Antimicrobial properties of model drugs in the systemic concept of health

Mykola Oseyko[1], Vasyl Shevchyk[2], Olena Pokryshko[3]

1 – National University of Food Technology, Kyiv, Ukraine
2 – "Vasyl Shevchyk's eye microsurgery", Chernigiv, Ukraine
3 – Ternopil State Medical University named after I.Ya. Grobachevsky, Ternopil, Ukraine

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Corresponding author:

Mykola Oseyko
E-mail:
nikios@ukr.net

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Abstract

Introduction. We analyzed the antimicrobial efficacy of the investigated preparations of the KTIOL-BF series on standard culture of microorganisms: S. aureus, Escherichia coli, P. aeruginosa and S. saprophyticus.

Materials and methods. The model preparations of the KTIOL-BF series (biofunctional) are studied. The preparations are based on vegetable and animal extracts containing iodine solution or do not contain it. As controls, preparations of povidone iodine and chlorophyll are used. The antimicrobial properties of the samples of the preparations were determined by the modified diffusion method ("wall" method) for increasing the upper range of evaluation.

Results and discussion. The scientific basis of this study is the systematic concept of health, developed on the basis of the KTIOL-I ecological-technological system and the physiologically functional system KTIOL-II. The preparation on the basis of herbal extract provided the initial good antimicrobial effect on all microorganisms studied. Introduction to the preparation based on extracts of plants and on the basis of plant and animal extracts with solution of nanosized particles of colloidal silver up to 35 wt. % slightly reduced the antimicrobial effect of the samples relative to S. aureus and S. saprophyticus. The sample on the basis of plant and animal extracts showed a good antimicrobial effect on microorganisms S. Saprophyticus, E. coli, P. aeruginosa. Two samples showed a good antimicrobial effect on all studied microorganisms.

Model samples of the preparation on the basis of two-phase plant modified enzymes produced a very good integral antimicrobial effect on all microorganisms studied. Of these, two samples based on extracts of plants and on the basis of plant and animal extracts showed high antimicrobial effects on the E. coli strain (30 mm growth retardation diameter).

The possibility of high antimicrobial action on E. coli strain (30 mm diameter growth delay) has been confirmed. This is due to the complex action of these two samples on the study of gram-positive and gram-negative strains of microorganisms.

Conclusions. The possibility of high antimicrobial activity of samples on the basis of two-phase plant extract and on the basis of plant extract and iodine solution on strain Escherichia coli was revealed and confirmed. The same specimens showed high and good antimicrobial properties, both in other strains, and in an integral manner.

Introduction

Modern livelihoods of Man contributes to the accelerated proliferation of pathogenic and the emergence of resistant microflora, which interacts with human saprophytic microbes and can affect our physical health. Saprophytic microbes are trillions of microbes living on the surface and inside our body.

It is also important for scientists to find evidence that intestinal bacteria use tiny strips of a genetic code called "miRNA" to change the way DNA acts in nerve cells [1].

In prophylaxis and treatment of infectious diseases are crucial the using of functional drugs for general and local therapy and/or the individual application of the systemic concept of health [2].

Kovan M.M. in the review [3] analyzed the possibility of using plant products as antimicrobial agents. The use of and search for drugs and dietary supplements derived from plants have accelerated in recent years. Ethnopharmacologists, botanists, microbiologists, and natural-products chemists are combing the Earth for phytochemicals and "leads" which could be developed for treatment of infectious diseases. While 25 to 50% of current pharmaceuticals are derived from plants, none are used as antimicrobials. Traditional healers have long used plants to prevent or cure infectious conditions; Plants are rich in a wide variety of secondary metabolites, such as tannins, terpenoids, alkaloids, and flavonoids, which have been found in vitro to have antimicrobial properties. This review attempts to summarize the current status of botanical screening efforts, as well as in vivo studies of their effectiveness and toxicity. The structure and antimicrobial properties of phytochemicals are also addressed. Since many of these compounds are currently available as unregulated botanical preparations and their use by the public is increasing rapidly, clinicians need to consider the consequences of patients self-medicating with these preparations.

In the author's opinion, it would be beneficial to standardize in vitro extraction and testing methods in order to more systematically find and facilitate the interpretation of results.

Gerontologists also recommend starting prevention as early as possible [4–6].

Now we can observe rasing of the microflora and hospital strains resistance to antibiotics and antiseptics, and as results - increasing in the frequency of secondary and postoperative infections [7].

The aim of the study. To reveal the antimicrobial properties of the different investigated specimens KTIOL-BF series, obtained from the systemic concept of health (KTIOL®) [3].

