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SILVER NANOPARTICLES AS PENICILLIN ACTION ENHANCERS

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Nowadays, the value of bactericidal nanomaterials research increases at the increasing number of bacteria strains resistant to the most highly potent antibiotics. In the review the characteristic of nanoparticles and methods for their production are done. The scope of nanoparticles application is observed, special attention is focused on silver nanoparticles usage in medicine, in particular, as bactericidal products. It is indicated that nanoparticles may have toxic effects.

Much attention is paid to nanoparticles application in the treatment of various diseases, for example, for targeted drug delivery, wound healing, bone regeneration, local heating of tumors in cancer pathology, immune system stimulation, for antibodies, viruses, bacteria detection, for liquids filtration.

Penicillins and their producers — *Penicillium* sp. characteristic is done. The mechanism of penicillin antimicrobial action is estimated.

It is revealed that silver nanoparticles usage in combination with antibiotics, particularly penicillin, leads to antibiotics antibacterial activity increasing against gram-positive and gram-negative microorganisms.

Key words: nanotechnology, silver nanoparticles, antibiotics, penicillin, *Penicillium* sp.

The field of nanotechnology is an intensively developing field as a result of its wide-ranging applications in different areas of science and technology. The term nanotechnology is defined as the creation, exploitation and synthesis of materials at a scale of 1–100 nm (1 nm = 10^{-9} m). The word «nano» is derived from a Greek word meaning «dwarf» or «extremely small». Nanobiotechnology is a multidisciplinary field and involves research and development of technology in different fields of science like biotechnology, nanotechnology, physics, chemistry, and material science [1, 2].

Nanoparticles (NPs) exhibit different shapes like spherical, triangular, rod, etc. (Fig. 1). Research on nanoparticles' synthesis is the current area of interest due to the unique visible properties (chemical, physical, optical, etc.) of nanoparticles compared with the bulk material [3, 4].

Nanoparticles have broad application prospects in biology and medicine [6–10]. Since many microorganisms seem to be less sensitive to most of the antibiotics, researchers started finding a new potential antimicrobial agent. With this respect, silver and silver-based compounds are having strong bacteriocidal and fungicidal activity [11].

Nanoparticles having larger surface area to volume ratio tend to pose higher antimicrobial activity [12]. Also, silver has a lower propensity to stimulate microbial resistance than many other antimicrobial agents [11]. Based on these properties, silver nanoparticles (Ag-NPs) have been used in wide range of applications such as to prevent infection, in (burn and traumatic) wound dressings, diabetic ulcers, coating of catheters, dental works, scaffold, and medical devices [13, 14].

Nanotechnology is an integration of different fields of science which holds promise in

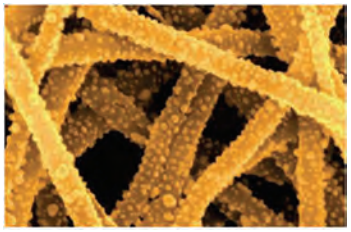

Fig. 1. **Silver nanoparticles with a diameter of 10–15 nanometers coat nylon nanofibers with a diameter of approximately 80 nanometers.** Photo: Cornell University Textiles [5]

the pharmaceutical industry, medicine, biotechnology and agriculture [2]. The unique properties of nanoparticles different from the bulk material have attracted the attention of several workers to use the multiple functionalities of nanoparticles. For example, the information about silver nanoparticles for water treatment and microbiological control was given at VII International Scientific conference of students and PhD Students «Youth and Progress of Biology» [15].

Silver NPs may exhibit antibacterial activity [16]. Furthermore, silver NPs were shown to enhance the antibacterial activity of such biotechnological products as penicillin G, amoxicillin, erythromycin, clindamycin, and vancomycin against *Staphylococcus aureus* and *Escherichia coli* [17].

