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# Sensitivity of Antibiotic-Resistant Clinical Strains of *Staphylococci* and *Enterococci* to Biodegradation Products of Ml-10 Magnesium Alloy

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## Abstract

**Introduction:** The problem of development of purulent-inflammatory infections such resulting from the surgical medical care and connected with the using of metal medical alloys is urgent in medical practice. Members of genus *Staphylococcus* and *Enterococcus* are the main causative agents of these infections. These microorganisms have numerous pathogenicity factors, including the ability to form biofilms on the surface of implants. Thus, it is important the study the biological properties of magnesium-based metal alloys that have bactericidal effect and prevent to form a biofilm on the surface of the implant.

**Aim of the Study:** The aim of the study was to identification the antibacterial properties of medical magnesium alloy ML-10 against clinical antibiotic resistant strains of *Staphylococci* and *Enterococci*, with further opportunity to use in surgical practice as implants that contribute to the prevention of nosocomial infections.

**Methods:** Studies have used the ML-10 magnesium alloy extract and antibiotic-resistant clinical strains of *Staphylococci* and *Enterococci* that was isolated from the wounds of patients with infectious postoperative complications. We have incubated different concentrations of these bacteria in the extract during 120 hours and studied the antimicrobial activity of ML-10 alloy's biodegradation products. Licensed computer software "Microsoft Excel 2010" and "Statistica for Windows 13" were used for statistical analysis.

**Results:** Research results have shown that antibiotic-resistant clinical strains of *Staphylococci* and *Enterococci* were sensitive to biodegradation products of ML-10 magnesium alloy. During process of the alloy biodegradation the corrosion products were formed and caused the increase pH of the medium from 7.2 to 9.3. Despite the fact that the destruction of the *Staphylococcus* spp. and *Enterococcus* spp. was slow, we found that the number of bacteria gradually decreased in the extract during the 120-hour incubation. This fact was confirmed by the decrease of the colonies number on the Mueller-Hinton agar after daily sowing from the extract. Prolonged incubation of *Staphylococci* and *Enterococci* in the extract led to complete destruction of the bacteria.

**Conclusion:** The biodegradation products of ML-10 magnesium alloy exhibit high antimicrobial activity against antibiotic resistant strains of *Staphylococci* and *Enterococci*. These results are making possible to use this metal in medicine as implants for prevention nosocomial infection.

***Keywords:*** *Products of Magnesium Alloy Biodegradation; Antibacterial Properties; Antibiotic Resistant Strains; Staphylococci; Enterococci*

## Introduction

One of the most pressing problems today is the development of infections associated with the provision of surgical care, the proportion of which are postoperative wound infections resulting from the use of metallic medical alloys. Thus, one of the causes of nosocomial

infection in patients of orthopedic and trauma hospitals is the use of metal - internal fixation devices during osteosynthesis. According to the authors, the etiofactor of exogenous osteomyelitis in 30 - 61% of cases are coagulase-positive staphylococci, in 33% - coagulase-negative *Staphylococci* and in 19% - members of the genus *Enterococcus* [1,2]. W. Zimmerli in his work showed that strains of *Staphylococcus* aureus, which are isolated from patients with osteomyelitis, express a variety of adhesins that play a role in the development of the infectious process [2]. Thus, most clinical isolates isolated from patients with osteomyelitis express FnBPA and FnBPB adhesion proteins, which ensure the adhesion of *Staphylococci* to the fibronectin of the bone matrix and to the surface of implants coated with plasma proteins [3]. 38 - 56% of *S. aureus* isolates associated with bone infection express collagen-binding adhesin (Cna), which together with bone sialoprotein binding protein (Bbp) interacts with bone sialoprotein (BSP), the most important component bone extracellular matrix [4]. The formation of adhesins by *Staphylococci* ensures the formation of biofilms, which reduces the viability of osteoblasts, bone repair and promotes the development of the inflammatory process [5].

