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Review Article

Priorities in the Field of Overcoming the Crisis of Antibiotic Therapy

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Abstract

The importance of the use of antibiotics by our civilization cannot be overestimated. Treatment and prevention of infectious diseases in humans and animals is the area of their application. Thanks to antibiotics, millions of human lives were saved, life expectancy was increased by 20 years and infant mortality was significantly reduced. Here is the chronology of the development of antibiotic therapy: 1928 - Penicillin, 1932 - Sulfonamide, 1943 - Streptomycin, 1948 - Cephalosporin, 1987 - Daptomycin. Destroying pathogens, they provided effective treatment for many infectious diseases. However, their effectiveness steadily declining, leading to an increase in mortality (more than 1 million people die every year from antimicrobial drug resistance and this figure will grow to 10 million by 2050). For this reason, tuberculosis is more difficult to treat (there is a steady growth of tuberculosis, characterized by resistance to the two most powerful anti-tuberculosis drugs.), Pneumonia (the length of stay in the hospital has increased 6 times), gonorrhea (more than 60 percent of Neisseria gonorrhoea isolates show resistance to the antimicrobial drug used ciprofloxacin, more than 20 percent of E. coli isolates are resistant to both ampicillin and co - trimoxazole and fluoroquinolones) and other diseases. In the US alone, about 3 million people become infected with drug-resistant bacteria each year, resulting in over 40,000 deaths per year. The World Health Organization has named antimicrobial resistance as one of the 10 global threats to public health [1].

Keywords: Antibiotic therapy, Benefits of biological antibiotics, Experience in the effective use of bee products, Forms of organization of production and use of natural antibiotics

The Crisis is Antibacterial Therapy

Medicine is trying to continue the fight against pathogens by further searching for and using new antibacterial drugs (natural, semi-synthetic, synthetic). But at the same time, new mutant microbes appear that are able to resist new generations of antibiotics. This is also facilitated by the massive uncontrolled and improper use of antibiotics. The result is the emergence and spread of antibiotic-resistant microbes on a monstrous scale. Increased resistance of pathogens to antibiotics is also facilitated by the excessive use of antibacterial drugs (one of the reasons for this is self-medication with antibiotics).

The massive use of antibiotics leads to the formation of free radicals, which in turn cause a few serious diseases. It is impossible to discount the use of antibiotics in animal husbandry, which can lead to human infection with dangerous infections that are resistant to them. The problems arising from the use of antibiotics should also be attributed to the non-selectivity of their action, which leads to a deterioration in the microflora (dysbacteriosis), adverse reactions (for example, allergies), narrow focus (that is, use only for certain diseases). Unfortunately, the search for new antibiotics lags behind the speed of getting used to him. Therefore, the search for new antibiotics does not stop, although it faces a huge increase in material and other costs. It is generally accepted that the cost of developing a new drug exceeds $1 billion and takes decades to achieve practical implementation, only about 0.1 percent of the total number of drugs undergoing preclinical studies.

Modern Mass Production of Antibiotics

The ever-increasing need for drugs caused further chemical and technical development of the pharmaceutical industry. The history of the development of pharmacology is the history of the development of chemistry and technology, the use of medicinal substances from simple to more complex (plants, minerals, synthetic substances, antibiotics, vitamins, enzymes, etc.). This is the history of the development of production from the first pharmacies to the mass production of medicinal chemicals, including suspensions, ointments, emulsions, syrups, etc. The main advantages of mass production: the production of large volumes of standardized products, observance of the given quality perimeters, reduction of the production cycle, the possibility of automating production, obtaining high profits. Mass production of drugs is based on the use of high-performance automated production pharmaceutical lines.

Often, thermal technological processes are used (this is heating, cooling, condensation, evaporation, etc.), the speed of which is determined by the rate of heat supply (or removal). The pharmaceutical industry followed the path least resistance, preferring to work with substances that are lossless of their properties lend themselves to chemical, thermal, electrophysical, mechanical, hydromechanical treatments. Despite the huge efforts and material costs for the search and production of new generations of antibiotics, it is not possible to achieve the main thing - the absence of resistance to them in certain pathogens. This has led to a lack of fundamentally new antibiotics in the present and near future. All in anticipation of the release of "miracle" drug developments, whose potential to radically change known treatments will reduce the side effects of antibiotic use.

Benefits of using Biological Antibiotics

A practical way out in the crisis of antibiotic therapy was the recognition by scientists of the importance of alternative methods of combating bacterial infections. These two methods are scaling up vaccinations and the use of natural antibiotics. The first will reduce the use of antibiotics, the second will increase the effectiveness of antibiotic therapy without providing an additional drug burden on the body. To date, about 30,000 antibiotics of natural origin are known. Here are some natural substances and products containing substances that define them antibacterial, antiviral and anti-inflammatory properties: garlic, honey, ginger, echinacea, Canadian goldenseal (hydrastis), cloves, oregano. A special place is occupied among natural antibiotics: Propolis is a brown sticky substance with which bees cover the gaps in the hives. Its most important properties: stimulation of immunobiological processes in the body, suppression of reproduction and destruction of many microorganisms, including tubercle bacillus, viruses and fungi [2].