Systemic concept of health (The systems KTIOL®). The system KTIOL-I (Comprehensive Technologies, Engineering, Equipment, Lines) was initially aimed at the synthesis of lipid-containing products of special purpose. The main principles of the system KTIOL-I: providing the structure of the product (preparation) at the micro and nano level; ecological and economic efficiency; a systematic approach to the methodology of producing safe food, pharmaceutical and cosmetic products and drugs'

The system of KIIOL-II (Integrated Therapy of Individual Health Improvement) was initiated from the analysis of indicators of quality and safety of water, food products, dietary supplements and preparations, environmental and endoecological aspects of personal health. The KIIOL-II system includes: hygiene of thoughts (positive thinking and positive mood); sleep hygiene (recovery, rehabilitation, treatment, rehabilitation); prevention (ophthalmologic, dental, endoecological, herrolontal); water is high quality and safe; nutrition organic and health-care; breathing health-curative; Individual systemic

exercise (walking, massage, swimming, tennis, Scandinavian walking, etc.); meditators and self-adjusting; individual know-how [2, 5, 8].

Means based on vegetable, ethereal oil and other sources. In recent data, we found information about the influence of the molecular structure of derivatives of 4-thiazolidine (about 70 compounds) on their antimicrobial activity was investigated by the QSAR method. Microorganisms were used as reference cultures: Candida albicans, S. Citrobacter freundii, Klebsiella pneumoniae, Pseudomonas aeruginosa and Staphylococcus aureus MSSA [9].

The influence of the evolution of the heterocyclic system on the antimicrobial properties of derivatives of 4-thiazolidines was demonstrated. An important role of electrostatic characteristics of their molecular structure was also shown. The compounds with the highest predictive value of antimicrobial activity against several cultures were selected as a result of virtual screening.

An international team of researchers and the Singapore Institute of Bioengineering and Nanotechnology created a biodegradable polymer. The activity of the polymer was tested on cultures of five ESKAPE pathogens, including Pseudomonas aeruginosa and methicillin-resistant Staphylococcus aureus (MRSA). It turned out that the substance destroys bacteria with 99-100 percent efficiency. Scientists also tested the activity and toxicity of the polymer in mice. The dose of polycarbonate needed for the survival of infected animals was lower or comparable to that of antibiotics for three of the four pathogens.

It is known that aqueous solutions of furatsillin, hydrogen peroxide, povidone-iodine (PVI), chlorhexidine, myramistin, alcoholic solutions of boric acid, liniment of syntomycin, ointment of salicylic acid, levorin, myraimystin, chlorhexidine are often used at the local application of medicinal antiseptic drugs. The disadvantage of these drugs is the narrow spectrum of antimicrobial activity, short-term antimicrobial activity, etc.

The paper [7] presents the results of the study of the antimicrobial properties of the antimicrobial agent palisept plus. The high sensitivity of strains of microorganisms (S. aureus, E. coli, K. pneumoniae, P. aeruginosa) to this drug is shown. According to the author's team, the palisept plus on the oral medication ecamotoxin provides an effective antimicrobial action for a long time.

Additional approvement of good antimicrobical activity of 4-thiazolidine was confirmed in another study [11].

Pharmacological screening of antimicrobial activity of synthesized isomanes is carried out.

Identified compounds with the expressive antimicrobial effect that can increase the sensitivity of clinical strains S. aureus and S. Haemolyticus to oxacillin, which can be used to create new combined antimicrobial chemotherapeutic agents.

Chinese, American and Singapore researchers [12] have synthesized a substance with antimicrobial properties that effectively destroys ESKAPE-bacteria, which was resistant to most antibiotics. The acronym ESKAPE combines the names of pathogens that are highly resistant to most antibiotics and cause most hospital infections worldwide.

Chemists and biologists synthesize antimicrobial peptides and polymers. Despite the efficacy and broad spectrum of action, antimicrobial peptides are toxic, and their production is rather expensive. Most of the described antimicrobial polymers are not decomposed and therefore can accumulate in the body and eventually become toxic. In addition, until now, their activity in living organisms has not been practically studied.

Despite the fact that scientists are constantly synthesizing new generations of drugs, bacterial resistance is still a significant problem.

The antimicrobial activity of the developed dermatological ointment with a two-phase extraction of black poplar kidneys using the method of diffusion into agar (the method of "wells") was studied [14]. As test cultures, eleven different strains of microorganisms were used. The results of microbiological studies have shown that the biphasic extracts of black poplars and ointment on its basis have a expected antimicrobial action against pathogenic microorganisms.

