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OCCURRENCE OF ANTIBIOTICS IN THE ENVIRONMENT

WYSTĘPOWANIE ANTYBIOTYKÓW W ŚRODOWISKU

Abstract

Antibiotics are the most commonly used group of pharmaceuticals used in human and animal treatment. The main sources are hospital and household sewage and waste from animal production. The paper is a review of the literature confirming the prevalence of antibiotics in wastewater influents and effluents, natural waters, sludge and sediments. Studies conducted around the world confirm that there is a risk of antibiotic accumulation in soil and their infiltration to drinking water despite advanced methods of water purification. The concentrations of several substances found in surface water samples exceed the levels considered as safe for the studied aquatic organisms several hundred times, which indicates a real threat to their lives.

Keywords: antibiotics, wastewater, surface water, sludge

Streszczenie

Antybiotyki są najczęstszą grupą farmaceutyków stosowanych w leczeniu ludzi i zwierząt. Głównymi źródłami tych leków są ścieki szpitalne, ścieki bytowo-gospodarcze i ścieki z produkcji zwierzęcej. W artykule dokonano przeglądu literatury potwierdzającej powszechną obecność antybiotyków w ściekach doprowadzanych do oczyszczalni, ściekach oczyszczonych, wodach naturalnych oraz osadach ściekowych i dennych. Analizy wykonane na świecie potwierdzają także ryzyko magazynowania się antybiotyków w glebie i przenikania do wody przeznaczonej do picia pomimo zaawansowanych metod uzdatniania. W przypadku kilku substancji, stężenia w wodach powierzchniowych przekraczały kilkaset razy poziomy uznawane za bezpieczne dla badanych organizmów wodnych, co wskazuje na realne zagrożenie dla ich życia.

Słowa kluczowe: antybiotyki, ścieki, wody powierzchniowe, osady

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1. Introduction

The consumption of pharmaceuticals in human and animal (veterinary) therapies has been steadily increasing for many years, while the issues of their occurrence and impact on the environment (aquatic and terrestrial) have been the subjects of worldwide research for only two decades. Nowadays, more and more research centers conduct research on the prevalence of pharmaceuticals in the natural environment, which seems to confirm the opinions on pharmaceuticals as a growing threat to the environment and animals. The most commonly used and prevalent group of pharmaceuticals, found in environmental samples in the largest quantities, are undoubtedly antibiotics [39]. Despite a more difficult access to this group of drugs (which are issued only on prescription) than in the case of anti-inflammatory drugs and painkillers, antibiotics are among the most abused drugs. In the case of many ailments with which patients go to the GP (general practitioner), therapy without antibiotics could be successful. However, some doctors still consider antibiotics as the only effective (and perhaps also the easiest) form of therapy of diseases caused by bacteria. This is despite the calls for reducing the excessive use of antibiotics, which affects the emergence of antibiotic resistance in patients, and which is a growing problem worldwide. Resistance to antibiotics is caused by both the correct application of the drug, as well as taking higher doses than prescribed or abandonment of therapy before its completion [4]. This applies to human as well as animal therapy. The bacteria carrying antibiotic resistance genes (ARGs) infiltrate the aquatic environment with sewage from urban treatment plants and livestock production, where the transmission of ARGs occurs between different bacterial species [14]. The prevalence and fate of these bacteria is currently relatively poorly understood. Due to the fact that ARGs are sometimes not completely eliminated during water purification processes [40] and they may be present in drinking water, we should focus on the source of the problem, which is the excessive antibiotic therapy of humans and animals. This paper is emphasizing the problem of antibiotic prevalence in wastewater and the environment.

2. Characteristics of selected antibiotics

Antibiotics are natural, semisynthetic or synthetic substances that act selectively on the cell structure (bactericidal) or the metabolism of microorganisms by inhibiting their growth and cell division (bacteriostatic). Antibiotics are produced by bacteria, actinomycetes, imperfect fungi (fungi imperfecti), rarely by basidiomycetes, lichens, green plants and animal cells [41]. The first discovered antibiotic in history was penicillin, found by Alexander Fleming in 1928. The structure of penicillin G, among other selected antibiotics, is presented in Fig. 1.

