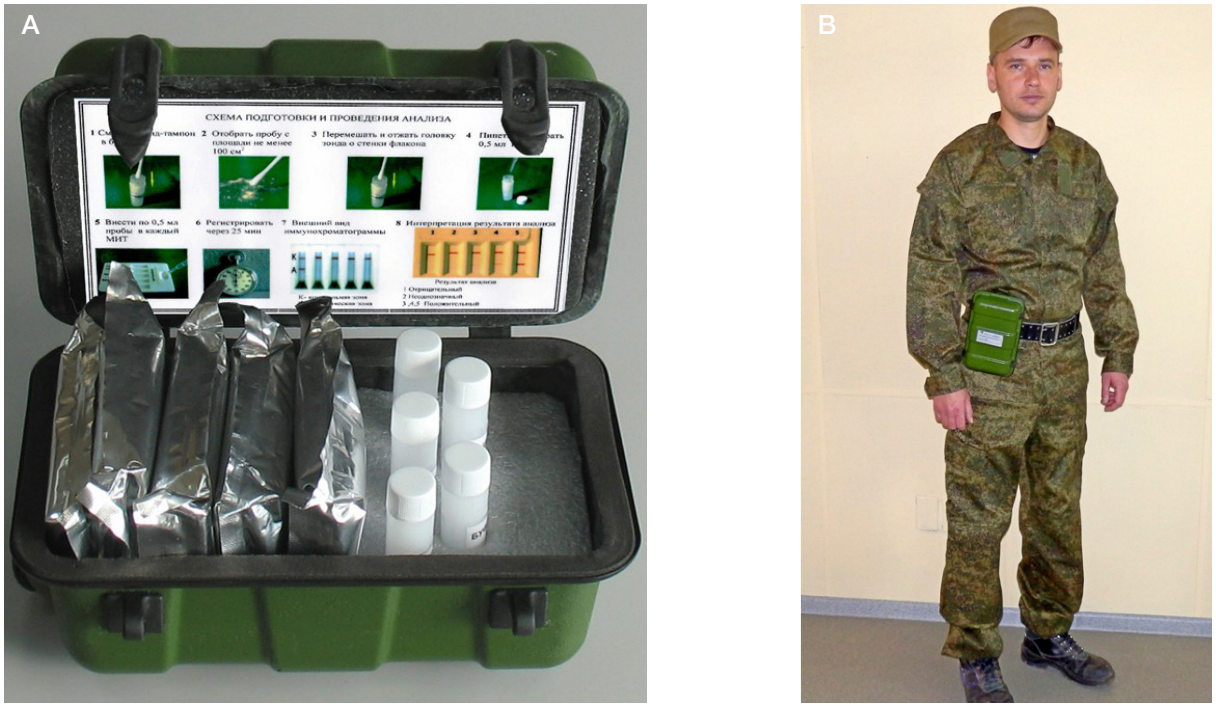

Fig. 4. Exterior view of the EkB-01 kit. **A**. Kit with open cover. **B**. Attachment of the kit to the operator's uniform

fluorescent tags, compared with NCG -based lateral flow immunoassays, and namely: for the spore form of the anthrax pathogen it is twice as much, for the vegetative forms of the plague pathogen it is twice as much, for the F1 antigen of the plague microbe it is five times higher, and for various types of botulinum toxin it is two to four times higher.

For the purpose of recording LFIA results, an experimental prototype reflectometer-fluorometer "Zondazh" was also developed to record the intensity of light reflection from an analytical or control zone of an lateral flow immunoassay in four spectral ranges of visible light: white (400–800 nm), red (650 nm), green (525 nm) and blue (470 nm). The spectral range of the instrument makes it possible to record reflectograms not only of CGN conjugates but also of colored latex particles of different colors, often used as a dispersed phase in the LFIA. In the luminescence intensity measurement mode the "Zondazh" instrument allows the recording of luminescent immunochromatograms. It provides a luminescence excitation wavelength of 380 nm and emission wavelength of 490 nm. The device operates based on the reflectometry of digital images of immunochromatograms, or the recording of luminescence intensity in the case of luminescence tests. Emitting LEDs are used as light sources. A solid-state video camera serves as an image receptor. The device is electrically powered (220V/50Hz) and weighs 1.30 kg. The software allows not only setting of recording parameters but also integral peak intensities of immunochromatograms and quantitative comparison of different samples. The LFIA logs are stored in memory and can be transmitted by email.