Silver as a biocide

Nanotechnology offers opportunities to re-explore the biological properties of already known antimicrobial compounds by manipulating their size to alter the effect. Silver has long been known for its antimicrobial properties, but its medical applications declined with the development of antibiotics. Silver (Ag) is a transition metal element having atomic number 47 and atomic mass 107.87. The medicinal uses of silver have been documented since 1000 B.C. Silver is a wellness additive in traditional Chinese and Indian Ayurvedic medicine [18]. Its action as an antibiotic comes from the fact that it is a non-selective toxic «biocide». Silver based antimicrobial biocides are used as wood preservatives. In water usage, silver and copper based disinfectants are used in hospital and hotel distribution systems to control infectious agents (for example, *Legionella*).

Nanomaterials can be toxic at the cellular, organ, and organism levels [19]. Cytotoxic effects of carbon nanotubes may be due to their ability to generate reactive oxygen species. The cytotoxic effect is due to oxidative damage of proteins, lipids and DNA, which in turn increases oxidative stress in cells and leads to their death by apoptosis or necrosis [8].

In medicine the most widely used are silver nanoparticles. Colloidal silver containing medicines collargol and protargol are produced since 1902 till nowadays. Except for nanosilver, nanogold, nanocopper, nanooxides of silicium, titanium, iron and zinc, calcium phosphate and hydroxyapatite ceramic nanoparticles, nanoparticles of polymers (polystyrene, latex, chitosane, cyclodextrin) are used [20].

Currently, silver sulfadiazine is listed by the World Health Organization as an essential anti-infective topical medicine [21]. Since silver works as a bulk material, the use of nanosize silver may also be appealing.

Methods of nanoparticle synthesis

Owing to the wide range of nanoparticles applications in different fields of science and technology, different protocols have been designed for their synthesis [13]. The nanoparticles can be synthesized using the top-down (physical) approach which deals with methods such as thermal decomposition, diffusion, irradiation, arc discharge, etc., and bottom-up (chemical and biological) approach which involves seeded growth method, polyol synthesis method, electrochemical synthesis, chemical reduction, and biological entities for fabrication of nanoparticles by means of biotechnological methods. Different synthesis methods involve the use of different types of chemical, physical, and biological agents to yield nanoparticles of different sizes and shapes [3].

Physical methods used for the synthesis of nanoparticles include thermal decomposition, laser irradiation, electrolysis, condensation, diffusion, etc. The thermal decomposition method is used for the synthesis of monodisperse nanoparticles. Fatty acids are dissolved in hot NaOH solution and mixed with metal salt solution which leads to formation of metal precipitate [22]. In diffusion method, crystals and short wires of copper are enclosed in glass ampoules and sealed at low pressure; further, the ampoules are annealed at 500 °C for 24 h. The crystals are removed from the ampoules and cooled on a metallic plate at room temperature. In the UV irradiation technique, polycarbonate films are cut and placed on glass microscope slide and exposed to UV radiation which results in the formation of hydroxyl groups on polycarbonate films. Further, these polycarbonate films are silanized with 3-(aminopropyl) triethoxysilane (APS) in denatured ethanol for 2 h and rinsed with deionised water which leads to the formation of silver film on the polycarbonate film [23]. The arc-discharge method involves use of two graphite electrodes which act as cathode and anode and are immersed in metal salt solution. The electrodes are brought in contact to strike an arc and separated immediately to sustain arc inside salt solution. The synthesis of nanoparticles is carried out at an open circuit and an optimized direct current [24].

The most often used method for the chemical synthesis of nanoparticles is the chemical reduction method, which deals with the reduction of metal particles to nanoparticles using chemical reducing agents like sodium borohydride or sodium citrate [25]. Other chemical agents utilized for the synthesis are N,N-dimethyl formamide (DMF), poly(N-vinyl pyrrolidine) (PVP), ethyl alcohol, tetra-n-tetrafluoroborate (TFATFB), etc. [26, 27]. Seeded growth method is a colloid chemical method for the synthesis of nanoparticles which involve preparation of seeds by reducing metal ions with the suitable reducing agent. The fine particles so formed are called seed particles which are then added to growth solutions containing metal ions and additives like L-ascorbic acid and hexadecyltrimethylammonium bromide (CTAB) [27]. Polyol is also used in the synthesis of nanoparticles. In the polyol method a metal precursor is dissolved in a liquid polyol in the presence of capping agent. The metal sol is prepared using methanol or ethyl alcohol as a solvent and reducing agent while PVP is used as a protective and capping agent [26]. Electrochemical synthesis method induces chemical reactions in an electrolyte solution with the use of an applied voltage. A wide variety of nanomaterials could be synthesized using this method.

