Vol. 18(1); May - June 2024

Despre Jurnalul nostru – 2024

About our Journal – 2024

Înființat acum 17 ani, Jurnalul *Medicamentul Veterinar / Veterinary Drug,* rămâne o prezența activă în peisajul revistelor de profil veterinar din țara noastră.

Concepută că un instrument de informare, revista prezintă rememorări valoroase în secțiunea “Educație continuă”, și date inedite în secțiunea “Lucrări originale”.

Parcursul revistei de alungul a aproape două decenii a atras indexarea în bazele de date internaționale, la această oră *Medicamentul Veterinar* fiind indexata BDI în numeroase surse, dintre care:

- Index Copernicus international (ICI),
- DOAJ,
- EBSCO,
- CABI,
- CiteFactor,
- Advanced Sciences Index (ACI), etc.

Concepută intr-un format prietenos, cu ergonomia spațiului și cu teme de interes jurnalul aduce noutăți în domeniul științelor farmaceutice veterinare cu toate aspectele specifice ale industriei medicamentului de uz veterinar.

Revista Asociației Naționale a Fabricanților de Produse de uz Veterinar își aduce aportul astfel la dezvoltarea și promovarea științelor medicale veterinare și implicit dezvoltarea medicinii!

Pe această dorim să mulțumim tuturor autorilor care au considerat revista noastră ca pe un bun mediu de publicare al ideilor și studiilor efectuate.

În speranța că jurnalul va rămâne în preferințele cititorilor și ale viitorilor autori vă dorim succes profesional, bunăstare și multă sănătate!

Founded 17 years ago, Jurnalul Medicamentul Veterinar / Veterinary Drug remains an active presence in the landscape of veterinary magazines in our country.

Conceived as an information tool, the magazine presents valuable memories in the "Continuing Education" section, and new data in the "Original Works" section.

The course of the magazine spanning almost two decades has attracted indexing in international databases, currently Medicamentul Veterinar is indexed by the BDI in numerous sources, among which:

- International Copernicus Index (ICI),
- DOJ,
- EBSCO,
- CABINETS,
- CiteFactor,
- Advanced Sciences Index (ACI), etc.

Designed in a friendly format, with space ergonomics and topics of interest, the journal brings news in the field of veterinary pharmaceutical sciences with all the specific aspects of the veterinary drug industry.

The Journal of the National Association of Veterinary Products Manufacturers thus contributes to the development and promotion of veterinary medical sciences and implicitly the development of medicine!

On this we would like to thank all the authors who have considered our journal as a good medium for publishing their ideas and studies.

In the hope that the journal will remain in the preferences of readers and future authors, we wish you professional success, well-being and good health!

Romeo T. Cristina
Head Editor

▼ *Educatie continuă / Continuous education*

Probiotics in fish nutrition: benefits and applicability

Probioticele în nutriția peștilor: beneficii și aplicabilitate

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***Key words*:**, probiotics, nutrition, aquaculture, antibiotic resistance, food industry, immunomodulation.
***Cuvinte cheie*:** probiotice, nutritie, acvacultura, antibiorezistenta, industria alimentara, imunomodularea.

Abstract

Probiotics play an essential role in fish nutrition, significantly contributing to their health and growth in aquaculture. By incorporating beneficial bacterial strains such as *Lactobacillus* and *Bacillus subtilis* into feed, the nutritional value of the feed is enhanced, enzymatic digestion is optimized, and pathogenic microorganisms are inhibited. Probiotics stimulate the immune response, increase intestinal microbial diversity, and have anti-mutagenic and anti-carcinogenic effects. Modern administration methods include bioencapsulation and the use of live foods, thus ensuring the probiotics' survival and effective colonization in the fish's digestive tract. Therefore, using probiotics in fish nutrition not only improves growth performance and health but also promotes sustainable and ecologically efficient aquaculture.

Rezumat

Probioticele joacă un rol esențial în nutriția peștilor, contribuind semnificativ la sănătatea și creșterea acestora în acvacultură. Prin includerea tulpinilor bacteriene benefice în furaje, cum ar fi Lactobacillus și Bacillus subtilis, se îmbunătățesc valorile nutritive ale furajelor, se optimizează digestia enzimatică și se inhibă microorganismele patogene. Probioticele stimulează răspunsul imunitar, cresc diversitatea microbiană intestinală și au efecte anti-mutagenice și anti-carcinogene. Metodele moderne de administrare includ bioîncapsularea și utilizarea alimentelor vii, asigurând astfel supraviețuirea și colonizarea eficientă a probioticelor în tractul digestiv al peștilor. Astfel, utilizarea probioticelor în alimentația peștilor nu doar îmbunătățește performanța de creștere și sănătatea acestora, ci și promovează o acvacultură sustenabilă și eficientă din punct de vedere ecologic.

1. Modern methods of administration of probiotics in fish feed

The concept behind the composition of probiotics in feed is to apply the beneficial bacterial strains in the feed using binding agents such as eggs and cod liver oil, to achieve beneficial microbial effects with more efficiency and a reduced environmental cost.

Most commercial preparations contain either *Lactobacillus* or *Saccharomyces cerevisiae*, nitrifying bacteria, *Streptococci*, *Roseobacter* and *Bacillus sp.* Beneficial effects of regular use of probiotics in fish feed in the UK and other European countries have been reported [3].

Fig.1. *Artemia shrimp* - **Source:** https://tropical-fish-keeping.com/wp-content/uploads/2018/10/Brine-Shrimp-Artemia.jpg [60]

In aquaculture, probiotics can also be encapsulated in feed or live foods such as rotifers and *Artemia* crustaceans [36].

Another effective application of probiotics for aquatic animals is through bioencapsulation or infusions in diets. Probiotic organisms used in food must be able to survive passage through the digestive tract, they must withstand gastric juices and exposure to bile. In addition, probiotics must be able to proliferate and colonize the digestive tract to be safe, effective, and to maintain their efficacy and potency throughout the shelf life of the product [5].

Fig. 2. *Euchlanis dilatata* – Rotifer – **Source:** https://www.canadiannaturephotographer.com/rotifers.html [61]

The benefits of including bacterial strains in feed ingredients include improved feed values, contribution to enzymatic digestion, inhibition of pathogenic microorganisms, anti-mutagenic and anti-carcinogenic activity, growth promoting factors and improved immune response.

Regarding the effects of *Bacillus subtilis* probiotics on intestinal microbial diversity and immunity of the *Epinephelus coioides* group of fish, it was shown that the innate cellular response and respiratory activity of the supplemented groups were significantly higher compared to the control group at 10 and 20 days after feeding and even more significant at 30 days [7].

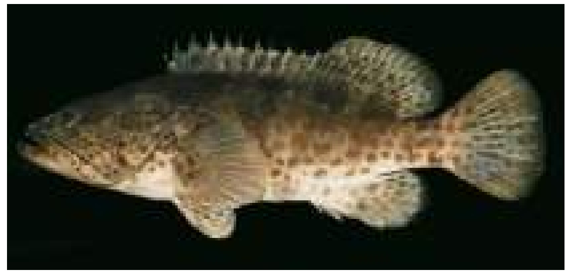

Fig. 3. Estuary cod **-** *Epinephelus coioides* – **Source:** *https://indiabiodiversity.org/species/show/232208* [62].

The probiotic *B. Subtilis* increases intestinal microbial diversity by stimulating the bacterial populations of *Paenibacillus sp., Lactobacillus oeni* strain 59b and *Methylacidiphilum infernorum* strain V4, which are beneficial to *E. coioides*.

The best dose of *B. subtilis* probiotic, based on growth performance, innate cellular responses and gut microbial profile of fish, is 0.1%, which showed equal efficacy to 1% diet.

Thus, the use of feed probiotics in aquaculture has opened up the possibility of sustainable commercial aquaculture [18].

2. Use of probiotics to increase feed efficiency in aquaculture

Certain probiotics and prebiotics can promote proper digestion, increase immune response, maintain water quality, and act as promoters of aquatic animal growth, survival, and health. In aquaculture, the intestines, gills, mucus on the skin of aquatic animals and their habitat, or even culture collections and commercial probiotic and prebiotic products can be Gram-positive and Gram-negative, as well as non-bacterial, such as bacteriophages, microalgae and yeast.

Finally, probiotic applications may include multiple strains or even a combination of prebiotics, symbiotics and live foams [47].

The use of probiotics can increase productivity in aquaculture, having beneficial ecological effects that can resist a wide range of pathogens and control infections.

Current research on probiotics for aquaculture, due to dietary supplementation with live microorganisms, shows improvements in intestinal digestibility and immune system in animals.

Probiotics can combat pathogenic bacteria such as *Lactobacillus sp., Bifidobacterium, Lactococcus and Streptococcus sp.* [10].

Aquatic animal protein contributes 43% to the global supply of animal protein, and the importance of aquaculture in the evaluation and decisions related to fish, mollusk and crustacean production is well recognized.

Fig. 4. Catfish (*Silurus glanis)* – **Source:** https://naturescu.com/wp-content/uploads/2021/06/Tipuri-de-peste-somn [63].

Probiotics, such as lactic acid bacteria and *Bacillus sp*., are ecological supplements in animal feed, reducing pathogen levels without side effects and improving digestibility and growth of cultured organisms [11].

Vibrio parahaemolyticus affects the development of aquaculture, and food additives have shown that seafood is a source of probiotics that act against Gram-positive and Gram-negative bacteria.

Various microorganisms, such as *Streptomyces panacagri and Streptomyces flocculus*, improve digestibility and act as antagonistic probiotics against foodborne pathogens, providing an alternative to antibiotics [6].

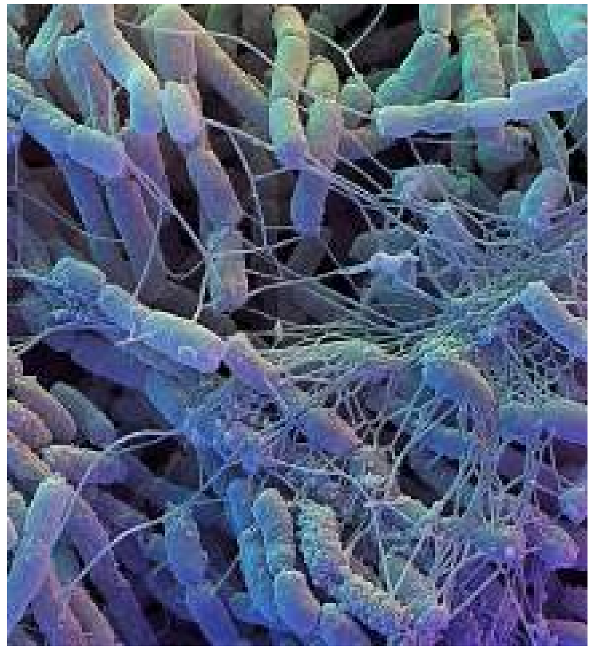

Fig. 5. *Streptomyces spp.* – **Source:** David Scharf / Science photo library [64].