*Staphylococci* and *Enterococci* play an equally important role in the development of sternal infection in cardiac surgery. Among the etiological factors should be noted the use for suturing and fixation of the sternum of metal wire sutures made of medical alloys [6]. Breakage, destruction and cutting of wire sutures is accompanied by the addition to the wound surface of known infectious agents. According to the literature, coagulase-negative types of *Staphylococci* and 26% of *Staphylococcus aureus* are isolated from patients with sternal infection in 43 - 64% of cases [7,8].

Currently, the medical market presents a large number of implants and structures made of metal alloys, characterized by different chemical composition of the material. Titanium alloys are most often used in practice, however, the experience of using such materials undoubtedly proves the ability of such materials to cause the development of hypersensitivity reactions, local and systemic inflammation [9,10].

Complications that develop when implanting such materials require the development of biocompatible alloys that would reduce the incidence of inflammatory infections in the area of implantation. Today, the study of biological properties of metal alloys based on magnesium ($Mg^{2+}$) is promising. It is known that $Mg^{2+}$ itself does not have antibacterial properties, but the biodegradation of magnesium alloys produces corrosion products (hydrogen gas, magnesium hydroxide, Mg salts), which locally increase the pH and cause bactericidal action. Such properties of magnesium alloys complicate the formation of microorganisms of a full-fledged biofilm on the surface of the implant, which in turn prevents the development of the inflammatory process [11]. In our research, we used a modified magnesium alloy based on industrial alloy ML-10, the characteristics of which allow its use in medical surgical practice. This work is a continuation of a series of studies to study the antimicrobial properties of a modified magnesium alloy based on industrial alloy ML-10 [12,13].

## Aim of the Study

Investigate the antibacterial activity of the modified magnesium alloy ML-10 against clinical strains of *Staphylococci* and *Enterococci*, in order to microbiologically substantiate the possibility of its use in surgical practice.

## Materials and Methods

The use of magnesium alloy extract, the original method of manufacture of which is given in our previous articles [12,13]. As test strains of microorganisms used serial dilutions ($10^9$ CFU/ml - $10^4$ CFU/ml) of daily cultures of *Staphylococci* and *Enterococci* isolated from patients with infection due to surgical care (5 isolates of *Staphylococcus aureus*, resistant to penicillins, caricillobases and macrolipofaf, 1 *Staphylococcus haemolyticus*, insensitive to penicillins, macrolides, lincosamides, 1 *Staphylococcus epidermidis*, resistant to penicillins, macrolides, 4 strains of *Enterococcus faecalis*, resistant penicillins and non-culture glycoside2). The study of susceptibility of these microorganisms to antibacterial drugs was performed according to the requirements of the European Committee for Antimicrobial Susceptibility (EUCAST. Version 9.0, 2019) disco-diffusion method using discs with antibiotics manufactured by Himedia Laboratories

Pvt. Limited (India). The culture method for experiments with coca cultures was similar to the method of culture for experiments with enterobacteria and non-fermenting gram-negative microorganisms, which ensured the reliability of the results, however, the incubation time of the extract with coca was increased to 120 hours. Studies of the antistaphylococcal activity of the magnesium alloy were performed in five replicates. For statistical analysis, we used the licensed computer program Microsoft Excel 2010 and Statistica for Windows 13 (StatSoft Inc., № JPZ804I382130ARCN10-J) which analyzed the distributions of quantitative data and determined the measures of the central trend - median (Me), measures of variation - interquartile scope in the form of 25 and 75 percentiles.