Since then, thousands of natural antibiotics were discovered, of which only a small portion may be used for the treatment of humans and animals due to their side effects. Side effects are divided into three basic groups: toxic (to kidney, liver or bone marrow), allergic reactions and dysbacteriosis (imbalance of body's bacterial flora). The consequences of dysbacteriosis are dangerous when microorganisms resistant to antibiotics appear in place of the natural bacterial flora, e.g. staphylococcus, which can even lead to death.

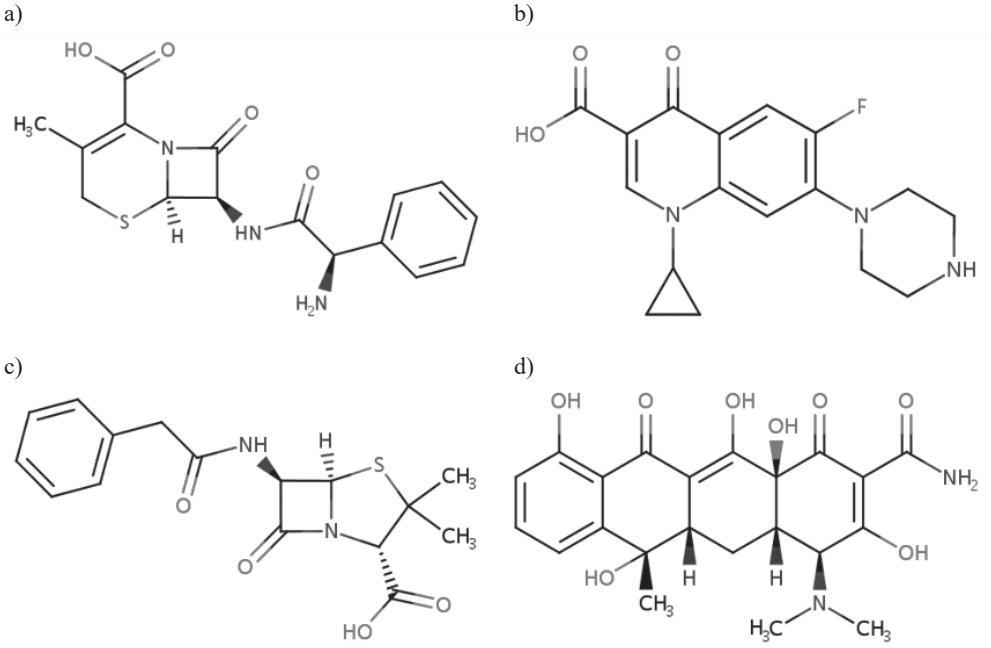

Fig. 1. Structures of selected antibiotics: a) Cephalexin, b) Ciprofloxacin, c) Penicillin G, d) Tetracycline [10]

For this reason, antibiotic therapy should be conducted only under the doctor's supervision and not exceed the recommended and prescribed doses. Table 1 contains the basic characteristics of commonly used antibiotics, which were detected in environmental samples (Table 2).

Table 1

Characteristics of selected antibiotics [10]

Compound	Formula	Molecular mass [g/mol]	CAS	Half-life
Amoxicillin	$C_{16}H_{19}N_3O_5S$	365.404	26787-78-0	1 h
Ampicillin	$C_{16}H_{19}N_3O_4S$	349.405	69-53-4	1 h
Azithromycin	$C_{38}H_{72}N_2O_{12}$	748.985	83905-01-5	68 h
Cefaclor	$C_{15}H_{14}ClN_3O_4S$	367.807	53994-73-3	0.6–0.9 h
Cephalexin	$C_{16}H_{17}N_3O_4S$	347.389	15686-71-2	1 h
Chlortetracycline	$C_{22}H_{23}ClN_2O_8$	478.88	57-62-5	6–9 h
Ciprofloxacin	$C_{17}H_{18}FN_3O_3$	331.342	85721-33-1	4 h
Clarithromycin	$C_{38}H_{69}NO_{13}$	747.953	81103-11-9	3–4 h
Clindamycin	$C_{18}H_{33}ClN_2O_5S$	424.983	18323-44-9	2–3 h