The intestine of healthy marine fish contains bacteria with antimicrobial effects and a broad spectrum of antimicrobial activity in strains of lactic acid bacteria, such as *Lactococcus lactis sp. lactis,* two *Enterococcus sp., Lactobacillus plantarum and Leuconostoc mesenteroides sp. mesenteroides*, which are effective against aquaculture pathogens including *Vibrio harveyi, V. splendidus* and *Photobacterium damselae*.

Actinomyces sp. isolated from marine sediments has demonstrated probiotic-like properties in several *in vitro* tests [9].

Although probiotics also contain bacteriocin, a bioactive compound, it was collected from marine animals and contains antibiotic peptides that fight pathogens [23].

The marine environment provides a wide variety of *Streptomyces* that can be used as probiotics in aquaculture. The MSU3IR mechanism of *Lactococcus gravieae* and *Lactobacillus sp*. increased bacteriocin levels, thereby inhibiting the pathogen *Listeria monocytogene* in shrimp.

Bacillus subtilis strain MMA7, isolated from the marine sponge *Haliclona simulans*, exhibits broad-spectrum antimicrobial activity against both Gram-positive and Gram-negative pathogens, as well as various pathogenic *Candida* species.

This antimicrobial effect is partly attributed to a newly discovered lantibiotic, which has been named subtilomycin. [19].

Fig. 6. *Haliclona simulans* – **Source:** https://inpn.mnhn.fr/espece/cd_nom/71649?lg=en [65].

2.1. The most widely used probiotics in feed

Probiotic microorganisms have beneficial effects on the gastrointestinal tract of aquatic animals, aiding in the digestion of dietary nutrients and energy production. The most common probiotic preparations used for this purpose are lactic acid bacteria [22].

The improvement in nutrient digestibility is due to the increased level of digestive enzymes (protease, amylase, cellulase, phytase, etc.) produced by the probiotic-modified intestinal microbial community in the host.

For example, some bacteria (*Rhodobacter sphaeroides* and *Bacillus sp.)* contribute effectively to digestion processes by significantly activating protease, lipase, amylase and cellulase enzymes in white shrimp (*Litopenaeus vannamei*) and bivalves [8].

Fig. 7. *Litopenaeus vannamei* – **Source:** https://euimg.eworldtrade.com/uploads/user_products/4/8/product-680338-g-0-t-1561046610-o.jpg [66]

In addition, recent studies have shown that probiotics can stimulate nutrient absorption by increasing the surface area of the host's gastrointestinal tract, based on quantitative changes in histological measurements of the area of intestinal folds, enterochromaffin cells, and microvilli [59].

To date, several bacteria (*Pseudomonas sp., Brevibacterium sp., Microbacterium sp., Agrobacterium sp. and Staphylococcus sp*.) have been reported to aid nutritional and metabolic physiology in Arctic trout (*Salvelinus alpines*) [44].

Different bacterial strains in the form of probiotics also contribute significantly by modulating the intestinal microbial population of host organisms, especially by synthesizing essential fatty acids, minerals, vitamins and amino acids [37].

Fig. 8. Arctic trout (*Salvelinus alpines)* **Source:**https://www.flickr.com/photos/72616463@N00/3798548888/ [67]

2.2. Bioencapsulation of probiotics in feed

Bioencapsulation involves encasing tissues or biologically active substances in a semipermeable membrane to protect enclosed biological structures from potentially hazardous processes in the immediate environment.

The field of application of bioencapsulation is wide. Bioencapsulation or bioenrichment is a process that can improve the nutritional status of living food organisms, either by feeding them or by incorporating them with various types of nutrients [35].

Probiotic encapsulation technology has the potential to protect microorganisms and deliver them to the gut. However, the inoculation of probiotics by bioencapsulation in live food such as microalgae, rotifers and Artemia is an interesting approach, although the administration process through enriched live food does not appear to be economically viable and is difficult to achieve in large-scale aquaculture practices. It is feasible to use microalgae cultures as vectors for the introduction of bacterial antagonists to combat bacterial pathogens in aquaculture [55].

However, the influence of the bacteria brought by the live food organisms was particularly dramatic during the first feeding. Following a study, the effects of different concentrations of probiotic *Bacillus spp.* at different intervals of bioencapsulation on the growth performance and survival rate of Persian sturgeon larvae were evaluated (*Acipenser persicus*).

Fig. 9. Persian sturgeon (*Acipenser persicus)*
Source: https://animalesenpeligrodeextincion.eu/wp-content/uploads/Acipenser-persicus1.jpg [68]

This study demonstrated significant conversion efficiency ratio, specific growth rate, feed conversion ratio, condition factor and daily growth coefficient ($p < 0.05$). However, the survival of all groups was not significantly different after 28 days [46].

An alternative would be the technique of controlled transfer of immunostimulants by incorporating *Artemia* and rotifers into live food.

After 12-24 hours of enrichment of newly hatched *A. franciscana* with a lipid source, a significant increase in the content of unsaturated fatty acids (HUFA) is detected. Thus, it was reported that *Bacillus subtilis and Lactobacillus plantarum* bioencapsulated in *Artemia* achieved good results against vibriosis [33].

Lactobacillus rhamnosus GG of human origin was used on tilapia (*Oreochromis niloticus*) to study growth performance, intestinal mucosal immunity, and humoral and cellular immune response, and a feeding experiment was performed by directly incorporating the bacteria into dry commercial pellets, having favorable results on their development and reproduction [12].

Fig. 10. Tilapia (*Oreochromis niloticus*).
Source: https://fish-commercial-names.ec.europa.eu/fish-names/species/oreochromis-niloticus_ro [69]

3. Improving growth performance and health of fish by administration of probiotics

The intestinal environment provides a favorable habitat for indigenous microorganisms, providing them with space, attachment sites, and nutrition. Balanced microbial communities are very important for maintaining gut health.

During disease, the natural microbial communities in the gut are disrupted, leading to various health problems.

Fish live in an environment surrounded by a vast population of pathogenic bacteria, fungi and deadly viruses. Restoring gut microbial communities by supplementing the diet with probiotics is an effective method to improve fish health [43].

However, the selection of probiotics varies significantly from one fish species to another to maintain the correct ratio of good to bad bacteria in the intestinal mucosa.

To date, several bacterial candidates have been tested for probiotic potential; however, several candidates from the genera *Bacillus, Micrococcus, Enterococcus, Phaeobacter, Shewanella,* lactic bacteria, and *Pseudomonas* have gained popularity in manipulating gut flora in fish.

In one study, the beneficial effects of three probiotics (*Shewanella sp*. AFG21, *Bacillus sp.* AHG22 and *Alcaligenes sp. AFG22*) were reported in *Tor tambroides*, which are able to alter the microbial composition in favor of beneficial bacterial populations [27].

Fig. 11. A species of carp (*Tor tambroides*).
Source: https://laukkancra.blogspot.com/2012/12/red-mahseer-tor-tambroides.html [70]

Several articles have reported that probiotics have positive effects on growth performance. For example, an indigenous LAB strain probiotic was mixed into the feed, while another indigenous *Bacillus* strain was added to the growth system, and both probiotics were combined for testing in tilapia culture.

This approach resulted in higher final fish weight, higher absolute growth rate and higher specific growth rate than in the control group. In addition, potential probiotics have been reported to produce high efficiency in low-protein diets, which may reduce production costs [15].

Moreover, different probiotic properties (high adherence and low adherence) showed different effects on feed conversion ratio and weight gain of hybrid tilapia.

Adverse effects of probiotics include reports of reduced growth in the fry stage of tilapia. In other studies, it was reported that supplementation of feed for pangasius fish (*Pangasianodon hypophthalmus*) with *S. cerevisiae* probiotic in freeze-dried microencapsulated form had major favorable effects on feed conversion ratio and growth performance was significantly improved [2].

Fig. 12. Pangasius (*Pangasianodon hypophthalmus*).
Source: https://www.fishhobbyist.net/2022/01/getting-to-know-pangasianodon.html [71]

The probiotic *Acinetobacter* KU011TH, used as a feed additive, produced improvements in growth performance and better survival rate in bighead catfish (*Clarias macrocephalus*) [14].

A previous study reported that the probiotic-supplemented diet in rainbow trout was highly effective in increasing the population of the beneficial bacteria *Bacillus subtilis* [25].

Fig. 13. Rainbow trout (*Oncorhynchus mykiss*).
Source: http://underwater-fish.blogspot.com/2011/11/rainbow-trout-oncorhynchus-mykiss.html [72]

It was also reported that colonization of *B. subtilis* on the intestinal epithelial surface conferred protection (increased immunity, reduced oxidative stress, increased serum lysozyme concentration and enhanced phagocytic activity of specialized cells) against pathogenic strains of *Aeromonas sp* [42].

In the same direction, a study performed on four species of fish (*Poecilia sphenops, Xiphophorus maculates, Poecilia reticulate and Xiphophorus helleri)* fed a diet containing *B. subtilis* reported an increase in the population of *B. subtilis* on the surface of the intestinal mucosa [38].

Fig. 14. Molly fish (*Poecilia sphenops*)
Source: https://aquaria.pro/product/poecilia-sphenops. [73]

Recently, the effects of two probiotic strains *Bacillus subtilis and Rhodococcus sp.* were evaluated on the intestinal microbiota of the species *Oreochromis niloticus*. The results of the study indicated a significant change in the intestinal microbial community (increase in the percentage of *Proteobacteria and Bacteroidetes*) in fish fed probiotics compared to those in the control group. The study also reported that bacteria belonging to the *Proteobacteria* family are important members as they are involved in the mineralization of organic compounds and nutrient recycling in fish [19].

The ability of two probiotics to restore gut microbiota was also tested in antibiotic-treated black molly fish (*Poecilia sphenops*). The results of the study indicated that both probiotic candidates (*Phaeobacter inhibens S4Sm and Bacillus pumilus RI06-95Sm*) were able to restore the microbial community to normal [14].