Biological agents used for the synthesis of nanoparticles include mainly bacteria, fungi [28, 29] and plants [30–33]. The biotechnological methods used for the synthesis of nanoparticles include both extracellular and intracellular methods [2, 34, 35]. The synthesis of nanoparticles using bacteria and actinomycetes usually involves the intracellular synthesis method, in which the bacterial cell filtrate is treated with metal salt solution and kept in a shaker in dark at ambient temperature and pressure conditions [36]. For the extracellular synthesis of nanoparticles using bacteria, the bacterial culture is centrifuged at 8,000*g* and the supernatant is challenged with metal salt solution [37]. In case of fungi also nanoparticles are intracellularly synthesized by treating the fungal mycelium with metal salt solution and further incubation for 24 h [38]. Dried mycelium of fungi is also used for synthesis of nanoparticles. In this method the fungal mycelium is harvested by centrifugation and subsequently freeze dried, and this freeze-dried mycelium is immersed in metal salt solution and kept on a shaker [39]. However, in the extracellular method the filtrate of the mycelium is treated with metal salt solution and incubated for 24 h [40, 41]. In algal synthesis of nanoparticles washed culture of algae without the presence of any medium is treated with metal salt solution and kept in dark with controlled pH and temperature conditions [42, 43]. The biotechnological synthesis of nanoparticles using yeast involves two steps which include firstly the synthesis of nanoparticles and next recovery of the synthesized nanoparticles [43]. For the synthesis process, yeast culture is challenged with metal salt solution and incubated in dark for 24 h. Further, the cells are separated from the medium by centrifugation and the cell-free extract is used for recovery of nanoparticles. For recovery of nanoparticles, specifically designed apparatus (polycarbonate bottle with sampling cup) is used, which separates nanoparticles from the extract by differences in thawing temperature. The cell-free medium containing nanoparticles is filled in the bottle up to the brim and kept at 20 °C in upright position. During freezing, the nanoparticles get denser than medium and settle down. The bottle is then kept at 0° C and allowed to thaw. The concentrated colloidal solution obtained in the sampling cup is centrifuged at 23,000 g for 24 h, the particles are suspended in distilled water, and further the particles are dried in vacuum [42].

Fields of application

Nanotechnology is an integration of different fields of science which holds promise in the pharmaceutical industry, medicine, biotechnology and agriculture [44]. The unique properties of nanoparticles different from the bulk material have attracted the attention of several workers to harness the multiple functionalities of nanoparticles.

Silver nanoparticles are utilized in the area of electronics, e.g. silica-coated Ag nanowires for electric circuits [45].

Colloidal silver nanoparticles can be used in the treatment of cancer and arthritis.

In cancer therapy it is proposed to use carbon nanotubes for the transport of drugs to the cancer cells [7], for DNA oligonucleotides transport to the nuclei of cancer cells for their selective destruction without damaging of normal cells [8]. In addition, carbon nanotubes by irradiation in the infrared are heated, due to this hyperthermic therapy of tumors is possible [46].

Fullerenes are biologically active and nontoxic, they are able to penetrate biological membranes, exhibit strong antioxidant and antiviral properties, increase the protective

functions of the immune system, and prevent the growth of malignant tumors. Metallofullerenes penetrate the plasma membrane of the tumor cells and effectively inhibit their proliferation, inhibit the vascularization of tumors and therefore prevent their malignancy, reduce metastasis. Their effect may be explained by their high antioxidant activity and blocking of specific cell receptors [9, 10, 47–49].