Continue Table 1

Compound	Formula	Molecular mass [g/mol]	CAS	Half-life
Cloxacillin	$C_{19}H_{18}ClN_3O_5S$	435.881	61-72-3	0.5–1 h
Doxycycline	$C_{22}H_{24}N_2O_8$	444.435	564-25-0	18–22 h
Enrofloxacin	$C_{19}H_{22}FN_3O_3$	359.4	93106-60-6	1.5–6 h
Erythromycin	$C_{37}H_{67}NO_{13}$	733.927	114-07-8	0.8–3 h
Lincomycin	$C_{18}H_{34}N_2O_6S$	406.537	154-21-2	4.5–6.5 h
Lomefloxacin	$C_{17}H_{19}F_2N_3O_3$	351.348	98079-51-7	8 h
Norfloxacin	$C_{16}H_{18}FN_3O_3$	319.331	70458-96-7	3–4 h
Ofloxacin	$C_{18}H_{20}FN_3O_4$	361.368	82419-36-1	9 h
Oxytetracycline	$C_{22}H_{24}N_2O_9$	460.434	79-57-2	6–8 h
Penicillin G	$C_{16}H_{18}N_2O_4S$	334.39	61-33-6	0.4–0.9 h
Penicillin V	$C_{16}H_{18}N_2O_5S$	350.39	87-08-1	0.5–0.7 h
Roxithromycin	$C_{41}H_{76}N_2O_{15}$	837.047	80214-83-1	12 h
Sulfadiazine	$C_{10}H_{10}N_4O_2S$	250.277	68-35-9	–
Sulfadimethoxine	$C_{12}H_{14}N_4O_4S$	310.329	122-11-2	–
Sulfamerazine	$C_{11}H_{12}N_4O_2S$	264.304	127-79-7	–
Sulfamethazine	$C_{12}H_{14}N_4O_2S$	278.33	57-68-1	–
Sulfamethizole	$C_9H_{10}N_4O_2S_2$	270.331	144-82-1	3–8 h
Sulfamethoxazole	$C_{10}H_{11}N_3O_3S$	253.278	723-46-6	10 h
Sulfathiazole	$C_9H_9N_3O_2S_2$	255.317	72-14-0	–
Tetracycline	$C_{22}H_{24}N_2O_8$	444.435	60-54-8	6–12 h
Trimethoprim	$C_{14}H_{18}N_4O_3$	290.318	738-70-5	8–11 h
Tylosin	$C_{46}H_{77}NO_{17}$	916.10	1401-69-0	–

3. Occurrence of antibiotics

Figure 2 shows the sources and routes of antibiotic contamination of aquatic and terrestrial environments. Unlike cytostatic drugs [2], the main sources of antibiotic pollution are not be only hospital and household sewage, but also, in an equally high degree, the wastewater from farms and animal production. In most cases, today's animal production is inherently associated with antibiotic therapy and often its main purpose is not so much a fight with possible animal diseases, but to accelerate their growth and ultimately increase production [26]. Hospital wastewater is also one of the main sources of pollution, especially if not pretreated before discharge to the municipal treatment plant. Concentrations of antibiotics in such waste can reach high values (10 000 ng/l cephalexin and 15 000 ng/l ciprofloxacin) [38]. However, the dominant sources of antibiotics are domestic sewage because the majority of infections requiring antibiotics is treated in-home after a visit to the clinic.