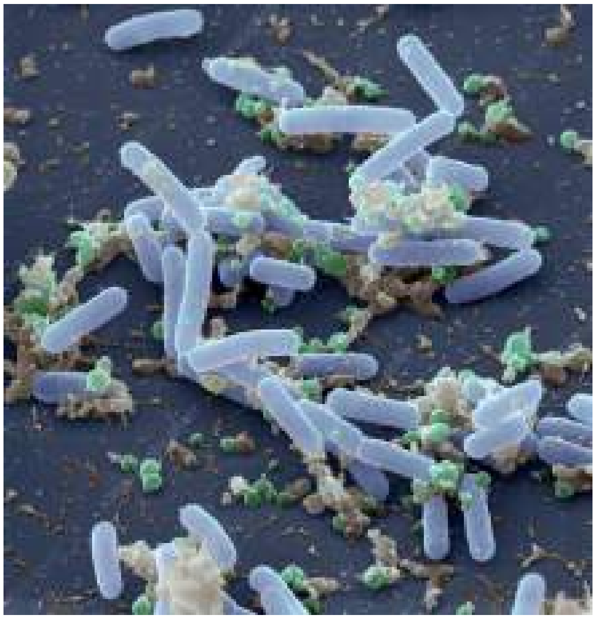

Fig. 15. *Bacillus pumilus* RI06-95Sm
Source:https://www.sciencephoto.com/media/12402/view [74]

Among the many probiotic strains, lactobacilli groups as probiotics in aquaculture have been extensively studied. It is well established that lactobacilli have a high colonization capacity and thus maintain for a longer period on the intestinal epithelial surface, conferring greater beneficial effects on the host and the intestinal microbiota [48].

Research in germ-free fish models has indicated that probiotics together with environmental factors have a large impact on the modulation of gut microbiota in terms of antibody production, stress release and resistant colonization. The ability of probiotics to manipulate the gut microbiota depends on several external/environmental (water quality, temperature and pH) and internal (fish age, probiotic binding strength, duration of probiotic-supplemented diet, administration system, etc.) factors. Changing any of these factors can affect the effectiveness of probiotics [13].

3.1. The role of probiotics in improving the immunity of aquaculture fish

Probiotics play a beneficial role as immunostimulators, helping to protect aquaculture species by reducing the impact of disease and preventing the entry of pathogens [20]. Thus, their use as immunostimulants is a very practical approach to improve success in aquaculture. Many authors have confirmed the use of probiotics to increase immune response, disease resistance and reduce malformations in carp species [17].

Their possible mechanism of action includes cellular and humoral immune responses, and the expression of IL-1b, TNFα and lysozyme-C increases when fish are fed a diet enriched with *Aeromonas veronii, Vibrio lentus and Flavobacterium sasangense* [30].

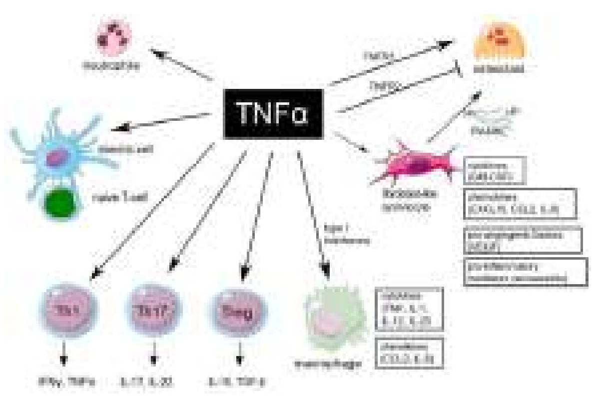

Fig. 16. TNFα (tumor necrosis factor) is a pleiotropic cytokine, which is involved in the function of various cells
Source: https://encyclopedia.pub/entry/20537 [75]

An experimental report claimed that probiotics, supplemented at 10 CFU/g diet for 2 weeks, act as immunomodulators by binding MAMPs (microorganism-associated molecular patterns) to pathogen pattern recognition receptors (PRRs) on immunogenic cells such as dendritic cells and macrophages, triggering an intracellular signaling cascade that leads to the release of specific cytokines and interleukins by activated T cells to exert antiviral, pro- or anti-inflammatory effects. Unfortunately, the specific role of probiotic supplementation on the expression of immunological parameters is not yet fully understood. [21].

3.2. Antiviral properties on aquaculture fish

Although data indicate that virus inactivation can occur by means of extracts from various probiotic bacterial strains in aquaculture, the exact mechanism by which they exert their action is not known. It is well established that probiotics such as *Pseudomonas sp. and Vibrios sp.* are highly effective against infectious hematopoietic necrosis virus (IHNV) [31].

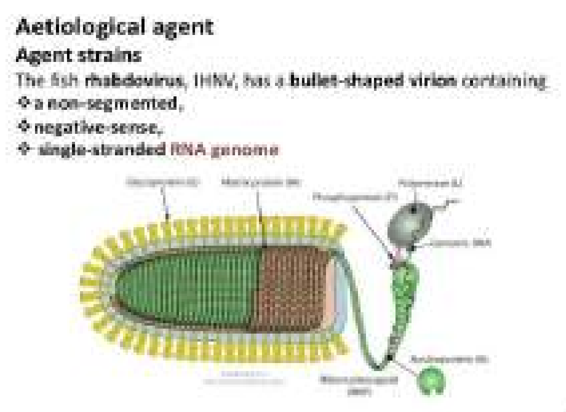

Fig. 17. Infectious hematopoietic necrosis virus
Source:https://www.slideshare.net/slideshow/infectious-heamopoietic-necrosis-virus/69788210 [76]

Moreover, *Paralychthys olivaceus* fed on food supplemented with Sporolac (*Lactobacillus sp.*) develops resistance against lymphocystic disease virus (LCDV). Similar experiments also demonstrated the increased power of resistance to viruses in grouper fish fed with the probiotic strain *Bacillus subtilis* E20 [22].

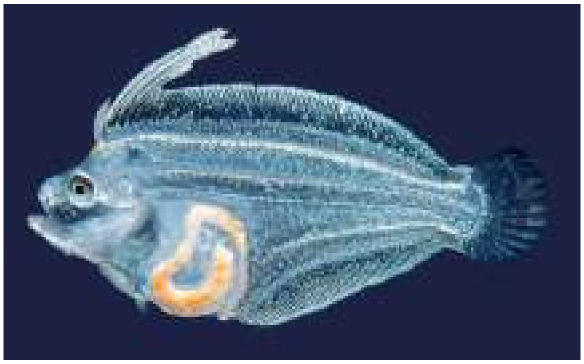

Fig. 18. A species of halibut (*Paralychthys olivaceus*)
Source:http://www.fishbiosystem.ru/PLEURONECTIFORMES/Paralichthyidae/Paralichthys_olivaceus2.html [77]

4. Probiotics and gut microbial diversity in fish

The main function of the gastrointestinal (GI) tract consists in the processes of digestion and absorption of nutrients present in the intestinal lumen. In addition to these nutrients from food, exogenous microorganisms such as bacteria, fungi, parasites and viruses can also enter the intestine.

The abundance of innate immune cells and adaptive immune cells that coexist with the trillions of beneficial commensal microorganisms in the gastrointestinal tract dictates the need for an effective barrier.

This barrier has the role of regulating host-microbiome interactions and maintaining tissue homeostasis.

4.1. Intestinal flora stimulant

Several researchers have reported that probiotics significantly stimulate gut microbiota to produce more metabolites, including short-chain volatile fatty acids, which play a vital role in maintaining gut health in fish.

Research has also shown that gut microbiota modulation by probiotics is not limited by fish age and maturity, as probiotics confer beneficial effects on all age groups, from larvae to adults [40].

5. Efficacy of probiotic strains in combating pathogens in aquaculture

5.1. Gram-positive bacteria

5.1.1. *Lactobacillus*

In an experiment, the diet of Indian white shrimp (*Penaeus indicus*) was supplemented with a single dose (5 × 10^6 CFU g−1) of various probiotics, including *Lb. acidophilus, S. cremoris, Lb. bulgaricus 56, or L. bulgaricus 57*, for 4 weeks.

At the end of the feeding period, the shrimp were experimentally exposed to *Vibrio alginolyticus* infection.

Fig. 19. *Vibrio alginolyticus*
Source: https://kswfoodmicro.com/category/vibrio-albensis/ [78]

The results showed significantly higher resistance (56–72%) compared to the control group (20%). Also, supplementing the diet with 10^10 CFU kg−1 of *Lb. plantarum* increased proPO and PE gene expression, improved PO and SOD activities, as well as resistance against *V. alginolyticus* in white shrimp [1]. In addition, a *Lactobacillus sp.* has been reported to improve survival (72%) and performance of the pearl mussel, *P. mazatlanica* [50].

Fig. 20. Mazatlan pearl oyster (*Pinctada Mazatlanica*)
Source: https://www.pearl-guide.com/threads/a-review-the-history-of-pearls-in-the-gulf-of-california-mexico-part-3.453033/ [79]

In a study with juvenile tiger shrimp (*Penaeus monodon*), Lb. acidophilus 04 (10^5 CFU g−1) administered for one month increased resistance (80% survival) after exposure to the pathogenic *V. alginolyticus* [4].

Fig. 21. Tiger prawns (*Penaeus monodon*)
Source:https://animaldiversity.org/accounts/Penaeus_monodon/ [80].

Feeding *E. faecium* MC13 and *Lactococcus garvieae* B49 protected post-larval shrimp, *P. monodon, against V. harveyi and V. parahaemolyticus* challenges. Similarly, feeding blue shrimp (*Litopenaeus stylirostris*) with the probiotic *P. acidilactici* increased protection against *V. nigripulchritudo* SFn1; mortality in the probiotic and control groups was 25% and 41.7%, respectively [29].

Fig. 22. Blue shrimp (*Litopenaeus stylirostris*)
Source: https://theoceaninsider.com/seafood-guide/blue-shrimp-everything-you-need-to-know-about-genus-neocaridina/ [81]

5.1.2. *Bacillus*

To study the protective effects of *Bacillus subtilis* BT23, black tiger shrimp were treated with 10^6-10^8 CFU ml−1 probiotic for 6 days and then challenged with *V. harveyi* infection. The results showed a significantly lower mortality in the treated groups [41]. One study attempted the combined administration of two probiotic strains (*B. subtilis* L10 and G1) to juvenile white shrimp, which were fed two levels of 10^5 and 10^8 CFU g−1 of selected probiotics for 8 weeks.

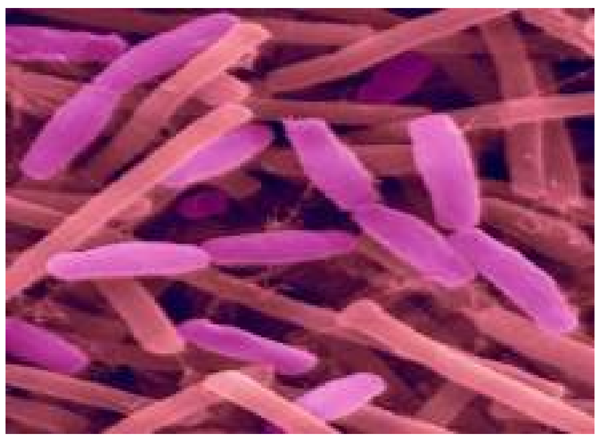

Fig. 23. *Bacillus subtilis* BT23
Source: Dennis Kunkel Microscopy/science Photo Library [82]

At the end of the feeding period, increased growth performance, digestive enzyme activity, up-regulated immunity-related genes, as well as resistance against V. harveyi were observed [53].

