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INSTRUMENTE INOVATOARE APLICATE ÎN EDUCAREA POPULAȚIEI PRIVIND REZISTENȚA LA ANTIMICROBIENE

INNOVATIVE TOOLS APPLIED TO EDUCATE THE POPULATION ON ANTIMICROBIAL RESISTANCE

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Rezumat
Rezistența la antimicrobiene reprezintă o adevărată criză de sănătate, în special în țările cu venituri mici și mijlocii, alimentată de lipsa acută de noi agenți antibacterieni. Evoluția rapidă a acestui fenomen se datorează utilizării excesive, asociată cu un nivel relativ scăzut de educație în acest domeniu. Pentru a crește nivelul de cunoștințe al populației generale privind rezistența la antimicrobiene și calitatea vieții legată de sănătate, a fost dezvoltat un instrument inovator de autoeducare – „REZISTENȚA LA ANTIMICROBIENE ȘI TRATAMENTUL ALTERNATIV CU FAGI ÎN ȚĂRILE CU VENITURI MICI ȘI MIJLOCII. CALENDAR DE BIROU DE POPULARIZARE A CUNOȘTINȚELOR", în cadrul inițiativei JPIAMR, de către echipa proiectului PhageLand implementat la Universitatea de Stat de Medicină și Farmacie „Nicolae Testemitanu" și promovat în cadrul mai multor evenimente științifice naționale și internaționale. Acest articol prezintă aprecierea acestui instrument de către comunitatea științifică.
Cuvinte-cheie: rezistența la antimicrobiene, țări cu venituri mici și mijlocii, campanii de educație și conștientizare, instrumente inovatoare, calitatea vieții legată de sănătate

Summary
Antimicrobial resistance is a real health crisis, especially in low- and middle-income countries, fueled by the acute shortage of new antibacterial agents. The rapid evolution of this phenomenon is due to overuse coupled with a relatively low level of education on the subject. To increase the literacy level of the general population on antimicrobial resistance and health-related quality of life, an innovative self-education tool was developed - "ANTIMICROBIAL RESISTANCE AND ALTERNATIVE TREATMENT WITH PHAGES IN LOW AND MIDDLE INCOME COUNTRIES. A KNOWLEDGE POPULARIZATION DESK CALENDAR", in the framework of the JPIAMR initiative by the PhageLand project team implemented at "Nicolae Testemitanu" State University of Medicine and Pharmacy and promoted in several national and international scientific events. This article presents the appreciation of this tool by the scientific community.
Keywords: antimicrobial resistance, low- and middle-income countries, education and awareness campaigns, innovative tools, health-related quality of life

Antibiotics became in the twentieth century the savior of the population against diseases such as plague, diphtheria and typhoid fever, but in just a few decades they have exhausted their effectiveness due to bacteria that have developed antimicrobial resistance [1, 2, 3]. Several studies and authors have determined that antimicrobial resistance is a multifactorial phenomenon, but the most important determinants are the misuse of antimicrobials in the medical system and the lack of general population antimicrobials' consumption supervision by qualified personnel [4 - 7].

The rapid rate at which this phenomenon is evolving is affecting the world population, causing deaths, prolonged lost work capacity and significant economic losses, with estimates showing that the number of deaths directly caused by AMR alone in 2050 will be 4 times higher than the one calculated in 2019 [6, 8, 9]. In economic terms, AMR will cause additional costs of more than one billion dollars over the next 25 years. Experts believe that the burden will be greatest for low- and middle-income countries, whose budgets and investments in health are limited. It is difficult to talk about massive investment in research or the purchase of new antimicrobials by these countries, because their gross domestic product is much lower than that of high-income countries, for example, Moldova's GDP is 5.2 times lower than that of Luxembourg (the richest country in the world), and the absolute poverty rate is 316 times higher, according to the World Bank and the National Bureau of Statistics [10 - 13].