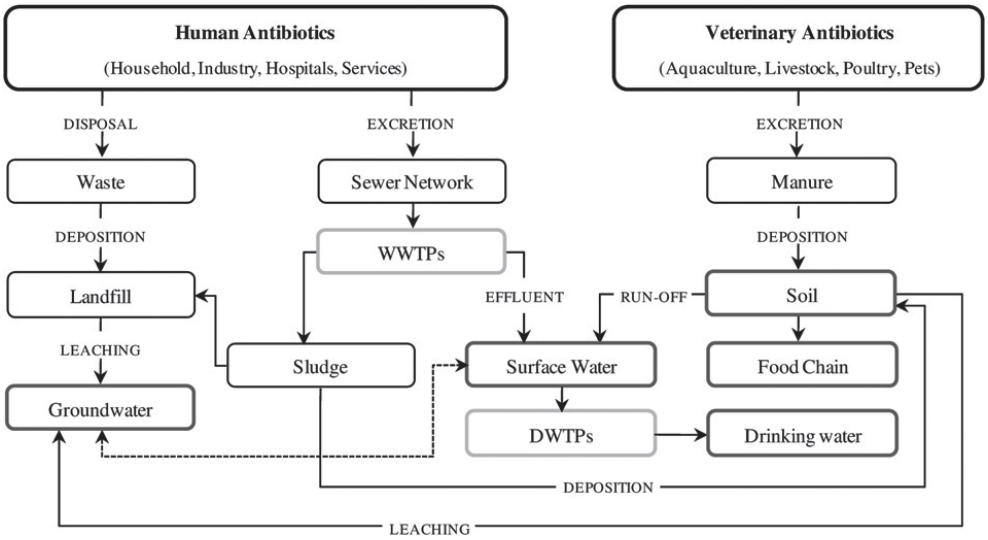

Fig. 2. Origin and principal contamination routes of human and veterinary antibiotics [13]

Excessive prescribing of antibiotics by GPs when it is not absolutely necessary, affects the growth of consumption and, consequently, increases the emissions of antibiotics to municipal treatment plants. Discontinuation of therapy before the scheduled end may cause only a partial elimination of pathogens from the body, while supporting the development of resistance to the antibiotic. Increased resistance to antibiotics poses not only a risk of creating bacterial strains completely resistant to the prescribed therapy, but also the use of increased doses of antibiotics (risk of dysbacteriosis) and the use of subsequent antibiotics when there are no health improvements. It is not surprising that, in the case of some municipal influent samples, the concentrations of antibiotics are higher than in the hospital wastewater (cephalexin 64 000 ng/l, penicillin V 13 800 ng/l, sulfamethoxazole 3000 ng/l, 4300 ng/l trimethoprim) [38].

Ineffective treatment of wastewater containing antibiotics results in their constant emission to effluent receivers. This is confirmed by the analysis of effluents, showing low to very high concentrations of antibiotics in the discharged wastewater effluent (ciprofloxacin 2,050 ng/l [20], ofloxacin 991 ng/l [19], sulfamethoxazole 2,000 ng/l [12], tylosine 3400 ng/l [38]). The result of pharmaceutical emission into the aquatic environment is its contamination and the risk of further migration of pollutants. Table 2 shows a summary of the analysis results showing the presence of antibiotics in the wastewater influents, wastewater effluents, surface and groundwater as well sludge and bottom sediments.

Not only the aquatic environment is being contaminated, as soils are being contaminated as well. One of the possibilities of sewage sludge management is its use in agriculture, which also creates certain risks. Particular attention should be payed to the risk of soil contamination as a result of this kind of sludge usage. Soil contamination can also occur as a result of leaching the residues of antibiotics by precipitation from landfills from animal production. There are known cases of significant antibiotic pollution of soil where the concentrations are higher than in sewage sludge (clarithromycin 67 μg/kg, ciprofloxacin 6–52 μg/kg, tetracycline 450–900 μg/kg) [17].