5.2. Gram-negative bacteria

5.2.1. *Vibrio*

In vitro research demonstrated inhibition of the growth of shrimp pathogens by the probiotic *V. gazogenes* NCIMB 2250.

Feeding white shrimp a diet supplemented with *V. gazogenes* NCIMB 2250 improved performance and health status, as well as reduced the number of *Vibrio sp*. in the intestinal microbiota.

Also, *Vibrio* NE17 isolated from egg samples improved the performance and immune parameters of the freshwater shrimp, *Macrobrachium rosenbergii* [58].

Furthermore, in marine gastropod mollusks, the combined administration of three probiotics (*Vibrio sp.* C21-UMA, *Agarivorans albus* F1-UMA and Vibrio sp. F15-UMA) using the macroalga *M. integrifolia* as a vector significantly increased survival over a period of 210 days [51].

Fig. 24. *Macrocystis integrifolia* algae
Source: https://www.inaturalist.org/taxa/528651-Macrocystis-integrifolia [83].

5.2.2. *Streptomyces*

The use of marine *Streptomyces* strains (CLS-28, CLS-39) in *Artemia* culture significantly increased the resistance of *Artemia* adults against *V. harveyi and V. proteolyticus* species, and adding 1% *Streptomyces* to the diet of black tiger shrimp postlarvae for 15 days, resulted in improved resistance against *V. harveyi* and growth performance in probiotic-fed shrimp [52].

6. Probiotics as a strategy for sustainable aquaculture

The future growth of the aquaculture industry will face many challenges, including biological challenges and legislative pressures, and sustainability will be supported by the use of natural feed additives, ensuring long-term profitability.

In this context, algae culture is above all a production method that contributes to potential solutions and to the sustainability of aquaculture, having a beneficial role for a healthy ecosystem.

There are ways to improve aquaculture practices by reducing the risk of fish loss, shortening periods of accelerated growth, setting fish size targets, facilitating access to urban markets and promoting low-cost investments.

Asia Pacific is expected to hold the largest share of the global market, with countries such as China occupying a leading position.

In India and Japan, production of animal feed additives has seen steady growth. Integrated multitrophic aquaculture also presents ecological and socioeconomic advantages, recycling the co-production of different fish species for increased nutritional impact and economic value [16].

In 2020, the global pandemic caused by the coronavirus has spread worldwide, and most countries have imposed quarantines and social distancing as the new norms.

Malaysia has implemented a Recovery Control Ordinance for the seafood sector, an important source of protein, supported by the aquaculture sector involving small and large scale fisheries [24].

One study evaluated the cost-effectiveness of fish production by supplementing the diet with certain additives such as probiotics (bacttocell), antibiotics (oxytetracycline) and vitamins (C and E); also, the addition of common culture fry in certain proportions was analyzed in terms of cost-effectiveness, with results showing higher fish growth and lower price compared to the use of Nile tilapia fish, common in Egypt [35].

Public policy decisions to restrict and eliminate the economic impacts of aquaculture farm management, together with the use of natural feed additives, have contributed to good cost-effectiveness and control of farm pollution.

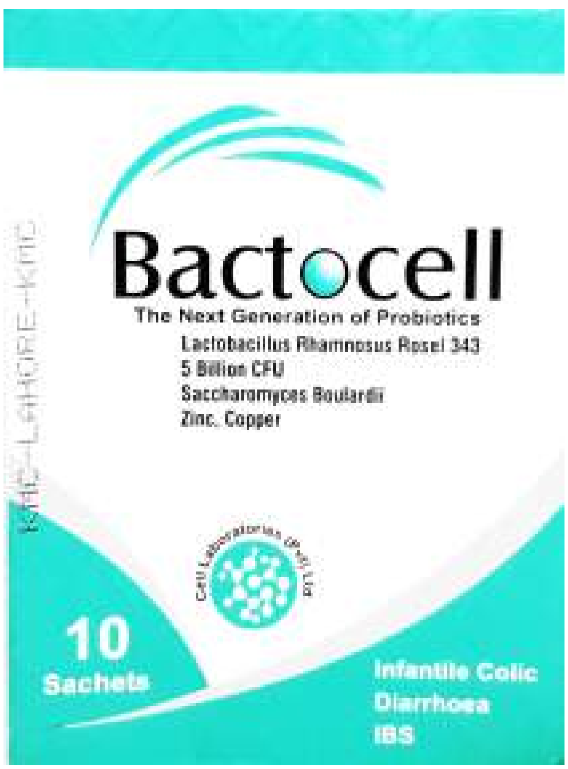

Fig. 25. Commercial probiotics Bactocell
Source: https://khasmart.pk/product/bactocell-sachets/ [84]

7. Conclusions

Current research is focused on optimizing the use of probiotics in the aquaculture industry, given the growing demand for these products.

The promising future application involves the identification and selection of the most suitable probiotic strains for the aquaculture system in order to improve its quality and functionality.

The research also aims to understand the effects and mechanisms of action of probiotics on reproductive performance and development in the industrial hatchery environment.

Although probiotic bacteria bring multiple benefits to the host, there are limitations because certain antimicrobial compounds produced by them are not specific for certain species of pathogenic bacteria.

Thus, strain improvement is necessary to enhance the effectiveness of probiotics. Modern molecular biology techniques, such as recombinant technology, can be applied to genetically modify probiotic strains, but are limited for probiotic candidates used in aquaculture.

Future investigations are needed to address these issues and develop more effective probiotics for the aquaculture industry.

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Utilizarea antibioticelor si evolutia antibiorezistentei în populatiile de animale – Un rezumat

The use of antibiotics and the evolution of antibiotic resistance in animal populations – A review

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Cuvinte cheie: *rezistența antimicrobiană; sănătate publică; importanță; România*
Keywords: *antimicrobial resistance; public health; importance; Romania;*

Rezumat

Rezistenta la antimicrobiană este o problemă de sănătate publica și animală, având dimensiuni globale, tributara utilizarii agentilor antimicrobieni, în medicina umana, în cea veterinara si in domeniul fitosanitar. În acest sens domeniile umane, animale si vegetale au o responsabilitate comuna in a preveni, sau a reduce la minimum presiunea selectiva care favorizeaza și amplifică rezistenta antimicrobiana atat a agentilor patogeni care afecteaza omul, cat si a celor care afecteaza alte specii. Prezentul material prezintă realitatea economică și aspecte importante legate de evoluţia antibiorezistențelor în populațiile animale în România, cu corelații între datele din țara noastră și U.E. Prezentul material a fost prezentat sub forma sa PPT la manifestări organizate în Romania pe baza acestui topic, dar importanța subiectului impune semnalarea acestui fapt și în publicația Asociației. Acest material se bazează pe studii stiintifice din ultimul deceniu, cărți, opinii ale expertilor si experienta personală a autorului. Desigur, ca parte a unui proces continuu de actualizare, acest punct de vedere (personal) trebuie adaptat periodic la cele mai recente cunoștinte științifice obtinute pe această temă.

Abstract

Antimicrobial resistance is a public and animal health problem, with global dimensions, due to the use of antimicrobial agents in human, and veterinary medicine and in the phytosanitary area. In this sense, the human, animal and plant domains have a common responsibility to prevent, or reduce to a minimum, the selective pressure that favors and amplifies the antimicrobial resistance of both pathogens that affect humans, and those that affect other species. This material presents the economic reality and important aspects related to the evolution of antibiotic resistance in animal populations in Romania, with correlations between the data from our country and the E.U. The present material was presented in its PPT form at events organized in Romania based on this topic, but the importance of the subject requires that this fact also be reported in the Association's publication. This material is based on scientific studies from the last decade, books, expert opinions and the author's personal experience. Of course, as part of a continuous updating process, this (personal) point of view must be periodically adapted to the latest scientific knowledge obtained on this topic.

Rezistența antibacteriană este capacitatea bacteriilor de a deveni rezistente la efectul medicamentelor antimicrobiene (inclusiv: antibiotice, antivirale, antifungice si antiprotozoarice) la care aceste microorganisme au fost anterior susceptibile.

Rezistența antimicrobiană (AMR) este prezentă la:

- oameni,
- animale,
- alimente,
- plante si
- în mediu.

Cel top 5 elemente care au stimulat rezistenta antimicrobiană (AMR):

1. Cererea crescută de hrana.
2. Schimbări majore în sistemele de productie animală.
3. Schimbarea tendintelor în comertul cu animale.
4. Circulatia crescută a animalelor si a produselor specifice.
5. "Specificitatea" cresterii animalelor = Lipsa de coerență

Medicamentul Veterinar / Veterinary Drug
Vol. 18(1); Mai - Iunie 2024

OCDE și FAO estimează că producția de animale și pește va crește cu 14% în perioada 2020-2030! In România tendința 2020-2023 pe specii de animale precum și numărul total de animale pe regiuni istorice în România este redată în figurile 2 și 3

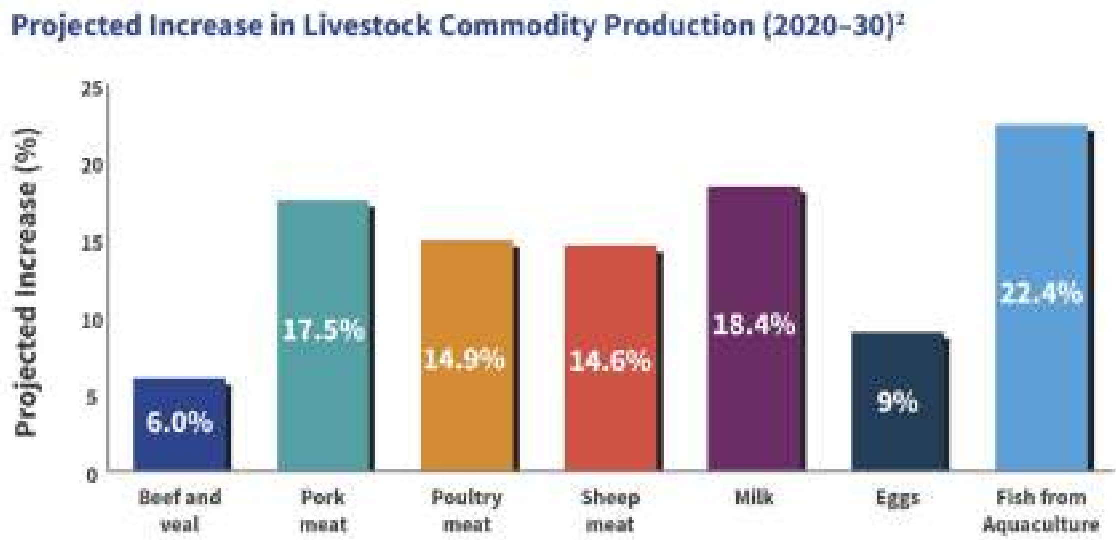
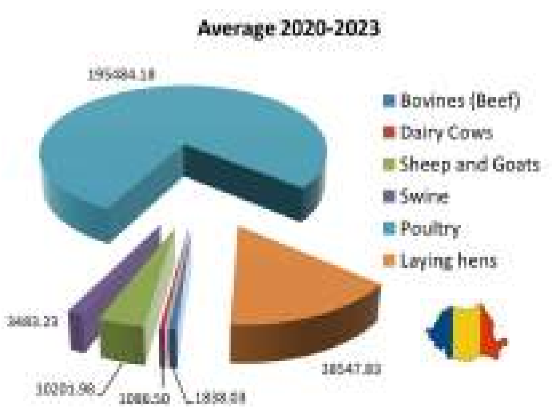
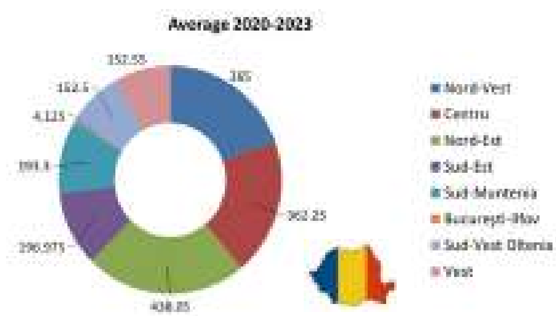