Taking into account these aspects, the increased rates of AMR in these countries, especially in the Republic of Moldova as a model country for small and medium-sized economies, and the results of the assessment of the general population's knowledge and attitudes on antimicrobials and antimicrobial resistance after the application of specially developed questionnaires, including in Moldova, which showed a relatively low level of literacy on these topics, the World Health Organization proposed to focus on campaigns to raise awareness and educate the population on various

aspects of AMR [14 - 21].

Following WHO recommendations, several countries have implemented various tools to promote awareness of the phenomenon of antibiotic resistance among the non-medically educated population [22-25]. Inspired by the success of these campaigns, and based on scientific and statistical aspects confirmed by various researchers worldwide, the Moldovan team of the transnational multi-lateral project "Phage treatment and wetland technology as intervention strategy to prevent dissemination of antibiotic resistance in surface waters (PhageLand)" developed the innovative tool - "ANTIMICROBIAL RESISTANCE AND ALTERNATIVE TREATMENT WITH PHAGE IN LOW AND MIDDLE INCOME COUNTRIES. A KNOWLEDGE POPULARIZATION DESK CALENDAR" in order to use it in various awareness and education campaigns by applying it at events dedicated to the given objective, including its distribution in the community, and also for self-education.

The desk calendar was conceived and developed for a 3-year period (2023-2025), thus it consisted of 37 pages. The cover contains the foreword to the topic of antibiotic resistance. The other 36 pages represent each month of the reference years. Each page contains a 4- to 5-sentence message and a personalized image reflecting it, be it Petri dishes with stylized cultures, or physician-microbiologists in the process of working in the laboratory (fig. 1). The information included in this promotion tool addresses 5 sub-domains of the antimicrobial resistance topic. The topic History of the discovery and research of antimicrobial preparations worldwide includes: notable personalities who contributed to the discovery of antibiotics (Alexander Fleming, Howard Florey, Albert Schatz), circumstances of the discovery and use of antibiotics. The Emergence and evolution of antimicrobial resistance (AMR) addresses the premises of the emergence of AMR, the causes of its emergence and the research done to understand, slow down and/or stop it. In the Antimicrobial resistance - global threat section, statistical data on AMR phenomenon (number of illnesses, risk groups), messages with social impact and information from WHO reports are presented. Antimicrobial resistance is also explored in the context of "one health", emphasizing the role of the environment in maintaining AMR and providing information on measures to combat AMR through targeted interventions on environmental components. Finally, information on modern/contemporary methods of combating AMR is included; phage therapy is emphasized as an innovative method and the history of its emergence as a treatment method (important personalities), its fields of application and possible uses (diseases treated with phages) are described. All described moments fit into social marketing programs for the general public. More than 40 sources were used as references for the scientific data including articles by Davies J et al, Hutchings MI et al, Manyi-Loh C et al and others [26-37]. It is worth mentioning that for the preparation of the Petri dish Art, strains of multi-drug resistant bacteria presenting resistance mechanisms and genes from *Klebsiella pneumoniae, Escherichia coli,* and *Pseudomonas aeruginosa* species were used, which are part of the group of pathogens known by the acronym ESKAPE - pathogens included in the WHO priority pathogens list for which new antimicrobial agents urgently need to be developed. This is yet another innovative element of this tool, besides the fact that such a form of presentation has never before been certified at national level and that it has been developed in 3 languages: Romanian, Russian and English. The whole methodology applied to the development of this tool was described in the article entitled "INNOVATIVE TOOL FOR PROMOTING KNOWLEDGE ON ANTIMICROBIAL RESISTANCE AND QUALITY OF LIFE IN LOW- AND MIDDLE-INCOME COUNTRIES" [38].