Table 2

Concentrations (min-max or max) of antibiotics in environmental samples

Compound	Influent (ng/l)	Effluent (ng/l)	Sludge µg/kg	Surface water (ng/l)	Groundwater (ng/l)	Sediments µg/kg
Amoxicillin	18-6940 [19],[38],[43]	30-50[19],[38]		200[38]		
Ampicillin	1805[24]	498[24]				
Azithromycin	98-711 [19],[42]	88-728 [19],[42]	146-599 [42]	2.1-569 [23],[33],[34],[42]	0.5-0.7 [33]	26.8-265 [11]
Cefaclor	6150[38]	1800[38]		200[38]		
Cephalexin	20-64000 [19],[38],[42]	10-1800 [19],[38],[42]		23-100 [38],[42]		
Chlor-tetracycline	0.14-970 [9],[19],[38]	0.3-250 [9],[19],[38]		2.6-68870[15],[17], [18],[32],[33],[38]	58-47444 [15],[33]	698.3[15]
Ciprofloxacin	0.82-1100 [6],[9],[16],[17], [19],[24],[38],[43]	0.4-2050 [9],[19],[16], [20],[24],[43]	2.09[43]	1.3-9660 [3],[11],[8],[15],[20],[32],[33], [34],[35],[38],[43]	0.28-40 [15],[20],[33]	6-2119 [15],[35],[37]
Clarithromycin	17.8-6524 [9],[19],[43]	3.5-621 [9],[12],[19],[43]	156[43]	0.89-2330[11],[12], [17],[23],[33],[34],[43]	0.5-0.7[33]	0.96-3.8 [11],[23]
Clindamycin	5.16-1870 [28],[38]	6.69-952 [28],[38]	2-80.6 [28],[29]	10-1000 [3],[38]		
Cloxacillin	15-4600 [19],[38]	700[38]				
Doxycycline	210-2480 [19],[38]	13.1-915 [7],[19],[38]		5.6-400 [7],[32],[33],[38]	2.7-64.2[33]	
Enrofloxacin	40[38]	2[38]		3.3-978.8 [15],[18],[32],[33],[38]	24.1-182.2 [15],[33]	82.1[15]
Erythromycin	15.5-10000 [6],[9],[16],[19],[21], [24],[43]	20-6000 [9],[12],[16],[19], [21],[43]	185[43]	0.78-3847 [6],[8],[12],[15],[17],[23], [33],[34],[43]	2.3-377.8[33]	2-26.7 [15],[23]
Lincomycin	15.2-1467 [6],[24],[28],[38]	3.92-300 [28],[38]	0.85-174 [28],[29]	19-21100 [6],[17],[38]		
Lomefloxacin				1.1-13.1[32],[33]	2.2-2.3[33]	
Norfloxacin	11.1-964 [6],[9],[19],[38],[42]	0.3-527 [9],[17],[19],[38],[42]	160-370 [42]	6.9-1150[8],[15],[17], [31],[32],[33],[35],[38],[42]	4.5-47.1 [15],[33]	6.8-801 [15],[35]
Ofloxacin	15.7-5560 [6],[7],[9],[19],[42],[43]	0.2-991 [7],[9],[19],[42],[43]	3.4-214 [42],[43]	0.65-11734.6 [6],[7],[8],[15],[31],[32] [33][34],[35],[42],[43]	1.9-382.2 [15],[33]	2.7-370.6 [15],[35],[37]
Oxytetracycline	0.2-350 [6],[9],[19],[38]	0.1-70[9],[38]		1.23-361107 [11],[15],[18],[32],[33],[38],[43]	4.1-1364.7 [15],[33]	162673[15]
Penicillin G	10[38]	300[38]		250[38]		
Penicillin V	160-13800 [19],[38]	80-2000[19],[38]		10[38]		
Roxithromycin	4.3-1500 [9],[19],[38],[42]	2.8-1000 [9],[12],[19],[38],[42]	14-87[42]	2-2251.6 [6],[12],[15],[17],[33],[38],[42]	2.9-146.2 [15],[33]	2581.8[15]

Continue Table 2

Compound	Influent (ng/l)	Effluent (ng/l)	Sludge µg/kg	Surface water (ng/l)	Groundwater (ng/l)	Sediments µg/kg
Sulfadiazine	0.14-5150 [7],[9],[19],[24]	15.3-194 [9],[19],[24]		1.3-4130 [7],[15],[17],[32],[33]	9.6-46.3 [15],[33]	5.6[15]
Sulfadimethoxine	0.2-460[9],[19]	0.02-2.1[9]		1.1-80[18],[32]		
Sulfamerazine	0.4-1530[9],[19]	3,6[9]		4.5-11.0[15],[33]	0.6-7.0[33]	5.7[15]
Sulfamethazine	1.1-4010 [6],[7],[9],[16],[19]	0.5-6.2[9]		0.7-580.4 [6],[7],[15],[18],[32],[33]	0.4-240 [12],[17],[33]	2.2[15]
Sulfamethizole	0.6-7.3[9]	0.3-1.2[9]				
Sulfamethoxazole	0.4-7910 [6],[7],[9],[16],[19],[21], [24],[28],[38],[43]	0.3-2000 [1],[7],[9],[12],[16], [19],[20],[21],[24], [27],[28],[38],[43],	31[28]	0.2-6000 [3],[6],[7],[8],[12],[15],[17],[18], [20],[21],[23],[31],[32],[3 3],[34], [35],[36],[38],[43]	0.1-1110 [12],[15],[17],[20], [21],[22],[33],[35]	2.4[15]
Sulfathiazole	0.8-10570 [9],[19],[38]	0.4-600 [9],[19],[38]		3.7-123 [38],[15],[33],[18]	1.4[33]	1.7[15]
Tetracycline	0.1-1300 [6],[9],[16],[19],[38]	0.09-850 [9],[16],[19],[38]		7.2-25537 [3],[38],[15],[33],[18],[32]	6-1082 [15],[17],[33]	6.5-16799 [15],[35]
Trimethoprim	0.14-6800 [6],[9],[16],[19],[21] [24],[28],[30],[38]	0.7-3050 [9],[12],[16],[19],[20] [21],[24],[27],[28],[38]	6.7-7.4 [29]	0.1-1808 [3],[6],[8],[12],[15],[17],[18], [20],[21],[23],[31],[33],[34], [35],[36],[38]	1.4-18 [15],[20],[21],[33]	1.6-87.55 [15],[22],[35]
Tylosin	44-60[6],[38]	3400[38]		9-187[6],[15],[17],[38]		11.2[15]