Figura 1. Creșterea previzionată a producțiilor animale în lume (pentru decada: 2020-2030)
Sursa: https://www.healthforanimals.org/reports/global-trends-in-the-animal-health-sector/



Specia / An	2020	2021	2022	2023
Bovine (carne)	1875.2	1826.8	1833.7	1816.4
Bovine (lapte)	1121.9	1081.9	1075.6	1066.6
Carne (bovine)	32.19	36.20	35.61	31.48
Ovine/ caprine	10281.5	10087.4	10247.4	10191.6
Carne (ovine/ caprine)	7.23	confidential		4.99
Suine	3784.5	3619.6	3328.7	3200.1
Carne (suine)	331.37	311.1	267.18	263.8
Gaini oua	38553.7	38530.2	38553.7	38553.7
Pui (carne)	193605.6	200152.2	196962.7	191216.2
Carne (pui)	462.32	465.3	491.22	510.69
Productii piscicole	12628	11793	11714	11212

Sursa: https://ec.europa.eu/eurostat/en/



Regiunea / An	2020	2021	2022	2023
Nord-Vest	368.9	361.4	355.1	374.60
Centru	341.0	353.4	374.1	380.50
Nord-Est	466.3	455.4	422.3	408.20
Sud-Est	216.2	190.7	190.10	190.90
Sud-Muntenia	206.2	195.5	185.30	186.20
Bucureşti-Ilfov	4.6	4.5	3.70	3.70
Sud-Vest Oltenia	165.3	160.0	144.30	140.40
Vest	154.8	154.3	151.90	149.20

Sursa: https://ec.europa.eu/eurostat/en/

Rezistenta antimicrobiană (AMR) apare atunci când germeni (bacterii, virusuri sau ciuperci) care cauzează infectii rezistă efectelor medicamentelor/moleculelor folosite pentru a le trata.

Consumul de medicamente de uz veterinar depăseste consumul de medicamente umane, si se recunoaste că medicina veterinară contribuie în mod semnificativ la aparitia si răspândirea rezistentei la antibiotice la oameni.

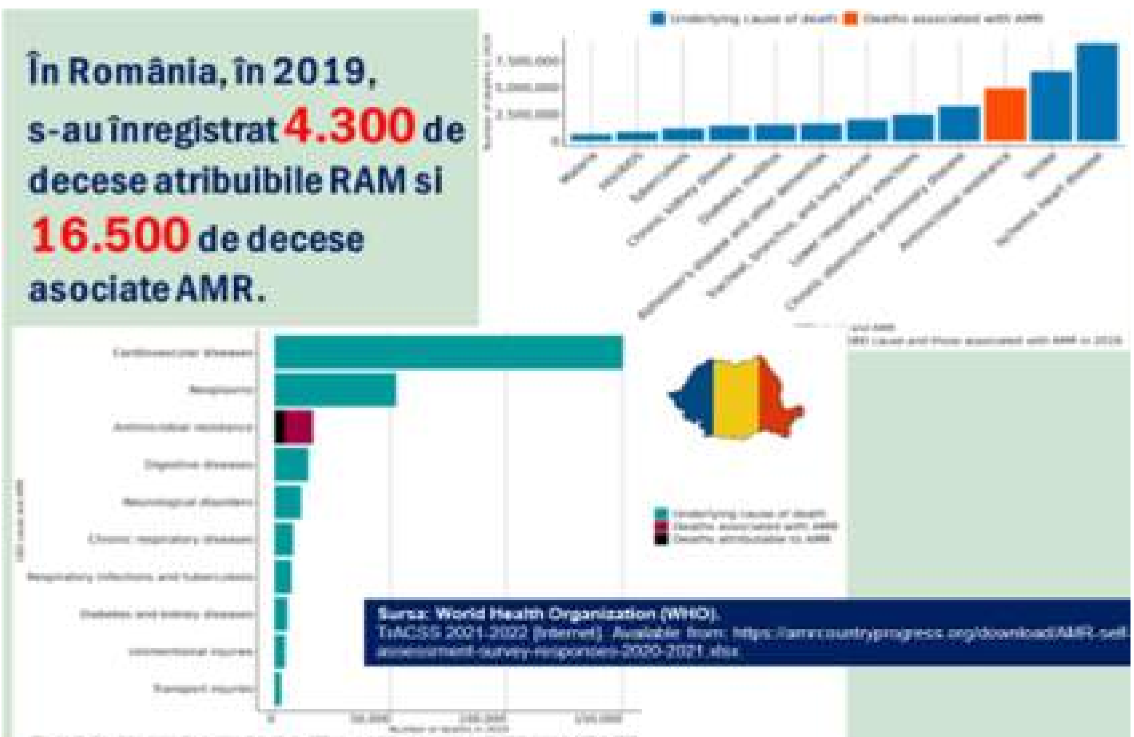
Fermierii folosesc aproximativ de zece ori mai multe tone de antibiotice decât sunt folosite în medicina umană!

Sursa: http://amrls.cvm.msu.edu/images/vph/HUMAN-HEALTH-IMPACT_3-copy.jpg

După documentul Tackling drug-resistant infections globally: Final report and recommendations' - The review on antimicrobial resistance de Jim O'Neill, **2016** - https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf; bacteriile rezistente infectează 800.000 de persoane în UE/EFTA în fiecare an (ECDC 2022. Costul estimativ al AMR pentru sistemele de sănătate doar în Europa este de 1.1 mld €/an.

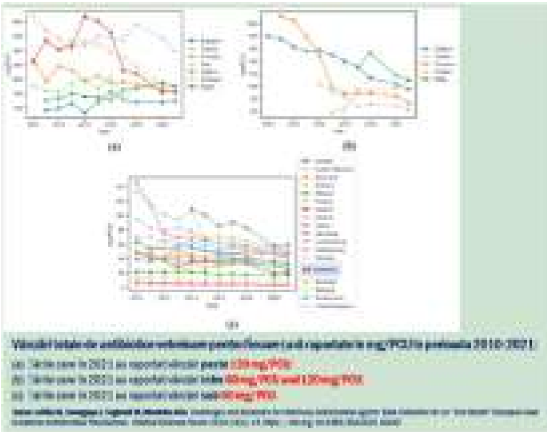
Datorită aparitiei AMR, marele avantaj câstigat în ultimul secol va fi pierdut in bolile infecţioase (pneumoniile, tuberculoza, HIV, malaria), oncologie (unde antibioticele sunt esentiale pentru a ajuta chimioterapia si implicit împotriva infectiilor asociate), sau procedurile chirurgicale (mai ales în transplantul de organe, cezariana, protezări, abdomenul acut sau operatiile pe tendoane).

În România, în 2019, s-au înregistrat 4.300 de decese atribuibile RAM si 16.500 de decese asociate AMR.



Sursa: World Health Organization (WHO). TrACSS 2021-2022 [Internet]. Available from: https://amrcountryprogress.org/download/AMR-self-assessment-survey-responses-2020-2021.xlsx

Trendul în rezistenta la antimicrobiene selectate în indicatorul E. coli la porci, și la puii broiler pentru perioada 2009-2021 în România este în scadere pentru ampicilină, cefotaximă, ciprofloxacină și tetraciclină, tara noastră fiind clasificată în grupul țărilor care în 2021 au raportat vânzări sub 60 mg/kgc, PCU



Sursa: Leitão M, Sarraguça J, Taghouti M, Monteiro ACG. Challenges and Obstacles for Veterinary Antimicrobial Agents' Data Collection for a "One Health" European Goal to Address Antimicrobial Resistances. *Medical Sciences Forum*. 2024; 24(1): 15. https://doi.org/10.3390/ECA2023-16430

În noiembrie 2011, Comisia Europeană prin Agenția Europeană a Medicamentului (EMA) a lansat primul plan de actiune pentru a aborda riscurile generate de rezistența antimicrobiană (AMR).

Planul de actiune se bazează pe o abordare holistică, în concordantă cu initiativa „One Health".

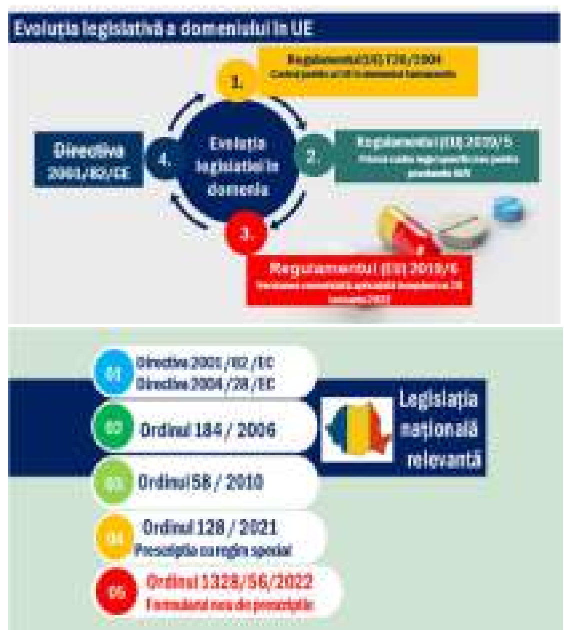
Planul de acțiune acoperă sapte domenii majore si stabileste douăsprezece măsuri specifice de luat în domeniul sănătății umane si / sau veterinare

Frecventa în crestere a rezistentei la chinolone în rândul tulpinilor umane/animale a fost deja demonstrată pentru *Salmonella enteritidis* si *Campylobacter spp*. Rezistenta multiplă la *Salmonella typhimurium* la: ampicilină, cloramfenicol, streptomicină, sulfamide, tetraciclină (ACSSuT), iar legătura AT / AMR a fost deja relevată statistic ($p<0,05$) pentru: fluorochinolone / *E. coli* la oameni / animale, cefalosporine generaţia 3 si 4 în *E. coli* la om; tetracicline si polimixine în *E. coli* la animale; carbapenemi si polimixine / *K. pneumoniae* la om.