These innovative elements allowed the team to obtain the Innovator's Certificate no. 6007, registered at *Nicolae Testemitanu* State University of Medicine and Pharmacy on March 23, 2023 and 3 copyright certificates (one for each language in which the tool was developed) issued by the State Agency for Intellectual Property for the codes OȘ 7538, OȘ

Figure 1. *Pages of "Antibioresistance and alternative treatment with phages in low- and middle-income countries. Knowledge popularization desk calendar".*

Figure 2. *Intellectual property objects obtained on the basis of the tool developed.*

7539 and OȘ7540 respectively in May 2023 (fig. 2) [39, 40, 41].

Like any population education tool to be used as an element of social marketing, the calendar has been tested and validated in workshops and round tables by measuring its impact on the level of knowledge and attitudes of the population on various issues related to antimicrobial resistance. In the piloting phase, post-implementation evaluations demonstrated an improvement in the knowledge and attitudes of the target group of around 47%, which led to the next stage of application of this tool and its promotion at various national and international scientific events, exhibitions, fairs and symposia.

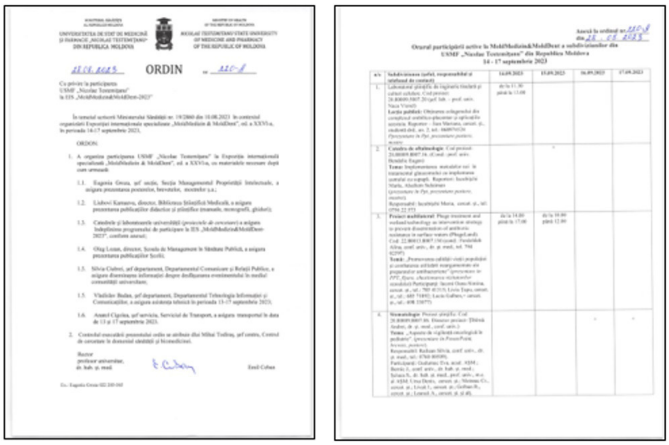

Figure 3. *Rector's Order no. 220-A of 28.08.2023.*

The first presentation of the tool developed by the PhageLand project team in Moldova was during the MoldMedizin & MoldDent 2023 International Specialized Exhibition, organized by the Ministry of Health of the Republic of Moldova, on 14-17 September 2023, participation confirmed by the Rector's Order (fig. 3). During this event, the team members presented the calendar to the visitors of the International Exhibition Center "MoldExpo" in 3 forms - the classic form (fig. 1), as a video that ran on the screens during the entire event and as a flyer. The two alternative forms of presentation were based on the messages included in the Calendar and were designed to facilitate distribution to and assimilation by the target population. The decision on these forms of presentation (fig. 4) was based on the fact that auditory and short messages are more easily perceived by people. The event was successful in achieving its objective: "Promoting the quality of life of the population and combating the unintended use of antibacterial preparations". More than 600 visitors to the team's stand were familiarized with the tool developed (n.n. Calendar), and the level of understanding of the information and the issue addressed was assessed by applying the KAP questionnaire developed within the same project.

A few days later, the tool was evaluated according to rigorous scientific and application criteria by the jury of the Excellent Idea 2023 International Exhibition of Innovation and Technology Transfer, at its second edition, organized by the Academy of Economic Studies of Moldova, in partnership with the Academy of Sciences of Moldova and the Ministry of Education and Research of the Republic of Moldova. The exhibition was held from September 19-21, 2023. During this exhibition, the Calendar was described, together with several other sociological tools for application in the field of Public Health, as "Tools for assessing the quality of life of the population and raising awareness of the phenomenon of antibiotic resistance in the Republic of Moldova", which was the theme of the poster presented for evaluation (fig. 5).

The complexity of the tool and its wide applicability without restrictions of age, gender, social class or ethnicity allowed the collective of authors to obtain the Diploma and the Gold Medal at the Exhibition (fig. 6).