In addition, it increases the level of gamma globulins in the body, has antitoxic properties, heals wounds, while maintaining the microflora of the body. That is, it has a positive complex effect on the body. The next super effective biological stimulant and natural antibiotic is royal jelly, a special food that bees use to feed the queen larvae and which the queen bee feeds throughout her life. Royal jelly has an immunomodulatory effect, increases the body's resistance to viral and bacterial infections, clinically proven antitumor activity. And - wax moth larvae are the only living creatures on Earth that feed on wax (which is important, from which bees build honeycombs, that is, containing vitamins and trace elements). Extracts and tincture of wax moth larvae are broad-spectrum antibacterial and antiviral drugs, an immunomodulator, their use promotes tissue healing without scarring, has an antioxidant and antitoxic effect [3,4].

Common to these natural antibiotics is high therapeutic efficacy, providing a therapeutic effect where other agents have been unsuccessfully used, and recovery occurs earlier than with the use of conventional agents in the absence of toxicity and side effects, the absence of pharmacological and medical risks, compatibility when used with pharmacological drugs. And, most importantly, the use of these natural antibiotics does not cause the development of resistance to their effects in microbes [5,6].

This is because the composition of these bee products has a unique feature - it is constantly changing, as it depends on the changing factors of their formation: on the variety of plants used by bees; changes in the morphological characteristics of the worker bee, fluctuations in climatic conditions. The use of preparations created on the basis of propolis, milk and wax moth is much more effective than their single use. The undoubted advantages of complex preparations include their economic availability [7,8].

Experience of Practical Application of Biological Antibiotics

Medicine has accumulated considerable experience in the use of bee products as natural antibiotics. First of all, this is their use in various dosage forms for acute bacterial infections, for the treatment of viral infections, and for fungal diseases [9]. Consider an example of the complex use of these products in the prevention of viral diseases (including coronavirus). This prevention scheme was developed by us in 2020 in Ukraine and tested in 2021-2022. The main results of the study were reported at the International Scientific and Practical Conference "Apiotherapy: scientific achievements and prospects for the development of the industry in Ukraine" [10]. The use of the above products provided effective protection against viral infections [11]. The use of the proposed prophylaxis allows you to activate the immune system in a short time and protect against viral attacks. The products used are absolutely safe, non-addictive and fully compatible with pharmacological preparations. The proposed scheme for the prevention of viral diseases is an effective and feasible strategy to combat the pandemic [12]. Trial of a viral disease prevention regimen, including COVID-19 conducted by volunteers during 2020-2022. For preventive purposes (based on 1 person), the following products are introduced into the diet in Recommended doses: Royal jelly (daily dose - 0.25-0.50 g); 2) Zabrus - (daily dose -30-40g); 3) Tincture of bee moth - (daily dose 8-4 drops / 10 kg of body weight); 4) Propolis oil - (daily dose 1-1.5 g) [13].

Mode of Application

1) Royal jelly (0.25-0.50 g) on an empty stomach, 30 minutes before the morning intake food, sublingually (by resorption under the tongue).

2) Zabrus (30-40 g) - after a morning meal, chew thoroughly for 15-20 minutes.

3) Wax moth tinctures - once a day - 4-2 drops / 10 kg of human body weight 30 minutes before the evening meal, previously diluted in 1-2 tablespoons of water [14].

4) Propolis oil (1-1.5 g) - it is necessary to lubricate the nasal mucosa before going outside (or going to work).

The mechanism of action of -substances ensures the prevention of viral diseases, including COVID-19, by strengthening immunity, improving metabolism, optimizing anticoagulant parameters, protecting the nasopharynx from the penetration of viruses, and increases the working capacity of the human body. The presence in the proposed substances of a significant amount of the enzyme catalase protects the cells lining the inner surface of the alveoli in the lungs, has an anti-inflammatory effect and regulates the production of cytokines that are involved in the body's immune response. In most cases, there is a concomitant [15].

The result is an increase in tone and performance. The course of prevention lasts 1.5 months and is carried out twice a year. It is better to start it from October to December, and from March to May. It should be noted that the incorrect application of the prevention scheme without taking into account the individual characteristics of the body can be harmful, which will cause disappointment and give rise to distrust in its effectiveness. Not a single case of morbidity, including COVID-19, was observed.

The limitation is a negative reaction to bee products, which is typical for about 7% of all population. The next example of the effective complex use of natural antibiotics is the SR-21 suspension mixture developed and tested by us. Its composition: native (live) royal jelly (100% Native Royal Jelly), powder from crushed ginseng roots (Panax), coenzyme Q10, auxiliary substance - honey from a white acacia. For patients undergoing antibiotic therapy, the use of this suspension mixture enhances the therapeutic effect of antibiotics, reduces toxicity and reduces the side effects of chemotherapeutic drugs, the antitumor properties of this mixture are due to an increase in immune status and resistance of the body, as an adjuvant in the treatment of neoplasms of the gastrointestinal tract and an additional agent in the treatment of precancerous diseases, prevents anemia, leukopenia, normalizes erythro-, neutrophil- and lymphopoiesis [16].