Macrolidele la animale au fost asociate cu rezistentă încrucisată la Campylobacter spp. la animale si la oameni; cefalosporinele de generatia a 3-a si a 4-a dau rezistentă încrucisată la fluoroquinolone / *E. coli* la oameni, iar fluoroquinolone / *Salmonella spp.* si *Campylobacter spp.* la oameni au fost legate de AT cu fluoroquinolone la animale.

Aparitia rezistentei la fluoroquinolone după infectiile comune cu *Campylobacter* si *E. coli* la oameni a fost clar rezultatul utilizării acestora în hrana animalelor, cu transmiterea bacteriilor rezistente la oameni prin carne si produsele animale
(**Sursa:**http://www.bio.umass.edu/micro/klingbeil/590s/Lectures/12590Lect23.pdf).

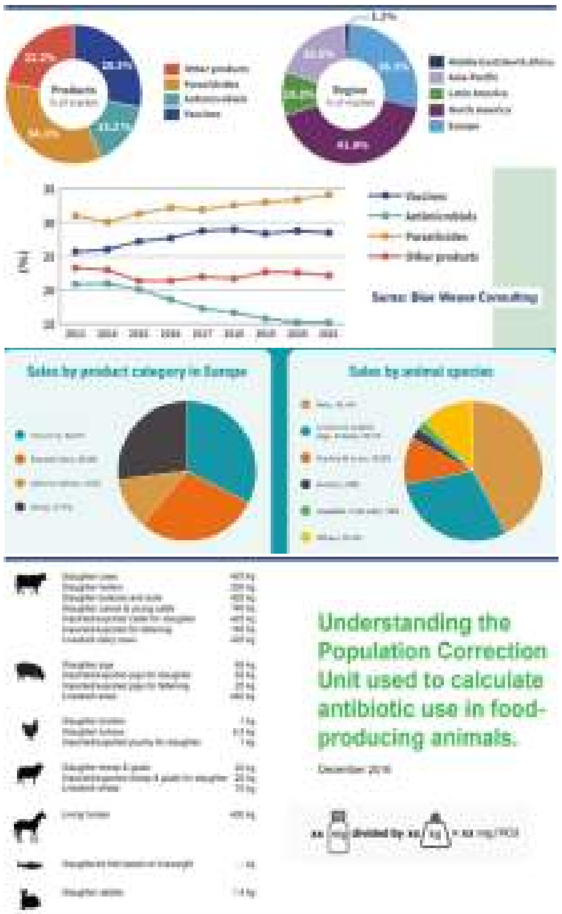
Legislația europeană s-a raliat la prvenirea și combaterea fenimenului prin legilația de profil, aceasta fiind urmată de modificările legislației Românești



Desigur aceste demersuri legislative au fost făcute în corelație cu tendințele în comerțul cu produsele medicinale a.u.v. și urmărindu-se categoriile de produse pe țări și regiuni.

Acest fapt a dus la apariția PCU **mg/PCU** (Unitatea de Corecție a Populației), care este o unitate de măsură dezvoltată de EMA pentru a monitoriza utilizarea și vânzările de antibiotice în U.E.

PCU se referă la numărul de animale dintr-o tară/an, corelat cu greutatea estimată a fiecărei specii la momentul tratamentului cu antibiotic.



Sursa: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/580710/1101060-v1-Understanding_the_PCU_gov_uk_guidance.pdf)

În meta-studiul UE: JIACRA (Analiza comună a consumului si rezistentei antimicrobiene între agentiile interinstitutionale) Report: EFSA Jurnal 2017;15(7):4872, 135 pp. doi:10.2903/j.efsa.2017.4872)

În ultimul deceniu, consumul mediu estimat total de antimicrobiene în mg substantă activă/kg greutate corporală a fost de:

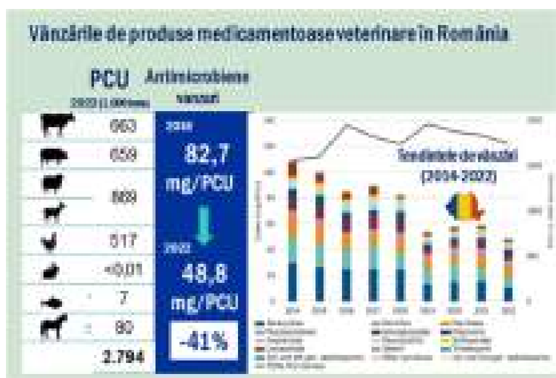
- 124 mg/kgc la om = media 118 mg/kgc și,
- 152 mg/kgc la animalele de rentă = media 67 mg/kgc

Țelul U.E. este reducerea cu 50% a vânzărilor totale de antimicrobiene pentru animalele de fermă si în acvacultură în UE până în 2030, trendul în ultimii ani aratând o reducere a utilizării antimicrobienelor, (calculată prin măsurarea cantitătii de antimicrobiene utilizate per kilogram de carne produsă de-a lungul anilor).

În țara noastră această tendință descrescătoare este respectată cu rezultate încurajatoare oglindite în PCU, date publicate de către Agentia Europeană a Medicamentului (EMA) în 13 ESVAC = Supravegherea Europeană a Consumului de Antimicrobiene Veterinare (Raportul pe 2022)

În România se fac eforturi continuă pentru colectarea datelor primare privind rezistența la antibiotice la animale pentru conectarea la sistemele oficiale de monitorizare a fenomenului (prezente deja în Europa de peste un deceniu).

Prezenta oficială a tării noastre a fost semnalată într-un studiu pe scară largă al UE încă din 2009.



Din acest rapot reiese că vânzările totale de antibiotice veterinare în 2022 pentru 31 de tări. Trendul din 2011 până în 2022 în cele 25 de tări participante în ESVAC arată o scădere a vânzărilor cu:

- 53.0% din vânzările totale,
- 49.0% din vânzările de cefalosporine din generatia a 3-a si a 4-a,
- 44.0% din vânzările chinolonelor,
- 81.0% din vânzările polimixinelor.

Totuși, utilizarea iresponsabilă a antibioticelor la animalele de fermă a dezvoltat rezistentă la animale sau la persoanele care au consumat carnea si produsele secundare.

Antibiorezistenta a apărut în principal prin utilizarea antibioticelor ca:

- biostimulatori
- în conservarea alimentelor de origine animală,
- prin administrarea irațională a antibioticelor,
- fără prescriptie si fără antibiogramă

Principalele cauze care favorizează aparitia fenomenelor de rezistentă la medicamente sunt:

- subdozarea sau administrarea inadecvată a antiinfecțioaselor,
- tratamentul bolilor virale la animale cu antibiotice,
- administrarea de antibiotice cu spectru larg în orice tratament, în timp ce antibioticele cu spectru îngust ar fi suficiente

Mecanisme & Consecinte ale AMR

Răspândirea si transmiterea genelor rezistentei s-a demonstrat că poate avea loc între:

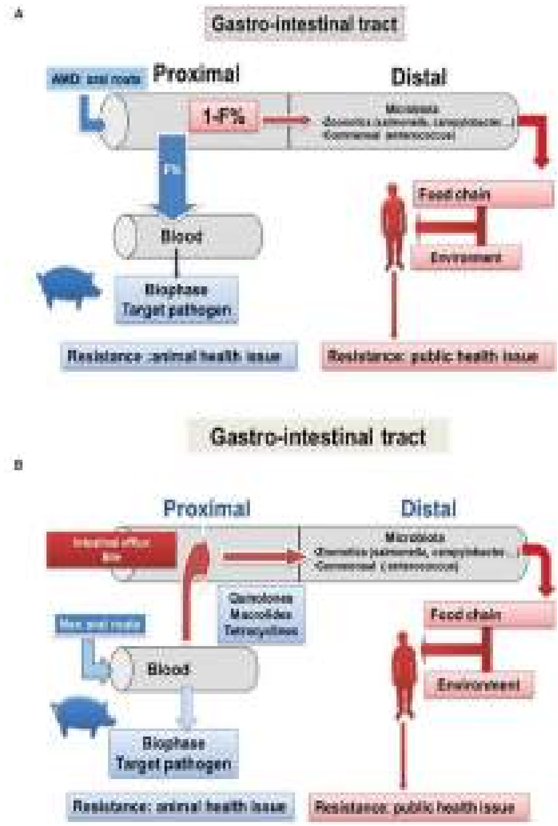
- oameni - animale,
- animale - oameni
- animale - mediu

Tratamentul veterinar antimicrobian sustenabil trebuie să fie legat de problemele de sănătate publică si nu de problemele de sănătate animală! Prin selectie, genomul bacterian a devenit aproximativ de 1000 de ori mai mic decât genomul animal / uman!

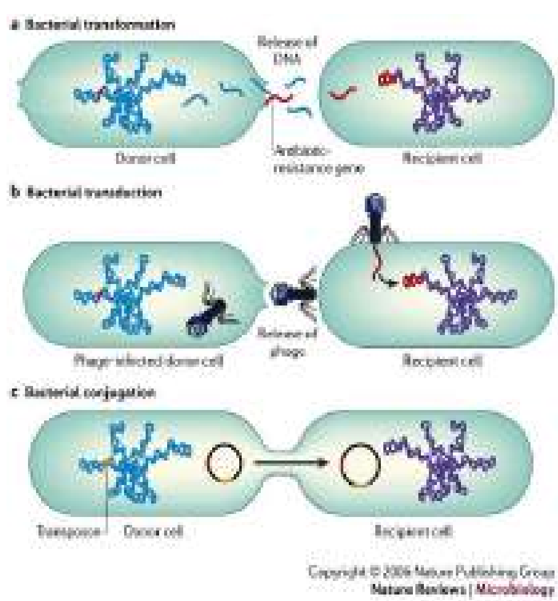
Acest fapt se datorează „rationalizării genomului". Între bacterii există o competitie pentru resurse. Pentru a se menține si reproduce genomul bacterian, este nevoie de: energie + resurse. Un genom mare necesită mai multă energie pentru a fi mentinut în funcțiune si replicat.

Un fapt essential este că antibioticele administrate animalelor nu sunt complet absorbite de acestea! Între 30 si 90% din antibiotic poate fi eliminat prin urină sau fecale în stare bioactivă, uneori intacta sau sub formă de metaboliti ai antibioticului.