(a)

(b)

Figure 4. *Forms of presentation of the developed tool: a) flyer b) movie (screenshots are shown).*

Figure 5. *Form of presentation and work description at the Excellent Idea 2023 Exhibition.*

Figure 6. *Diploma at the Excellent Idea 2023 Exhibition.*

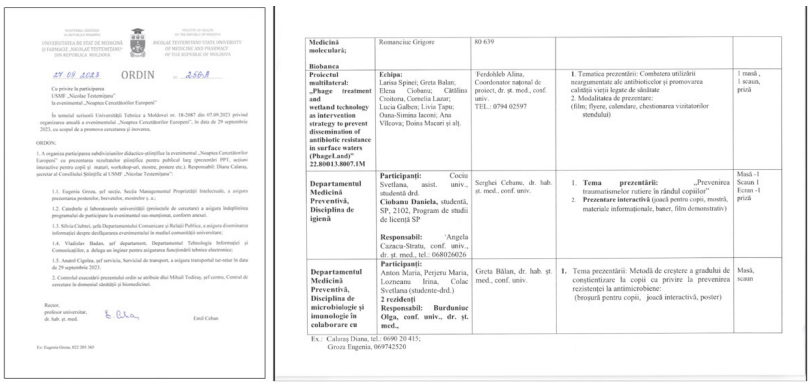

Figure 7. *Rector's Order no. 256-A of 27.09.2023 on the participation of Nicolae Testemitanu State University of Medicine and Pharmacy in the European Researchers' Night, 2023 Edition*

Figure 8. *Public interaction with the Desk Calendar*

Dissemination of the Calendar to the general population continued with a second phase, implemented during the European Researchers' Night organized by the Technical University of Moldova on 29 September 2023. The participation of the PhageLand project team was ensured by Order No. 256-A of 27.09.2023 of "Nicolae Testemitanu" State University of Medicine and Pharmacy (fig. 7).

During this event, all the above-mentioned forms of presentation of the calendar (Figures 1 and 4) were used to capture the attention of the stand visitors. During the event, which lasted 6 hours, more than 400 people familiarized themselves with the tool developed by the authors' collective (fig. 8). As in the previous dissemination phase, their knowledge and attitudes towards the antimicrobial resistance phenomenon were assessed by means of the KAP questionnaire (the results of the survey will be presented in a separate publication).

The uniqueness and strengths of the Calendar, including the fact that there are no limits of applicability to various social groups, it promotes positive lifestyle changes and at the time of application people are not subject to external risks or influence by third parties, the Calendar being a mean of passive training, were described, argued and published for participation in the International Specialized Exhibition "InfoInvent" [42]. The organizer of this exhibition is the State Agency for Intellectual Property, the institution that recognized the novelty of this tool. The event took place on November 22-24, 2023, during which the tool was evaluated by a well-established jury consisting of representatives of the Academy of Sciences of Moldova, the State Agency for Intellectual Property, the National Agency for Research and Development, the Ministry of Culture, the Ministry of Education and Research and the State Chancellery of the Republic of Moldova, as well as members of the jury of the International Exhibition of Inventions in Geneva (Switzerland) and the Forum of Romanian Inventors. It was presented alongside other tools in the work: "Cycle of tools developed for the analysis of the population's knowledge on antibiotic resistance and popularization of the quality of life related to their health", as a poster (fig. 9). Following the evaluation, the author group (the authors of the Calendar) managed to obtain the Diploma and the bronze medal (fig. 10) at the Salon, thus ranking the work in the top 3 inventions among the more than 1000 works that participated in the Salon and beating more than 60 works presented in the Compartment IV: Innovative Products and Services by institutions such as: National Institute for Research-Development in Pathology and Biomedical Sciences "Victor Babes", Institute of Medical Scientific Research "Academician Nicolae Cajal", Technical University of Cluj-Napoca, University "Stefan cel Mare" of Suceava (Romania) and Technical University and State University of Moldova.