Detection of viruses is generally performed by either antigens (immunoassays) or genome sequences (polymerase chain reaction-based methods). However, sensitivity of such detection techniques is a problematic issue. There is novel sandwich-enzyme immunosorbent method for direct detection of adenoviruses with the help of covalently coated monoclonal anti-hexon antibodies onto highly fluorescent europium (III)-chelate doped nanoparticles (~10^7 nm).

Carbon nanotubes are offered to use for antibodies detection, including the cases of autoimmune diseases, for the detection of nucleotide sequences, as ion channel blockers, as biosensors for detection of DNA, glucose, cholesterol, and nitric oxide [7].

The technique of nanofiltration is a novel method to remove both enveloped and non-enveloped viruses [50]. There are reports of removal of IgG-coated non-enveloped viruses including bovine parvovirus and bovine enterovirus with the help of 20- and 50-nm-sized nanofilters [51].

Nanoparticles due to its biocompatibility and strong interaction with bases like thiols play a major role in the treatment of cancer [52]. Epithelial ovarian cancer a common malignancy of female genital tract could be cured with the use of gold nanoparticles. Vascular endothelial growth factor (VEGF) performs a vital role in the progression of ovarian cancer and also tumor growth and gold nanoparticles possess the capability to inhibit the progression of ovarian tumor growth and metastasis. Also, in case of multiple myeloma (MM), a cancer of plasma cells, nanoparticles are observed to inhibit the function of VEGF which induces cell proliferation. This inhibition of VEGF further leads to upregulation of cell cycle inhibitor proteins like p21 and p27 which inhibit proliferation [52].

Chronic lymphocytic leukemia (CLL), a cancer caused due to the overproduction of lymphocytes. Chronic leukemia starts in the bone marrow but could spread to other organs also. Nanoparticles possess the ability to inhibit the function of growth factor secreted by CLL cells, and induce apoptosis [52].

Rheumatoid arthritis which is considered as an incurable disease, bare nanoparticles are found to serve as a possible cure.

Nanoparticles can be used in the construction of miniaturized devices, which can be helpful in drug delivery [6, 7, 53].

Thiol-stabilized nanoparticles are used as «bio-catalyst». Nanoparticles can be used as fluorescence labeling system in microbial detection. Nanoparticles can be widely used as signal reporters to detect biomolecules in DNA assay, immunoassay and cell bioimaging [54].

It is prospectively to use carbon nanotubes as mechanically strong micro catheters that do not affect coagulation parameters [7].

Catheters coated with nanocrystalline silver serve as a tool to prevent infections. Silver nanoparticles are found to be active against most of the nosocomial infections related to catheters and also predominantly accumulate at the site of insertion. Thus, silver nanoparticles function as a protective agent against infection has no risk of systemic toxicity [55].

Nanosilver dressings are found to induce major improvements in the healing of wounds with respect to antimicrobial efficiency, ease in using and faster re-epithelialization. It was reported that re-epithelialization in a patient with a third-degree burn was observed as a result of the treatment of nanosilver dressing as it provided a protection against infections and also promoted early formation of neodermis and uncomplicated wound closure [3, 56].

Titanium nanoparticles are particularly useful for the production of pigments, paints and cosmetics [57].

The bone cells interact with nanostructured materials as the collagen fibrils, hydroxyapatite and proteoglycans found in bone tissues in the nanometer scale. Hence, nanomaterials are efficiently used for the regeneration and repair of bone tissues. It is observed that the bone cells could elicit desired cellular functions like adhesion, migration and proliferation. Nanomaterials can mimic the constituent components of bone, may be used for bones and neurons growing [7, 58]. Examples of bone implants include nanoceramics, nanopolymers, nanometals and composites [59].

Characteristics of penicillin and *Penicillium* spp.

Penicillin (sometimes abbreviated PCN or pen) is a group of antibiotics derived from *Penicillium* fungi (Fig. 2). They include penicillin G, procaine penicillin, benzathine peni-

cillin, and penicillin V. Penicillin antibiotics are historically significant because they are the first drugs that were effective against many previously serious diseases such as syphilis and infections caused by staphylococci and streptococci. Penicillins are still widely used today, though many types of bacteria are now resistant. All penicillins are beta-lactam antibiotics and are used in the treatment of bacterial infections caused by susceptible, usually Gram-positive, organisms [60].