Unlike other types of pharmaceuticals and similar to estrogen [25], some antibiotics have negative effects on aquatic organisms at relatively low concentrations. PNEC (Predicted No Effect Concentration) estimated for ciprofloxacin, ofloxacin, sulfamethoxazole and tetracycline are respectively 5, 11.3, 27 and 90 ng/l [15]. It means that, in the analyzed natural water samples, concentrations of antibiotics significantly exceeded (220x for sulfamethoxazole, 280 for tetracycline, 1900x for ciprofloxacin) the level estimated as safe for the tested organisms. Regarding the concern for the environment and aquatic organisms that live in it, we should not allow the continuous emission of antibiotics into the environment.

The presence of antibiotics in the source water for the water purification plants poses a risk of exposure to consumers of drinking water. Even very low levels of antibiotics consumed with the water can have a negative impact on the human body and its natural bacterial flora. In addition, it should be kept in mind that a low dose of antibiotic will not be able to eliminate pathogens from the body, and at the same time can support the formation of resistance to antibiotics. Unfortunately, antibiotics infiltrate into the water intended for human consumption, as it was confirmed by analysis - 0.2 ng/l clarithromycin, 5 and 13.8 ng/l erythromycin, 19.8 ng/L trimethoprim [5] and 12.7, 13.7 [5] and 66 ng/l sulfamethoxazole [17].

4. Conclusions

Antibiotics are commonly found in the environment, which is the result not only of excessive consumption of pharmaceuticals in health care, but also their use in animal production to increase productivity. The data from Table 2 shows that antibiotics have the potential to pollute almost every part of the aquatic environment – surface waters, groundwater, bottom sediments. The first step to protect the environment should be preventive measures to reduce the use of antibiotics or possibly withdraw them from use if they are not absolutely necessary. It seems crucial to point out that agriculture is a big contributor to antibiotic pollution of the natural environment and withdrawing from excessive use of antibiotics in farms would be beneficial not only for the environment, but also for consumers of the produced meat.

Next, hospital wastewater should be initially pretreated, with particular focus put on the elimination and degradation of antibiotics before their discharge to municipal treatment plants. Another source of antibiotics, the household sewage, is a problem far more difficult to solve. Reducing consumption of antibiotics in households requires a greater awareness of primary care physicians and choosing the therapy without the use of antibiotics. The sewage system for households is incomparably more diffused than in the case of hospitals – hospital waste produced by all patients can be collected and purified. For residential development, such a possibility does not exist. The only possibilities of elimination of antibiotics from household sewage are efficient and effective processes used in municipal wastewater treatment plants.

Unfortunately, not all antibiotics are effectively eliminated from the wastewaters, thus environmental pollution occurs. Antibiotics present in surface waters, being the effluent receivers, seep into groundwater, accumulate in the sediments, and in some cases, they penetrate into the drinking water. In these cases, there is a risk of unconscious antibiotic consumption at very low doses, which may lead to the formation of resistance to the consumed antibiotic. We should make every effort to decrease the emission of antibiotics into the environment, for example by improving the efficiency of municipal wastewater treatment processes.

Although it seems natural to focus primarily on providing the highest purity and quality of drinking water, it should not be our only goal. Ignoring the problem of antibiotic pollution of the environment, especially water, can have serious consequences, such as the development of resistance of pathogenic bacteria and wide transfer of resistance genes between different types of bacteria. The emergence of strains of pathogenic bacteria resistant to most or at least some of the antibiotics used in therapy poses a very serious threat to human life and health.

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