The study was conducted to evaluate the in vitro antibacterial activities of 18 essential oils chemotypes from aromatic medicinal plants against streptococcus S. Pyogenes [15].

The chemical composition of oil was analysed by GC and GC-MS. the reducing power, antioxidant and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging activities of the essential oil were studied. The reducing power was compared with ascorbic acid, and the other activities were compared with 2,6-di-tert-butyl-4-methyl phenol (BHT, butylated hydroxytoluene). The results showed that the activities were concentration dependent. The antioxidant activities of the oil were slightly lower than those of ascorbic acid or BHT, so the oil can be considered an effective natural antioxidant. Antimicrobial activities of the essential oil from the leaves of Origanum syriacum was also determined on 16 microorganisms tested using the agar-disc diffusion method, and showed antimicrobial activity against 13 of these.

Antibacterial activity of essential oils was investigated using disc diffusion method. Minimum Inhibitory Concentration of essential oils was measured using broth dilution method. Out of 18 essential oils tested, 14 showed antibacterial activity against S. pyogenes. Among them Cinnamomum verum, Cymbopogon citratus, Thymus vulgaris CT thymol, Origanum compactum, and Satureja montana essential oils exhibited significant antibacterial activity. The in vitro results suggest that, for patients (if aromatherapy is used) these essential oils, considered as potential antimicrobial agents, should be preferred.

The authors plan additional studies of essential oils in clinical strains regarding the potential clinical use in therapeutic therapy (to determine whether they can effectively replace antibiotics or may be used in combination) [18].

Adiantum Linn. of Adiantaceae family is one of the most common and widely distributed species. Ethnomedicinally, the genus is important and popularly known as “Hansraj” in Ayurvedic System of Medicine.

In the present study its four important species, i.e. Adiantum capillus–veneris, Adiantum peruvianum, Adiantum venustum and Adiantum caudatum were collected and extracted with methanol. These extracts were tested for their antimicrobial agents against five gram positive, six gram negative (including multiresistant bacteria Staphylococcus aureus) and eight fungal strains using standard microdilution assay. The maximum activity was exhibited by the methanolic extract of Adiantum venustum followed by Adiantum capillus–veneris, Adiantum peruvianum and Adiantum caudatum. The methanolic extract of Adiantum capillus–veneris had very low MIC value (0.48 μg/ml) against Escherichia coli whereas, Adiantum venustum extract against Aspergillus terreus with MIC of 0.97 μg/ml. Total phenolic constituents of Adiantum species viz. Adiantum venustum, Adiantum capillus–veneris, Adiantum peruvianum and Adiantum caudatum were 0.81% (w/w), 0.83% (w/w), 0.71% (w/w) and 0.52% (w/w), respectively (as gallic acid equivalent); implying that the observed activity could be related to the amount of phenolics [19].

In [16], the authors studied antimicrobial activity of lipophilic complexes obtained from Galium species. The study was conducted in vitro by agar diffusion. Staphylococcus aureus was found to be the most susceptible to the studied lipophilic complexes. Escherichia coli and Proteus vulgaris showed low sensitivity. Pseudomonas aeruginosa and Bacillus subtilis showed moderate sensitivity. The obtained results provided the basis for

further in-depth studies of the antimicrobial and antifungal activity of the lipophilic complex of the genus Galium L.

The exponential growth of bacterial resistance to antibiotics raises a problem for clinicians regarding endophthalmitis in postcataract surgery through multidrug-resistant (MDR) organisms. Treatment options are limited and the results are bad. Therefore, prompt surgical prophylaxis provides the best treatment solution. There are currently no recommendations for surgical prophylaxis in patients with bacterial colonization of multi-resistant (MDR) organisms.

The current ESCRS (European Society Cataract and Refractive Surgery) recommendation for a 3-minute exposure to 5%PVI is effective for gram-negative bacteria and most gram-positive cocci. However, 5%PVI is ineffective for enterococci and requires exposure to chlorhexidine for 5 minutes.

Materials and methods

Materials

Strains of Gram-positive and Gram-negative microorganisms, were used: S. aureus (ATCC 6538), S. saprophyticus (ATCC 15305), E. coli (ATCC 25922), P. aeruginosa (ATCC 9027). The density of the microbial suspension was determined according to the standard of turbidity 0,5 by McFarland (equal to 1.5x108 colony-forming units (CFU)/ml).