Directions for improving LFIA for pathogen indication

Ways to improve LFIA are to increase sensitivity, specificity and speed of the method. A review of the literature suggests that a pre-analytical sample concentration procedure, the selection of high affinity receptor molecules, the use of colloidal tags with a low detection threshold, instrumentation and methods for recording these tags are promising for this purpose. The use of magnetosorbents to concentrate bacteria and viruses is effective in the pre-analytical phase [15, 16]. In order to select the most efficient receptor molecules, it should be taken into account that immune reactions in LFIA are carried out in a kinetic mode. Therefore, it does not matter whether the detected complexes dissociate within hours or days. Their number is determined primarily by the kinetic association constants, which are similar in magnitude and vary within a limited range for receptors and antigens with the same structure. Additionally, the affinity can be increased by genetic modification (targeted design) of the antibody active centre. The use of these methods is still very limited, despite the confirmation of their efficacy [17].

With the development of molecular biology techniques, the production of modified traditional receptors (antibodies) and new receptors — aptamers [18–20], single domain antibodies [21] are becoming available. Targeted immobilization of antibodies on the dispersed phase via receptor staphylococcal protein A and streptococcal protein G, avidin-biotin interactions [22–25], occurs without loss of antibody affinity, as often occurs with physical adsorption on the dispersed phase, indicating the utility of this approach.

In the search for optimal markers, attention should be paid to the use of new optical markers based on highly branched colloidal gold [26, 27], colloidal carbon [28–30], graphene oxide and carboxylated graphene oxide [31]. The limitation to the registration of only surface label molecules existing in LFIA is of no relevance to analytical methods in which label registration is based on other physical principles. A temperature contrast amplifier reader has been developed for the registration of gold nanoparticles on immunochromatographic membranes [32]. This reader reduces the detection limit by a factor of eight for influenza virus LFIA, also for malaria, Clostridium difficile LFIA, compared to an optical reader.

The magnetic properties of the nanodispersed tag are also used to record the LFIA signal [33–35]. In recent studies, a commercially available glucometer with electrochemical detection has been proposed as a recorder of LFIA results [36].

Future test systems should be expected to be integrated with recording systems (reflectometers, fluorometers) as well as tools for collecting, storing and processing information to record and record results. The literature summarizes trends in the transformation of LFIA from a visual to an instrumental method [37] and presents the current state of the art in mobile/ smartphone based analytical technologies [38, 39].

CONCLUSION

Data from the literature and the authors' own studies show that LFIA is widely used for the identification of human pathogenic bacteria, viruses and toxins.

A comparison of the technical characteristics of the developed sets and kits for pathogen indication with similar foreign samples (Table 1) showed that our work followed the global trend of the method development: from the creation of mono-type individual lateral flow immunoassays to multiplex analysis, the search for the most sensitive methods of registration, and the expansion of the range of pathogens detected [40]. Kits EkB and EkB-01 are better than foreign analogues as they have a wider range of detected pathogens, automation of registration of results of the analysis (EkB) at comparable, or better threshold of sensitivity. The indicated means of pathogen indication are in demand in practice of centers of hygiene and epidemiology, specialized laboratories of other departments, providing biological safety.

The ways of improvement discussed in this review suggest that immunochromatographic analytical systems will be able to detect pathogens of bacterial, viral- rickettsial and toxin nature more effectively. At the same time, the specificity of the analysis will increase to the strain level, in the case of bacterial pathogens, making it possible to carry out a process of specific indication of pathogens and toxins on a new technological basis.

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