## Results

In the study of the bactericidal activity of the alloy extract against clinical strains of *Staphylococci* and *Enterococci*, it was found that their disposal was quite slow. However, over time of incubation, the number of cocci in the extract decreased significantly, which was confirmed by a decrease in the number of colonies on Mueller-Hinton agar after each seeding from the extract (Table 1). Among the studied cultures of staphylococci, two strains (*S. aureus* №80, *S. epidermidis*) were found to be weakly sensitive to the action of the extract, but 120 hours of incubation of the extract with bacteria led to almost complete neutralization of the latter. Thus, after the first seeding from the tubes to which the highest concentration of bacteria was added the day before ($10^9$ CFU/ml), the number of colonies on agar in most experiments could not be counted due to their significant number and almost drain growth. But in 48 years, incubation of the extract, the number of colonies of *S. aureus* №80 was 1195 (1150-1280), after 72 hours - 726.8 (820-862), after 96 years - 263.4 (131-315), after 120 years - 71.2 (44-82). The corresponding indicators for the strain *S. epidermidis* were 1027 (925-1160), 846 (790-930), 340.4 (290-320) and 26.4 (21-33). $10^8$, $10^7$, $10^6$, $10^5$ CFU/ml *Staphylococcus aureus* and $10^8$, $10^7$, $10^6$ CFU/ml epidermal were also slowly neutralized. At the same time, complete disinfection of $10^4$ CFU/ml *S. aureus* №80 took place within 72 - 96 hours and *S. epidermidis* $10^5$ CFU/ml and $10^4$ CFU/ml in 72 - 120 hours. and 48 - 120 hours. in accordance. Despite the obtained results, it is safe to say that the biodegradation products of the studied magnesium alloy ML-10 cause a significant bacteriostatic and bactericidal effect against *Staphylococci*. Our conclusion confirms the fact that the other 4 cultures of *S. aureus* and *S. haemolyticus* strain were highly sensitive to the extract: the death of the highest concentration of these microorganisms ($10^9$ CFU/ml) was recorded within 3 - 4 days, the lowest - during the day.

| № s/n | Strain | | Incubation time, h | 24 | 48 | 72 | 96 | 120 |
|---|---|---|---|---|---|---|---|---|
| | name | № | Sowing dose, KUO/ml | Number of staphylococcal colonies (Me (Q25-Q75)) | | | | |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| 1 | *S. aureus* | 80 | $10^9$ | X | 1195 (1150-1280) | 726,8 (820-862) | 263,4 (131-315) | 71,2 (44-82) |
| | | | $10^8$ | 1017,6 (890-1211) | 824 (750-890) | 446 (320-600) | 155 (108-200) | 29,4 (24-32) |
| | | | $10^7$ | 400 (192-562) | 275,6 (110-386) | 176 (59-212) | 67,8 (50-85) | 4,4 (1-8) |
| | | | $10^6$ | 243,6 (109-321) | 105 (65-112) | 31,2 (9-48) | 5,4 (2-11) | 0,6 (0-1) |
| | | | $10^5$ | 46,8 (33-54) | 28,8 (12-50) | 10 (0-3) | 2 (0-2) | 0,2 (0-0) |
| | | | $10^4$ | 7,4 (5-9) | 1 (1-1) | 0,2 (0-0) | 0 | 0 |
| 2 | | 81 | $10^9$ | 324,6 (249-421) | 80,4 (15-122) | 9,2 (2-15) | 0,6 (0-1) | 0 |
| | | | $10^8$ | 48,2 (28-54) | 21 (12-25) | 1,4 (0-2) | 0 | 0 |
| | | | $10^7$ | 16 (15-21) | 2 (1-4) | 0 | 0 | 0 |
| | | | $10^6$ | 3,2 (1-5) | 1,2 (0-0) | 0,2 (0-0) | 0 | 0 |
| | | | $10^5$ | 0,2 (0-0) | 0 | 0 | 0 | 0 |
| | | | $10^4$ | 0 | 0 | 0 | 0 | 0 |