The study used samples of the KTIOL-BF series. These functional and antioxidant drugs have been obtained on the basis of the systemic concept of health. As model samples, the preparations of the KTIOL-BF (biologically functional) series were used. The preparations KTIOL-BF5, KTIOL-BF6 and KTIOL-BF7 are based on plant extract and iodine solution. The preparations KTIOL-BF25, KTIOL-BF26 and KTIOL-BF27 on the basis of plant and on the basis of plant and animal extracts and solution of nanosized particles of colloidal silver. KTIOL-BF49 based on plant and animal extract and KTIOL-BF69 on the basis of plant extract and iodine solution.

The preparations KTIOL-BF31 and KTIOL-BF32 are based on a two-phase plant extract. The preparations KTIOL-BF36, KTIOL-BF37, KTIOL-BF38 and KTIOL-BF39 on the basis of plant extract and iodine solution. Povidone-iodine, PVI (pharmaceutical preparation BETADINE is based on a solution of povidone-iodine, surface-active and auxiliary substances) and Chlorophyllipt (CHL) based on two phases of plant extract were used as controls.

Order of conducting researches

Analysis of the methodology. Preparation of exploratory strains of Gram-positive and Gram-negative microorganisms, model preparations of the KTIOL-BF series and control drugs. Execution of planned research, processing and discussion of the results, conclusions.

Description of the methodology

As the references, strains of Gram-positive and Gram-negative microorganisms, were used: S. aureus (ATCC 6538), S. saprophyticus (ATCC 15305), E. coli (ATCC 25922), P. aeruginosa (ATCC 9027). The density of the microbial suspension was determined according to the standard of turbidity 0,5 by McFarland (equal to 1.5x108 colony-forming units (CFU)/ml) [14].

An antimicrobial activity of drug samples were determined by the agar-well diffusion method. In one Petri dish the activities of four or five different samples were studied. The investigated samples were dissolved in formamide in a ratio of 1:10. 10 ml of a sterile melted meat peptone agar (MPA) was poured into a Petri dish. After cooling of this medium layer, sterile glass cylinders were placed in it (height 10 mm, internal diameter 6 mm) and then 15 ml of melted MPA mixted with overnight suspension of the test-microbe were added. When the second layer of medium became solidified, the cylinders were removed and into the wells that were formed, the 0,5 µl of the drug samples were delivered under the aseptic condition. After incubation period for 24 hours at 37 °C the results were determined. The the inhibition zones (no growth) of the test-microorganisms around wells were measured in millimeteres.

Working out of research results

According to the diameter of the microbial growth inhibition zone the degree of a susceptibility of microorganisms to the antibacterial solutions were adopted: as high susceptibile to drug sample – if the diameter of the growth inhibition zone of microorganisms exceeded 20 mm; susceptibile if the diameter was from 14 to 20 mm; and low susceptibile - from 8 to 14 mm. All tests were perfomed triplicate and average values were recorded.

After the second layer of the agar was sealed, the cylinders were also removed in the formed wells; the samples of the investigational drugs were 0.3±0.03 ml. In one cup, Petri studied the activity of four or five different samples.

The seeds were incubated at 37 °C. for 48 hours. The results were determined in the presence of zones of growth retardation test-microorganisms, which were clearly visible around the walls.

By the degree of sensitivity of microorganisms to antibacterial solutions, we measured the diameter of the zone of suppression of microorganisms.

As a scientific and practical basis in the planning and implementation of this study, the systemic concept of health [3] was used. This concept includes two systems of KTIOL.

Results and discussion

Taking into account the principles of the systemic concept of health and the physiologically functional system of KTIOL-II, samples of type KTIOL-BF [2, 8] included hydrophilic lipophilic extracts from plant and/or animal raw materials, antioxidants, biologically active and auxiliary components. The results of the study are presented in Tables 1 and 2.

The analysis of the data in Table 1 in comparison with the control sample PVI the following. From samples KTIOL-BF5, KTIOL-BF6 and KTIOL-BF7 on the basis of initial extracts only sample KTIOL-BF7 provided an initial good effect on all microorganisms being studied.

When the nanoparticles of colloidal silver were introduced into the original extracts (KTIOL-BF5, KTIOL-BF6, KTIOL-BF7), specimens KTIOL-BF25, KTIOL-BF26 and KTIOL-BF27 were respectively obtained. Colloidal silver slightly reduced the antimicrobial effect of these samples on S. aureus and samples KTIOL-BF26 and KTIOL-BF27 relative to S. saprophyticus. Note that only a sample of 25 nanoscale colloidal silver showed a good antimicrobial effect on the microorganisms S. Saprophyticus, E. coli, P. aeruginosa examined.