A final presentation and dissemination of the Calendar to the general population was made at the International Student Scientific Research and Innovation Exhibition - "Cadet INOVA'24", organized by the Land Forces Academy "Nicolae Balcescu" in Sibiu, Romania, event held from 11-13 April 2024. This time, however, the authors' group followed a different approach than the one applied to the previously described scientific events. During the Cadet INOVA Salon, the authors described the methodology applied to the creation of the tool, emphasizing not only the strengths related to social marketing, but also the innovative elements of the Calendar. In order to participate in the Salon, the authors first prepared a scientific article describing in detail the methodology applied for the development of the Calendar [38], published in the Scientific Bulletin of the Academy of "Nicolae Bălcescu" Land Forces with the title:

Figure 9. *Poster presented at InfoInvent 2023.*

Figure 10. *InfoInvent Exhibition Diploma of Bronze Medal 2023.*

"Innovative tool for promoting knowledge on antimicrobial resistance and quality of life in low- and middle income countries". The International Jury of the Salon, bringing together representatives of the Forum of Romanian Inventors, the State Office for Inventions and Trademarks (Romania), the University of Malaysia Perlis (Malaysia), Inventarium-Science (Portugal), the Academy of Medical Sciences (Romania), the National Institute of Gerontology and Geriatrics "Ana Aslan" (Otopeni, Romania), "Dunărea de Jos" University of Galati, "Alexandru Augustin" Military Emergency Hospital in Sibiu, "Iuliu Hațieganu" University of Medicine and Pharmacy in Cluj-Napoca, and "Stefan cel Mare" University of Suceava awarded a score of 95% out of a possible 100% to the paper presented by the PhageLand project team, thus passing the paper to the second stage of the competition. At this stage, a representative of the team had to present the developed tool in a video of maximum 10 minutes, published on YouTube, which can be watched by clicking on the link: https://www.youtube.com/watch?v=URLdhZYT8g0 . In this video the innovative elements of the Calendar were emphasized, namely: 1. The lack of such a tool at regional level; 2. The preparation and use of images on Petri dishes using multi-resistant bacterial strains from the ESKAPE group of pathogens, some of them presenting also ESBL resistance mechanisms (fig. 11), along with the demonstration of making process of images by Art Agar technique. The team effort was rewarded with 2 diplomas and a medal. The Desk Calendar was awarded the Diploma and Gold Medal of the Cadet INOVA 2024 Salon and the Salon Diploma of Excellence awarded by the World Invention and Intellectual Property Associations (fig. 12).

Buddha said that "Every human being is the author of his own health or disease", and antimicrobial resistance is the disease of modern society fed by the lack of knowledge of each individual. The team of PhageLand multilateral project wanted that through the innovative self-education tool - "Antibioresistance and alternative phage therapy in low- and middle-income countries. Desk calendar of knowledge polularization" to remove this lack of knowledge and raise awareness about this worrying phenomenon. The appreciation of the tool by specialists at national and international exhibitions, fairs and symposia devoted to research and innovation is an unquestionable argument of the calendar's applicability and impact in the process of educating the population. The diplomas and medals awarded to the team's work is an unfailing motivation to continue efforts to understand and combat the phenomenon of antibiotic resistance, especially in low- and middle-income countries, in order to improve the quality of life of each individual.

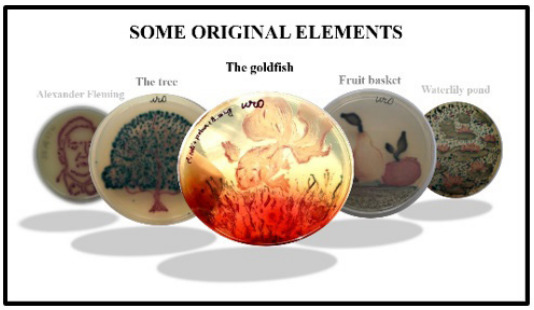

Figure 11. *Screen-shot of original calendar elements (video Cadet INOVA 2024).*

Figure 12. *Cadet INOVA 2024 Salon Awards.*

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