For postoperative patients, it increases physical activity during the rehabilitation period, stimulates the restoration (regeneration) of tissues, stabilizes blood pressure and heart function, normalizes metabolism and restores the functioning of the reproductive and endocrine systems. Contraindication to use is intolerance to bee products, as well as disease adrenal glands. In 2018, we developed an ointment formulation based on royal jelly and propolis [17]. The high clinical efficacy of its use for the period from 2018 to 2022 was confirmed in the treatment of a number of diseases (treatment of trophic ulcers, erysipelas, wounds, psoriasis), when the use of conventional means was unsuccessful. The high efficiency of the treatment of chronic bacterial prostatitis was also confirmed in the case of unsuccessful use of conventional medicines with our developed rectal propolis suppositories with native royal jelly-100% Native Royal Jelly (not lyophilized, when the frozen product goes through the drying stage in a special chamber; not adsorbed, that is, preserved with a special food adsorbent, but live). Ingredients: propolis (Propolis), native milk (100% Native Royal Jelly), natural cocoa butter (Fresh, Cacao Gold), total weight - 3.3 g [3].

Royal jelly, as the most powerful bio stimulant, significantly increases the effect of propolis. The effectiveness of propolis suppositories with native milk increases significantly. In addition, with this method, royal jelly is absorbed 100%. In addition to local action, the components that make up the composition, being absorbed into the blood, beneficial effect, first of all, on the pelvic organs, helping to restore male and female health. In addition to the above indications for use, these suppositories are recommended after surgery and serious illnesses (strokes, heart attacks and chemotherapy), with impotence and infertility [18,19].

Their intake is also recommended in order to stabilize blood pressure and heart function, normalize metabolism and resume the functioning of the reproductive and endocrine systems. A contraindication to the use of these suppositories is intolerance to bee products, as well as adrenal disease. At present we are working on the use of wax moth suspension medicine in the treatment of coronavirus diseases (as the main drug). Positive stable results were obtained (15 patients were observed). Full recovery occurs on days 7-10, no complications were observed.

Results

The use of drugs based on natural antibiotics, in modern conditions, has shown its high efficiency in overcoming the crisis of antibiotic therapy. But there are factors limiting their mass application. Objective - not manufacturability of biological substances containing natural antibiotics (for example, at room temperature in 2 hours, royal jelly completely loses its unique properties, high stickiness of propolis, etc.), the impossibility of synthesizing them at the current level of development of science and technology. And, as a consequence of this, the unreality of the organization of mass production with all its benefits.

The solution to this problem can be the organization of the manufacture of such drugs in the conditions of pharmacy organizations. The advantages of extemporaneous production (ex tempore - as needed) of these drugs with a limited shelf life, which do not have industrial analogues, include the possibility of individual selection of the composition and dosage, taking into account the age, concomitant chronic diseases of the patient, taking into account the tolerance of certain substances, to optimize the cost of purchasing medicines, to minimize side effects.

Technological progress in the production of modern laboratory equipment, mobile individual ice packs, new types of containers and packaging contributes to the increase in the efficiency of such production. Without competing with mass production, the pharmacy will successfully occupy the niche to produce natural antibiotics, and their use will solve the problem drug resistance to antimicrobials. The subjective factor is the lack of potential

consumers of any knowledge about natural antibiotics, their properties and the effectiveness of their treatment of many diseases, the possibility of parallel use with traditional drugs, the absence of side effects [20].

When choosing medicines, 30% of patients listen to the advice of pharmacists, a quarter make their choice based on personal experience or recommendations from friends, and the rest - with the help of family doctors. Based on this, in modern conditions, medical and educational work can be carried out with the help of the Internet, family doctors and pharmacy workers. It is necessary to create a special resource providing access to a comprehensive knowledge base on natural antibiotics and the experience of their effective use [21].

It is necessary to share practical experience and answer questions from readers. The purpose of the resource is to raise the level of awareness of family medicine doctors, pharmacists and patients in the practical use of natural antibiotics. Mutual communication in the form of questions and answers is important. This is an opportunity for a multilateral discussion of the problem that has arisen, in which each participant can take part [22].

This is the opportunity to choose the main speaker not on a territorial basis, but from the standpoint of his competence and knowledge of the problem under discussion. The idea of using Internet technologies to obtain knowledge, which is created by the joint efforts of numerous online communities that have replaced professional knowledge created by individuals, is timely and technically feasible. The task of the World Health Organization is to create and finance outside the national Internet society of doctors, pharmacists, patients for the use of natural antibiotics in a crisis of antibiotic therapy [23].

Discussion on the Limitations

The limitation is a negative reaction to bee products, which is typical for about 7% of the total population, as well as adrenal disease.

Ethical Consideration

A verbal commitment was received from volunteers for the use of beekeeping products.

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Conflict of Interest

The authors declare no conflict of interest. Author Sergey Roslyak is an independent researcher, not an employee of government agencies and private companies offering contract development services for the pharmaceutical industry.

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