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|
| 3 | *S. aureus* | 82 | $10^9$ | 23,6 (12-36) | 4,4 (2-5) | 0,6 (0-1) | 0 | 0 |
| | | | $10^8$ | 5,4 (2-8) | 1 (0-1) | 0,4 (0-0) | 0 | 0 |
| | | | $10^7$ | 0,8 (1-1) | 0,4 (0-1) | 0 | 0 | 0 |
| | | | $10^6$ | 0 | 0 | 0 | 0 | 0 |
| | | | $10^5$ | 0 | 0 | 0 | 0 | 0 |
| | | | $10^4$ | 0 | 0 | 0 | 0 | 0 |
| 5 | | 96 | $10^9$ | 1306 (1250-1360) | 512,2 (420-620) | 186,4 (172-212) | 16,4 (12-21) | 0 |
| | | | $10^8$ | 371,6 (325-480) | 109 (85-125) | 27 (12-41) | 1,4 (0-1) | 0 |
| | | | $10^7$ | 90,2 (86-112) | 19,6 (16-29) | 4,2 (2-5) | 0,4 (0-1) | 0 |
| | | | $10^6$ | 16,2 (8-21) | 1,8 (0-2) | 0,2 (0-0) | 0 | 0 |
| | | | $10^5$ | 0,9 (0-1) | 0,2 (0-0) | 0 | 0 | 0 |
| | | | $10^4$ | 0 | 0 | 0 | 0 | 0 |
| 6 | | 97 | $10^9$ | 21,4 (14-28) | 4,4 (2-7) | 0 | 0 | 0 |
| | | | $10^8$ | 17,8 (2-20) | 1 (0-2) | 0 | 0 | 0 |
| | | | $10^7$ | 1,4 (0-2) | 0,6 (0-1) | 0 | 0 | 0 |
| | | | $10^6$ | 1 (1-1) | 0 | 0 | 0 | 0 |
| | | | $10^5$ | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | |
| 7 | *S. epidermidis* | 95 | $10^9$ | X | 1027 (925-1160) | 846 (790-930) | 340,4 (290-320) | 26,4 (21-33) |
| | | | $10^8$ | 1234 (1250-1400) | 705,2 (626-830) | 275 (121-320) | 87 (20-118) | 17,4 (1-18) |
| | | | $10^7$ | 460,6 (365-550) | 182,4 (140-242) | 27,4 (7-48) | 2,8 (0-2) | 1 (0-0) |
| | | | $10^6$ | 96,4 (97-106) | 38,6 (3-64) | 16,2 (1-28) | 0,8 (0-1) | 0,1 (0-0) |
| | | | $10^5$ | 70,2 (28-98) | 18,2 (2-29) | 3,4 (0-3) | 0,4 (0-1) | 0 |
| | | | $10^4$ | 3 (1-4) | 1 (0-1) | 0,4 (0-0) | 0,2 (0-0) | 0 |
| 8 | *S. haemolyticus* | 98 | $10^9$ | 13,2 (7-18) | 2,2 (2-2) | 0,2 (0-0) | 0,2 (0-0) | 0 |
| | | | $10^8$ | 4,6 (4-5) | 1,4 (0-2) | 0 | 0,2 (0-0) | 0 |
| | | | $10^7$ | 0,8 (0-1) | 0 | 0 | 0 | 0 |
| | | | $10^6$ | 0,2 (0-0) | 0 | 0 | 0 | 0 |
| | | | $10^5$ | 0 | 0 | 0 | 0 | 0 |
| | | | $10^4$ | 0 | 0 | 0 | 0 | 0 |

***Table 1:*** *The results of the study of the survival of staphylococci in the extract of magnesium alloy, Me (Q25-Q75). Explanation: «X» - counting colonies is impossible.*

Among the strains of *Enterococcus* faecalis, the most sensitive to the action of biodegradation products of the magnesium alloy ML-10 was the strain *E. faecalis* №99: neutralization of the highest concentration of *Enterococci* ($10^9$ CFU/ml) in the extract occurred within 96