Table 1

Antimicrobial properties of samples of model drugs KTIOL-BF on the basis of extracts (in mm, retarded growth zone)

Drug samples	Growth inhibition, mm (Mean ±SD)			
	S. aureus	***S. saprophyticus***	***E. coli***	***P. aeruginosa***
Control PVI	10±0.2	12±0.5	10±0.4	12±0.2
KTIOL-BF5	0	0	0	0
KTIOL-BF6	14±0.5	12±0.8	0	0
KTIOL-BF7	14±0.3	14±0.6	18±0.5	14 ±0.4
KTIOL-BF25	12±0 .7	16±0.4	18±0.6	16±0.5
KTIOL-BF26	12±0.5	12±0.4	18±0.5	20±0.5
KTIOL-BF27	12±0.4	12±0.3	14±0.8	20±0.6
KTIOL-BF49	16±0.4	16±0.5	22±0.6	24±0.8
KTIOL-BF69	18±0.6	16±0.3	14±0.3	18±0.6

Table 2

Antimicrobial properties of samples of model drugs KTIOL-BF on the basis of extracts with biologically active components (in mm, retarded growth zone)

Drug samples	Growth inhibition, mm (Mean ±SD)			
	S. aureus	***S. saprophyticus***	***E. coli***	***P. aeruginosa***
KTIOL-BF31	20±0.4	18±0.5	18±0.5	18±0.3
KTIOL-BF32	24±0.6	18±0.6	30±0.5	16±0.4
KTIOL-BF36	20±0.6	18±0.5	18±0.7	18±0.4
KTIOL-BF37	16±0.5	16±0.7	22±0.4	12±0.5
KTIOL-BF38	24±0.2	22±0.6	30±0.8	20±0.7
KTIOL-BF39	14±0.4	14±0.5	20±0.6	16±0.6
control 52	10±0.3	12±0.4	10±0.4	10±0.4

Also modified and samples 49 (based on the iodine content extract 7) and 69 (based on the iodine content extract 6 and plant extract) were also studied. Sample KTIOL-BF49 showed a good antimicrobial effect on all microorganisms studied. Sample KTIOL-BF69 (Improved Sample KTIOL-BF6) neutralized the defects of sample KTIOL-BF6 and provided antimicrobial effect on all microorganisms under study.

The analysis of the data in Table 2 in comparison with the control sample 52 (pharmaceutical preparation Chlorophyllipt on the basis of a two-phase plant extract) revealed the following. Samples KTIOL-BF31 and KTIOL-BF32 on the basis of two-phase plant extracts provided a very good integral antimicrobial effect on all investigated microorganisms: S. aureus, S. saprophyticus, E. coli, P. aeruginosa. For the first time, a high antimicrobial effect of samples KTIOL-BF32 and KTIOL-BF38 on strain E. coli was detected.

Modified model samples KTIOL-BF36, KTIOL-BF38 and KTIOL-BF39 (were also studied. Samples KTIOL-BF37 and KTIOL-BF39 showed a good antimicrobial effect on all microorganisms being studied.

The high integral sensitivity to the sample of the preparation KTIOL-BF38 was revealed by all strains of microorganisms examined (the diameter of their growth delay

exceeded 20 mm). Also the possibility of a high antimicrobial action on the E. coli strain (growth delay diameter of 30 mm) was confirmed. Also, the possibility of a high antimicrobial action on E. coli strain (diameter growth delay of 30 mm) was confirmed. This is due to the complex action of the drug KTYOL-BF38 on the study of gram-positive and gram-negative strains of microorganisms.

Conclusions

On the basis of analytical and experimental research new data on the antimicrobial properties of samples of model preparations of KTIOL-BF on the basis of two-phase extracts from animal and plant raw materials were obtained.

For the first time the possibility of high antimicrobial action of samples of the preparation of KTIOL-BF32 and38 on the E. coli strain (30 mm growth retardation diameter) was confirmed.

It was found that samples of the KTIOL-BF model preparations compared with the control agents (BETADINE /PVI, Chlorophyllipt) showed higher and good antimicrobial pro perties for S. Aureus, S. Saprophyticus, E. coli, P. Aeruginosa and integral strains.

The obtained data confirmed the expediency of further in- depth studies of antimicrobial and antifungal activity of hydrophilic and/or lipophilic drugs of a number of KTIOL in the systemic concept of health, in particular in the treatment of ophthalmic and gerontological prophylaxis, treatment and rehabilitation.

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