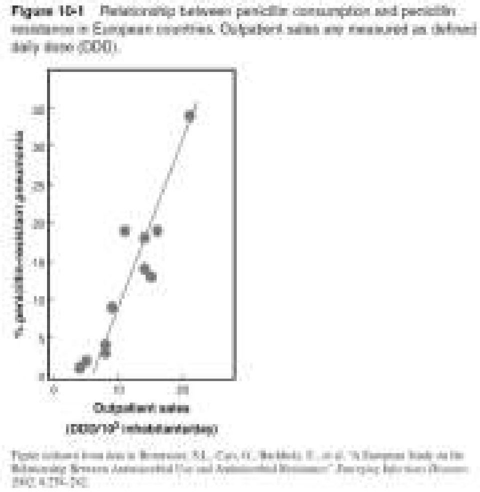
Antibioticele administrate animalelor ajung adesea în sol si în apă prin deseuri medicale si/sau medicamente eliminate necorespunzător sau prin praful din facilitătile de crestere industrială.

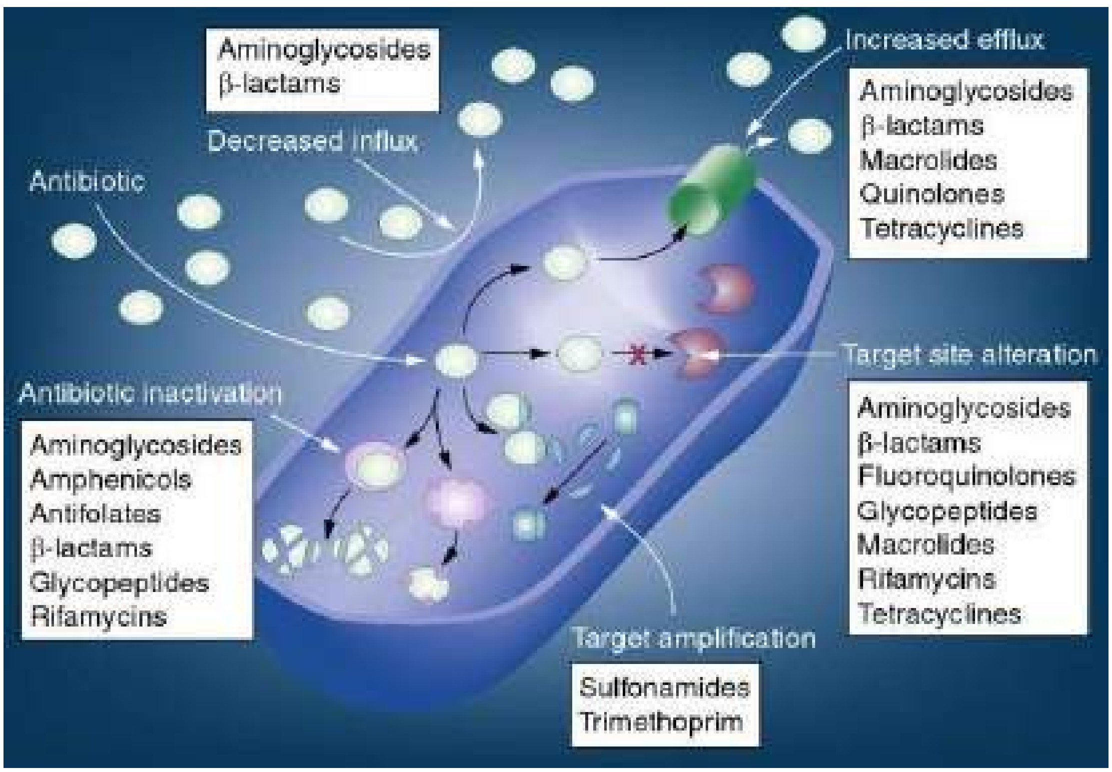


Consecinta directa a AMR: evolutie, selectie natural, mutatie genetică



Utilizarea masivă a medicamentelor, în special a antiinfecțioaselor, exercită o presiune de selectie majoră care duce la aparitia microorganismelor rezistente în populatiile umane si animale. De exemplu în Franța, Spania si România, prevalenta declarata a rezistentei la penicilină este de **25-50% !**





Sursa: http://images.forbes.com/media/magazines/forbes/2006/0619/Forbes_0619_p70_f1.gif

De exemplu, in cazul mecanismelor de efflux, relative recent, au fost descoperite cinci tipuri de pompe de eflux:

- superfamilia ABC (casetă de legare ATP),
- superfamilia MFS (facilitatorului major),
- superfamilia MATE (expulzării compusilor multidrog si toxici),
- superfamilia MDR (rezistentei multi-drog),
- superfamilia RND (diviziunii r-nodulație).

Una din amenințările majore este scăderea ratei de apariție a noilor sinteze de molecule antiinfecțioase în ultimii treizeci de ani, ceea ce face că alternativa alegerii unor molecule total eficiente să fie tot mai restrânsă, mentinerea eficacitatea antimicrobienelor actuale fiind o cerință vitală în actualul context.

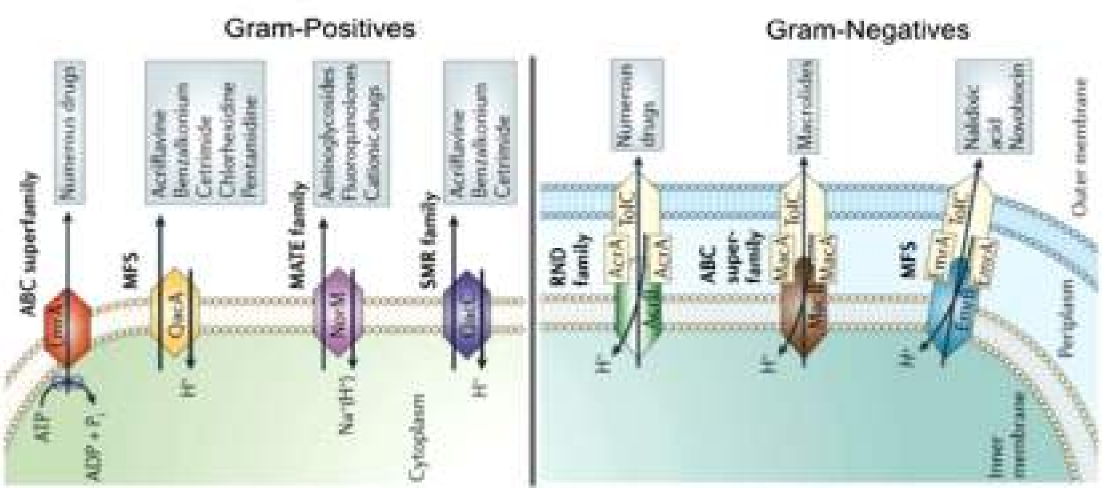
Din punct de vedere practice, limitările antibioticelor folosite în prezent includ:

- bioadisponibilitatea nesatisfăcătoare,
- efectul limitat,
- citotoxicitatea,
- tratamentele lungi și frecvente.

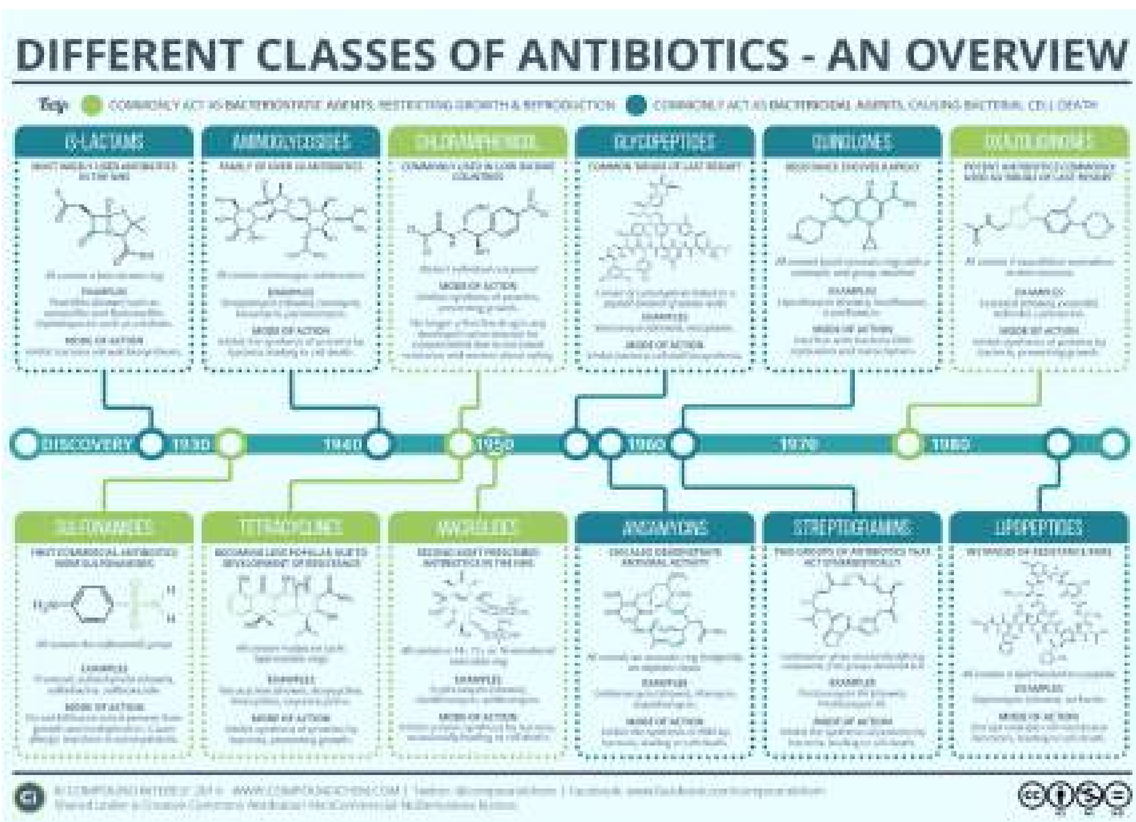
În acest context, sunt necesare noi caracteristici specifice care pot reduce morbiditatea si mortalitatea!

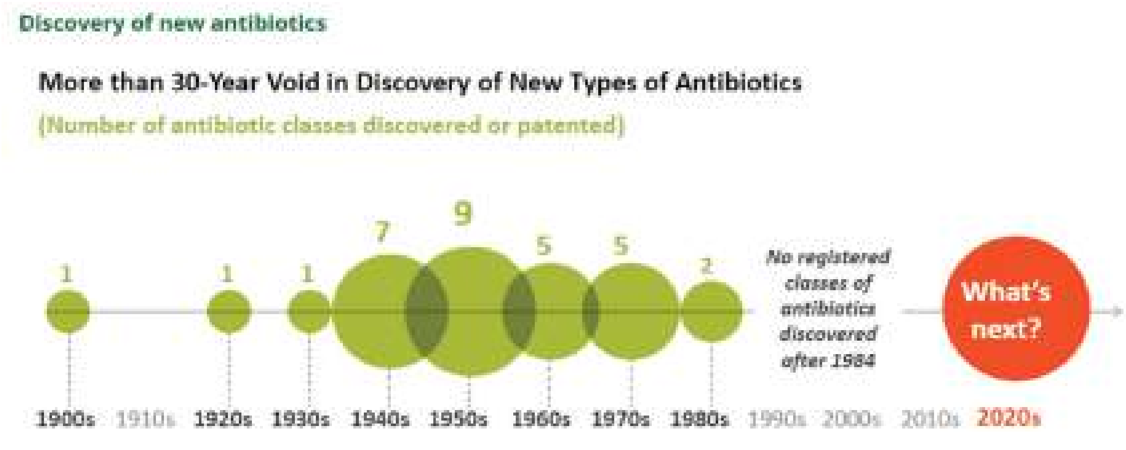
Deasemenea, prescrierea excesivă de antibiotice nu este singura sursă de antibiotice care poluează mediul!