- 120 hours, growing on agar, with each sowing decreased rapidly: from 166.6 (154-182) after 24 hours. incubation of the extract, up to 45.2 (35-58) - after 48 hours, 8 (7-9) - after 72 hours and up to 0.2 (0-0) - after 96 hours and after 120 hours incubation in all replicates of the study of colony growth was not registered. Destruction of $10^8$ and $10^7$ CFU/ml of this strain was registered within 72 - 96 hours, $10^6$ CFU/ml - 48-72 hours, $10^4$ and $10^5$ CFU/ml - 24 - 48 hours. The other three strains of *E. faecalis* (№№ 29, 49, 102) were moderately sensitive to the extract, their disposal was quite slow, but despite this, with each seeding the number of enterococcal colonies on Mueller-Hinton agar decreased due to the gradual destruction of bacteria in the extract over time. Thus, after the first seeding from tubes to which $10^9$ CFU/ml of *Enterococci* were previously added, the number of colonies on agar could not be counted due to their significant number and drain growth (Table 2). But with the incubation time of the extract there was a gradual neutralization of bacteria and, as a result, after 120 hours of incubation of the extract, on a dense medium increased in total 20.4 (0-32) (*E. faecalis* №29), 9.8 (0-15) (*E. faecalis* №49), 56.8 (34-82) (*E. faecalis* №102) colonies. Disposal of $10^8$, $10^7$, $10^6$ and $10^5$ CFU/ml of these isolates was also slow, but after each sowing the number of enterococcal colonies on a dense medium decreased, which clearly confirms the presence of bactericidal properties of the studied alloy against *Enterococci*.

| **№ s/n** | **№ strain** | **Incubation time, h** | **24** | **48** | **72** | **96** | **120** |
|---|---|---|---|---|---|---|---|
| | | **Sowing dose, CFU/ml** | **Number of colonies of *Enterococcus* faecalis (Me (Q25-Q75))** | | | | |
| **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** |
| 1 | 29 | $10^9$ | X | 838,4 (465-1180) | 486,8 (96-850) | 124,4 (12-128) | 20,4 (0-32) |
| | | $10^8$ | 1147,4 (982-1340) | 525 (125-560) | 326,4 (18-360) | 122,8 (11-218) | 11 (0-15) |
| | | $10^7$ | 542 (154-742) | 229,2 (32-220) | 164 (28-281) | 66, 6 (12-115) | 13,4 (0-22) |
| | | $10^6$ | 167, 4 (84-253) | 41 (21-51) | 20,4 (3-20) | 8, 4 (0-12) | 2,4 (0-1) |
| | | $10^5$ | 28 (5-26) | 26,8 (1-30) | 14,2 (0-15) | 7,4 (0-12) | 0,4 (0-1) |
| | | $10^4$ | 8,4 (1-14) | 4,8 (0-11) | 0,8 (0-1) | 0 | 0 |
| 2 | 49 | $10^9$ | X | X | 209,2 (68-420) | 40,6 (21-54) | 9,8 (0-15) |
| | | $10^8$ | 983,8 (924-955) | 520,2 (320-710) | 121 (22-215) | 20 (1-32) | 2,8 (0-2) |
| | | $10^7$ | 456,6 (222-700) | 147,8 (14-214) | 49,6 (2-112) | 12,4 (0-20) | 1 (0-1) |
| | | $10^6$ | 267,6 (205-300) | 35,6 (12-26) | 16,2 (0-4) | 2,6 (0-0) | 0 |
| | | $10^5$ | 167 (20-25) | 5,4 (1-2) | 0,4 (0-1) | 0 | 0 |
| | | $10^4$ | 2 (1-3) | 0 | 0 | 0 | 0 |
| 3 | 99 | $10^9$ | 166,6 (154-182) | 45,2 (35-58) | 8 (7-9) | 0,2 (0-0) | 0 |
| | | $10^8$ | 55,4 (34-75) | 10,2 ( 3-14) | 2,6 (2-3) | 0 | 0 |
| | | $10^7$ | 48,4 (22-72) | 6,2 (2-5) | 0,6 (0-1) | 0 | 0 |
| | | $10^6$ | 27,2 (14-41) | 2,6 (0-3) | 0 | 0 | 0 |
| | | $10^5$ | 4,4 (2-6) | 0 | 0 | 0 | 0 |
| | | $10^4$ | 1,2 (0-1) | 0 | 0 | 0 | 0 |
| 4 | 102 | $10^9$ | X | X | 637,6 (350-720) | 342,6 (148-290) | 56,8 (34-82) |
| | | $10^8$ | 1186 (1100-1250) | 688,8 (650-720) | 261,8 (220-315) | 105,4 (81-95) | 28,6 (28-31) |
| | | $10^7$ | 791,8 (715-850) | 499,4 (320-720) | 149,2 (82-208) | 51,4 (37-65) | 16,8 (11-22) |
| | | $10^6$ | 269,8 (220-308) | 150,2 (126-178) | 40,4 (15-64) | 8,2 (0-14) | 7,4 (0-16) |
| | | $10^5$ | 44,4 (35-52) | 16,4 (14-16) | 5,8 (2-8) | 2,6 (0-5) | 2,6 (0-1) |
| | | $10^4$ | 3 (1-3) | 0 | 0 | 0 | 0 |