Fig. 2. **Laboratory Petri-dish culture of the fungus *Penicillium chrysogenum* growing on agar with the produced antibiotic penicillin.** Geoff Tompkinson/Science Photo Library [5]

Bacteria constantly remodel their peptidoglycan cell walls, simultaneously building and breaking down portions of the cell wall as they grow and divide. β-Lactam antibiotics inhibit the formation of peptidoglycan cross-links in the bacterial cell wall, but have no direct effect on cell wall degradation. The β-lactam moiety (functional group) of penicillin binds to the enzyme (DD-transpeptidase) that links the peptidoglycan molecules in bacteria. The enzymes that hydrolyze the peptidoglycan cross-links continue to function, which weakens the cell wall of the bacterium (in other words, the antibiotic causes cytolysis or death due to osmotic pressure). In addition, the build-up of peptidoglycan precursors triggers the activation of bacterial cell wall hydrolases and autolysins, which further digest the bacteria's existing peptidoglycan. This imbalance between cell wall production and degradation is responsible for the rapid cell-killing action of this class of drugs, even in the absence of cell division. In addition, the relatively small size of the penicillin molecule allows it to penetrate deeply into the cell wall, affecting its entire depth. This is in contrast to the other major class of cell wall synthesis inhibiting antibiotics, the glycopeptide antibiotics (which includes vancomycin and teicoplanin) [61].

Penicillin shows a synergistic effect with aminoglycosides, since the inhibition of peptidoglycan synthesis allows aminoglycosides to penetrate the bacterial cell wall more easily, allowing its disruption of bacterial protein synthesis within the cell.

Penicillin is a secondary metabolite of fungus *Penicillium* that is produced when growth of the fungus is inhibited by stress. It is not produced during active growth. Production is also limited by feedback in the synthesis pathway of penicillin [61]:

α-ketoglutarate + AcCoA → homocitrate →
→ L-α-aminoadipic acid → L-Lysine + β-lactam.

The by-product L-Lysine inhibits the production of homocitrate, so the presence of exogenous lysine should be avoided in penicillin production [62].

The *Penicillium* cells are growing using a technique called fed-batch culture, in which the cells are constantly subject to stress, which is required for induction of penicillin production. The carbon sources that are available are also important: glucose inhibits penicillin production, whereas lactose does not. The pH and the levels of nitrogen, lysine, phosphate, and oxygen of the batches must also be carefully controlled [61].

The biotechnological method of directed evolution has been applied to produce by mutation a large number of *Penicillium* strains. Appropriate techniques include PCR, DNA shuffling etc. [62].

Penicillium is a genus of ascomycetous fungi of major importance in the natural environment as well as food and drug production (Fig. 3). It produces penicillin, a molecule that

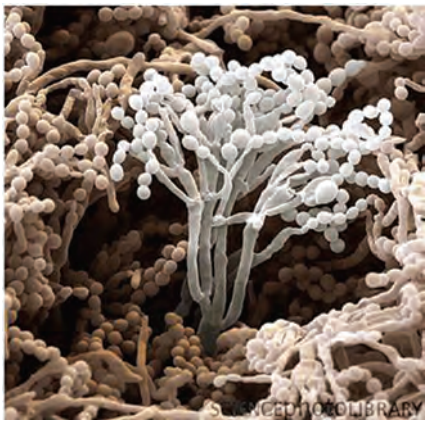

Fig. 3. **Penicillium chrysogenum, coloured scanning electron micrograph (SEM) at magnification ×1250.** The round structures are conidia, the asexual reproductive spores of the fungus. Eye of Science/Science Photo Library [5].

is used as an antibiotic, which kills or stops the growth of certain kinds of bacteria inside the body. The widespread genus contains over 300 species [63].

Penicillium is classified as a genus of anamorphic fungi in the division *Ascomycota* (order *Eurotiales*, class *Eurotiomycetes*, family *Trichocomaceae*) [64]. The genus name is derived from the Latin root «penicillium», meaning «painter's brush», and refers to the chains of conidia that resemble a broom [65].

The thallus (mycelium) typically consists of a highly branched network of multinucleate, septate, usually colorless hyphae. Many-branched conidiophores sprout on the mycelia, bearing individually constricted conidiospores. The conidiospores are the main dispersal route of the fungi, and often green.

Sexual reproduction involves the production of ascospores, commencing with the fusion of an archegonium and an antheridium, with sharing of nuclei. The irregularly distributed asci contain eight unicellular ascospores each [66].

Combined action of penicillin and nanoparticles

With the emergence and increase of microbial organisms resistant to multiple antibiotics, and the continuing emphasis on healthcare, many researchers have tried to develop new, effective antimicrobial reagents free of resistance. Such problems and needs have led to the resurgence in the use of Ag-based antiseptics that may be linked to broad-spectrum activity and far lower propensity to induce microbial resistance than antibiotics [67]. Research in antibacterial material containing various natural and inorganic substances has been intensive [68]. Among metal nanoparticles (Me-NPs), silver nanoparticles (Ag-NPs) have been known to have inhibitory and bactericidal effects. It can be expected that the high specific surface area and high fraction of surface atoms of Ag-NPs will lead to high antimicrobial activity as compared with bulk silver metal [68]. The biomedical application of silver nanoparticles also attracted increasing interest, such as antimicrobial activity of silver nanoparticles for wound healing, and silver nano-coated medical devices, etc. [69]. There were investigated that silver ion or metallic silver as well as silver nanoparticles can be exploited in medicine for burn treatment, dental materials, coating stainless steel materials, textile fabrics, water treatment, sunscreen lotions, etc. and posses low toxicity to human cells, high thermal stability and low volatility [70].

In 2007, three papers have been published reporting the use of blue aggregated mixtures of drugs and NPs, rather than of stable red conjugates [71–73]. Such a color change and transmission electron microscopy (TEM) images unambiguously indicated NP aggregation. The drugs used were aminoglycoside antibiotics (streptomycin, gentamicin, kanamycin, and neomycin), quinolones (ciprofloxacin, gatifloxacin, and norfloxacin), ampicillin (a penicillin antibiotic), and 5-fluorouracil (an antimetabolite of nucleic metabolism). The preparations were tested for antibacterial activity toward gram-positive (*Bacillus subtilis, Staphylococcus aureus, Micrococcus luteus*) and gram-negative (*E. coli, Pseudomonas aeruginosa*) microorganisms and they also were examined for antifungal activity toward *Aspergillus fumigatus* and *Aspergillus niger* (Fig. 4, 5). The basic experimental tests for the determination of antibacterial activity were the disk diffusion method and the agar diffusion method. Depending on the antibiotic used, increase in the activity of the antibiotic-colloidal-silver mixture ranged from 12 to 40%, as compared with the activities of the native drugs. So, the antibacterial activities of the antibiotics were enhanced through the use of silver NPs.

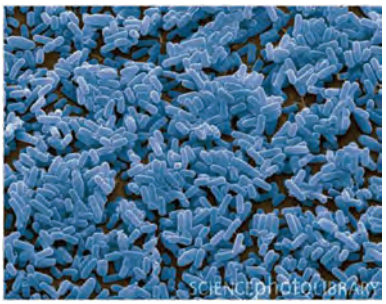

Fig. 4. **Coloured scanning electron micrograph (SEM) of *Bacillus subtilis* bacteria at magnification ×12000.**
Steve Gschmeissner/Science Photo Library [5]

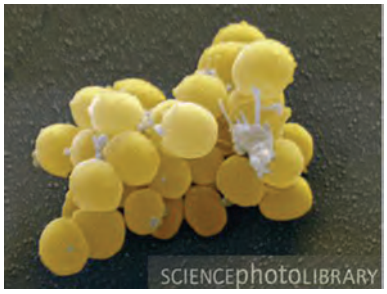

Fig. 5. **Coloured scanning electron micrograph (SEM) of *Staphylococcus aureus* bacteria at magnification ×16000.**
Eye of Science/Science Photo Library [5]