***Table 2:*** *The results of the study of the survival of Staphylococci in the extract of magnesium alloy, Me (Q25-Q75).*

*Explanation: «X» - counting colonies is impossible.*

## Discussion of Research Results

The development of a bacterial infection in patients after surgery involving the use of medical metal alloys requires a constant search for materials that would prevent infectious complications, ensure the safety of life and quickly restore the patient's health. Modern research focuses on the development of medical alloys that would have antibacterial properties and undergo biodegradation in the body, performing its function of osteosynthesis or comparison and healing of wound tissue. It is known that the introduction of $Mg^{2+}$ in the metal alloy allows the latter to gradually break down in the human body after performing its function. The destruction of such an alloy is accompanied by the formation of magnesium salts and changes in the pH of the medium in the alkaline direction, which ultimately causes a bactericidal effect [11]. Thus, in the process of decomposition of the magnesium alloy ML-10 studied by us, the pH of the medium changed from 7.2 to 9.3. Despite the ability of *Staphylococci* and *Enterococci* to survive at elevated pH, the biodegradation products of this alloy showed high bactericidal activity against these antibiotic-resistant microorganisms. Despite the fact that some strains of *Staphylococci* and *Enterococci* were characterized by the ability to survive long-term exposure to the extract, its bacteriostatic properties did not allow bacteria to multiply, and adverse living conditions eventually led to the incessant death of cocci. Guanping He (2015) showed similar results in its work by detecting a high sensitivity of the reference test strain *S. aureus* (ATCC 25922) to the biodegradation products of magnesium alloys containing calcium, strontium and zinc. However, He G did not focus on studying the antimicrobial activity of magnesium alloys against antibiotic-resistant staphylococcal strains [14]. A significant bactericidal effect of medical magnesium alloy with the addition of aluminum was proved by Di Tie and co-authors in the study of the sensitivity of methicillin-resistant strain *S. aureus* DSMZ 20231 (*Staphylococcus aureus* Rosenbach 1884, German Collection of Microorganisms and Cell Cultures).

It should be noted that we did not find reliable evidence to prove a link between the resistance of our cultures to antibiotics and their sensitivity to the extract, but we found that cultures of clinical strains of *Staphylococci* and *Enterococci* showed different sensitivity to the biodegradation products of magnesium alloy ML. 10. The rate of destruction in the extract of individual isolates of *Enterococci* and *Staphylococci* differed significantly. This fact needs further study in order to develop alloys with more effective antibacterial action [15,16].

## Conclusion

1. Products of biodegradation of the extract of magnesium alloy ML-10 have high bactericidal activity against antibiotic-resistant clinical strains of *Staphylococci* and *Enterococci*.