Nowadays one of the nanobiotechnology tasks is metal nanoparticles construction and usage. Nanoparticles are known for a long time, and they are used in different areas of human activity. Silver nanoparticles have a wide range of applications in pharmacy, medicine, biotechnology and agriculture. From the literature data analyzing there was given information about nanotechnology development in face of silver nanoparticles in the combination with antibiotics. Silver nanoparticles are in active usage as «naked» as in the combination with antibiotics, in particular with penicillin, for enhancing of their action. The silver nanoparticles can be synthesized by the means of physical, chemical and biological methods. Penicillin produced by filamentous fungi *Penicillium* sp. is the first discovered antibiotic; it is still applied in medicine. But many bacteria for the long time have developed the resistance to it. Researches show that penicillin in the combination with the silver nanoparticles give the highly effective bactericidal action against different bacteria, especially *Bacillus subtilis* and *Staphylococcus aureus*.

Nanobiotechnology is prospective for medicine. Nanocomposites creation and application are especially important. Nanoparticles usage offers great opportunities for diagnostics and treatment patients with bone and joint pathology, bacterial and virus infections, injuries, autoimmune diseases, cancer, etc.

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НАНОЧАСТИНКИ СРІБЛА ЯК ПІДСИЛЮВАЧІ ДІЇ ПЕНІЦИЛІНУ

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На цей час зростає значення досліджень бактерицидних наноматеріалів у зв'язку зі збільшенням кількості штамів бактерій, резистентних до більшості сильнодійних антибіотиків. В огляді подано характеристику наночастинок і способів їх одержання. Розглянуто галузі застосування наночастинок, особливу увагу приділено використанню наночастинок срібла в медицині, зокрема як бактерицидних препаратів. Зазначено, що наночастинки можуть справляти токсичну дію.

Велику увагу приділено застосуванню наночастинок в терапії різних захворювань, наприклад, для спрямованого доставлення ліків, загоєння ран, відновлення кісткової тканини, локального нагрівання пухлин при онкологічних захворюваннях, стимуляції функцій імунної системи, для визначення антитіл, вірусів, бактерій, для фільтрації рідин.

Наведено характеристику пеніцилінів та їхніх продуцентів — *Penicillium* sp. Розглянуто механізм антимікробної дії пеніциліну.

Виявлено, що застосування наночастинок срібла в комбінації з антибіотиками, зокрема з пеніциліном, сприяє посиленню антибактеріальної активності антибіотиків стосовно грампозитивних і грамнегативних мікроорганізмів.

Ключові слова: нанотехнологія, наночастинки срібла, антибіотики, пеніцилін, *Penicillium* sp.

НАНОЧАСТИЦЫ СЕРЕБРА КАК УСИЛИТЕЛИ ДЕЙСТВИЯ ПЕНИЦИЛЛИНА

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В настоящее время возрастает значение исследований бактерицидных наноматериалов в связи с увеличением количества штаммов бактерий, резистентных к большинству сильнодействующих антибиотиков. В обзоре дана характеристика наночастиц и способов их получения. Рассмотрены области применения наночастиц, особое внимание уделено использованию наночастиц серебра в медицине, в частности в качестве бактерицидых препаратов. Указано, что наночастицы могут обладать токсическим действием.

Большое внимание уделено применению наночастиц в терапии различных заболеваний, например, для направленной доставки лекарств, заживления ран, восстановления костной ткани, локального нагрева опухолей при онкологических заболеваниях, стимуляции функций иммунной системы, для определения антител, вирусов, бактерий, для фильтрации жидкостей.

Дана характеристика пенициллинов и их продуцентов — *Penicillium* sp. Рассмотрен механизм антимикробного действия пенициллина.

Установлено, что применение наночастиц серебра в комбинации с антибиотиками, в частности с пенициллином, приводит к усилению антибактериальной активности антибиотиков по отношению к грамположительным и грамотрицательным микроорганизмам.

Ключевые слова: нанотехнология, наночастицы серебра, антибиотики, пенициллин, *Penicillium* sp.