2. High sensitivity to the action of biodegradation products of magnesium alloy ML-10 resistant to antibiotic *Staphylococci* and *Enterococci* is confirmed by their gradual disinfection during 120 hours of incubation in the extract.

3. The obtained research results confirm the possibility of using a metal alloy based on magnesium ML-10 as implants that help prevent nosocomial purulent-inflammatory infections.

## Bibliography

1. Aytac S., *et al*. "Posttraumatic and postoperative osteomyelitis: surgical revision strategy with persisting fistula". *Archives of Orthopaedic and Trauma Surgery* 134 (2014): 159-165.

2. Zimmerli W and Sendi P. "Orthopaedic biofilm infections". *Acta Pathologica, Microbiologica et Immunologica Scandinavica* 125 (2017): 353-364.

3. Saddif A., *et al*. "*Staphylococcus aureus* Fibronectin Binding Proteins Are Essential for Internalization by Osteoblasts but Do Not Account for Differences in Intracellular Levels of Bacteria". *Infection and Immunity* 69.5 (2001): 2872-2877.

4. Wiśniewska K., *et al*. "Clonal distribution of bone sialoprotein-binding protein gene among *Staphylococcus aureus* isolates associated with bloodstream infections". *Folia Microbiologica* 59.6 (2014): 465-471.

5. Sanchez CJ., *et al*. "Staphylococcus aureus biofilms decrease osteoblast viability, inhibits osteogenic differentiation, and increases bone resorption in vitro". *BMC Musculoskeletal Disorders* 14 (2013): 187.

6. Shvedova MV., *et al*. "Metodi osteosintesa grudini b lechenii i profilactike osloznenii sredinnoy cternotomii". *Sibirsky Medicinsky Jurnal* 31.3 (2016): 26-32.

7. Chernyavsky AM., *et al*. "Infeksii v cardiohirurgii [Infections in cardiac surgery]". *Hirurgia* 5 (2016): 64-68.

8. Rehman SM. "Risk factors for mediastinitis following cardiac surgery: the importance of managing obesity". *Journal of Hospital Infection* 88.2 (2014): 96-102.

9. Rozhnova OM., *et al*. "Biological compatibility of medical devices based on metals, the reasons for the formation of pathological reactivity (review of foreign literature". *Bulletin of Siberian Medicine* 14.4 (2015): 110-118.

10. Petersen RC. "Titanium implant osseointegration problems with alternate solutions using Epoxy/Carbon–Fiber– Reinforced". *Composite Metals* 4.4 (2014): 549-569.

11. Witte F., *et al*. "Degradable Biomaterials based on Magnesium Corrosion". *Current Opinion in Solid State and Materials Science* (2009).

12. Chornyi VM., *et al*. "Resultati vivchennya *In vitro* antibacterialnoy activnosti modificovanogo magnievogo splavu shchodo test-shtamiv *E. coli* ta *P. aeruginosa* [Results of the in vitro study of the antibacterial activity of modified magnesium alloy in experiments with *E. coli* and *P. aeruginosa* test-strains]". *Pathologia* 3.44 (2018): 337-340.

13. Chornyi VM. "Antibacterial properties of a modified magnesium alloy in vitro with clinical strains of non-fermentative gram-negative microorganisms". *Zaporizhzhya Medical Journal* 1 (2020): 103-106.

14. He G., *et al*. "Addition of Zn to the ternary Mg–Ca–Sr alloys significantly improves their antibacterial properties". *Journal of Materials Chemistry* 3 (2015): 6676-6689.

15. Tie D., *et al*. "Antibacterial biodegradable Mg-Ag alloys". *European Cells and Materials* 25.25 (2013): 284-298.

16. Kim BS., *et al*. "Genome sequence of type strain of *Staphylococcus aureus* subsp". *Aureus Gut Pathogens* 6.6 (2014).

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