Încă din anii 1970, antibioticele puteau fi găsite în carnea bovinelor, porcilor si păsărilor, iar aceleași antibiotice (!) au fost ulterior identificate în sistemele de apă municipală si subterană sau în sol, cu consecintele dramatice aferente!



Sursa: Munita si Arias, modificat dupa Piddock, Nat Rev Microbiol. **2006**; 4(8): 629–636.





Source: ECA based on "A sustained and robust pipeline of new antibacterial drugs and therapies is critical to preserve public health", Pew Charitable Trusts, May 2016.

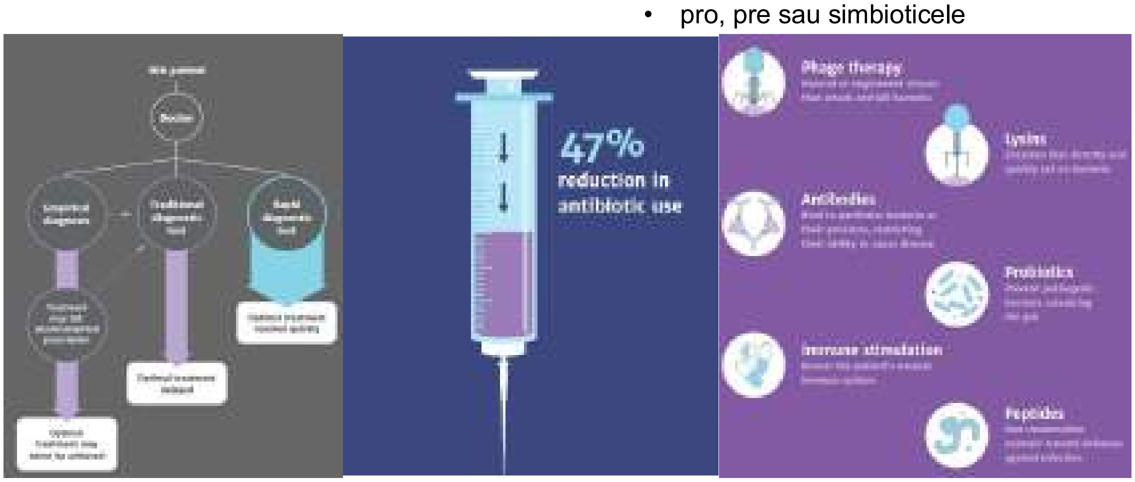
Alternative și posibile soluții

Dr. Margaret Chan, Director General al WHO afirma "Astăzi, antibioticele sunt rareori prescrise pe baza unui diagnostic definitiv". Testele de diagnostic pot arăta dacă un antibiotic este într-adevăr necesar si care anume. De exemplu dintre cei 40.000.000 de americani care iau antibiotice pentru probleme respiratorii pe an, 27.000.000 le iau degeaba

Vaccinologia ca știință ar putea fi pusă cu success în slujba luptei anti-AMR! Sally Davies, Chief Medical Officer for England afirma: „O gamă largă de abordări și dezvoltarea de alternative la antibiotice, la oameni și animale, este esențială pentru luptă. Vaccinurile au un rol vital în combaterea rezistenței la medicamente, prin prevenirea infecțiilor în primul rând."

Alternative atrăgătoare ar putea fi de asemenea și:

- anticorpii patogeni specifici,
- agentii imunomodulatori,
- bacteriofagii,
- peptidele antimicrobiene si
- pro, pre sau simbioticele

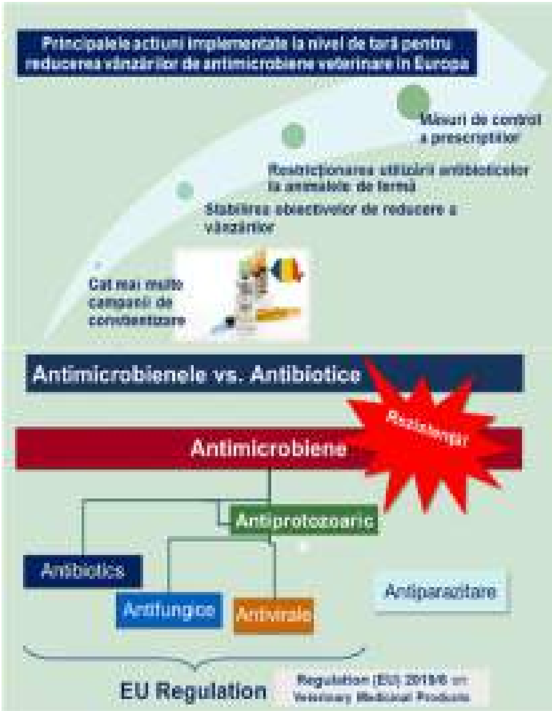


Sursa: https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf

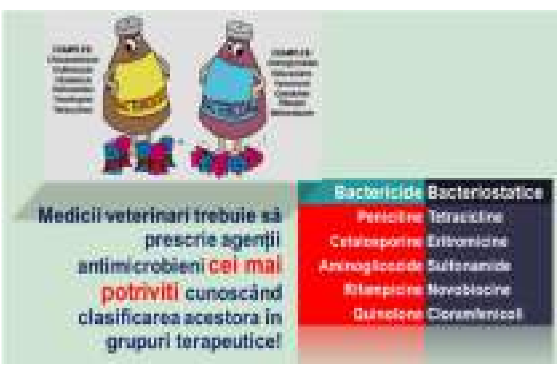
Cum putem reduce impactul ?

Prevenția este "cheia" si se realizează prin:

- Biosecuritate
- Întreținerea animalelor
- Igienă
- Observația zilnică
- Campaniile de vaccinare
- Identificarea corectă a animalelor în tratament
- Înregistrarea corectă în registrul de consultații



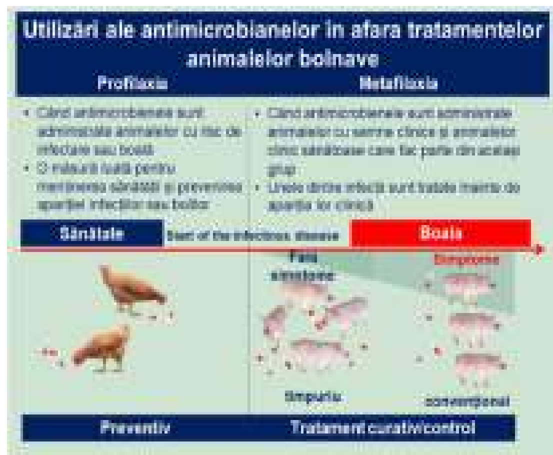
Astăzi, cele mai multe rapoarte fac referire la tendința cresterii utilizării substantelor antimicrobiene în doze subterapeutice la pui si păsări.

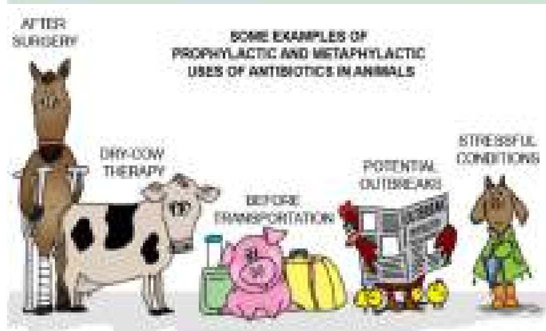


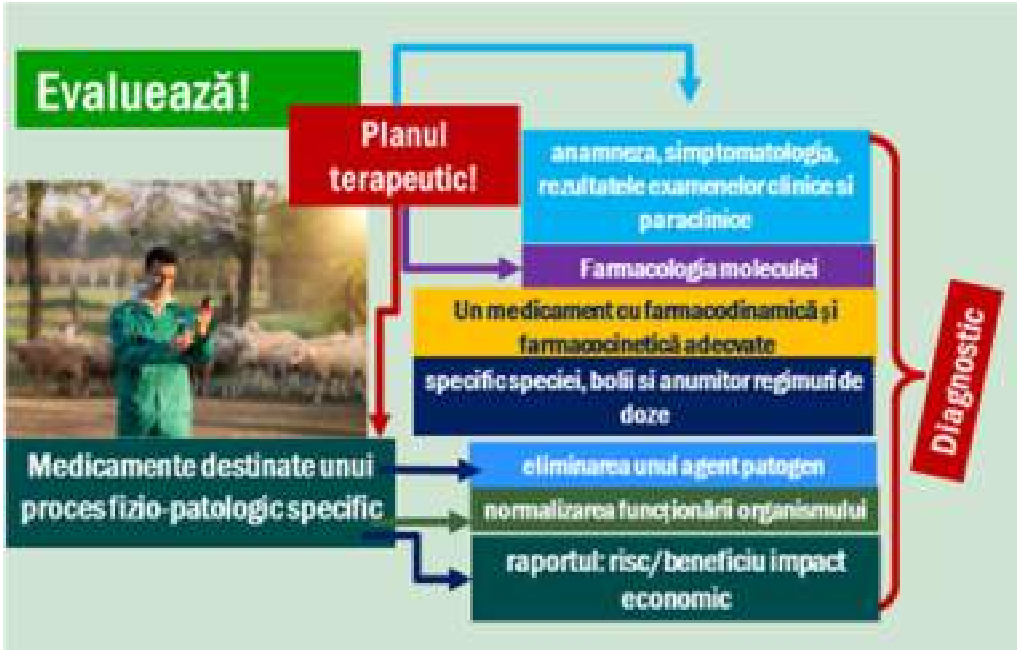
Utilizări ale antimicrobianelor în afara tratamentelor uzuale

Atât dovezile moleculare, cât si cele epidemiologice indică faptul că prevalența rezistenței la antibiotice în rândul oamenilor a fost declansată de introducerea enrofloxacinei în hrana pentru păsări, ceea ce a determinat FDA să interzică utilizarea acestui medicament în păsări în 2011.

Antimicrobienele ar trebui să fie utilizate în metafilaxie doar atunci când riscul răspândirii unei infectii / boli infecțioase e ridicat si când nu există alte alternative disponibile.

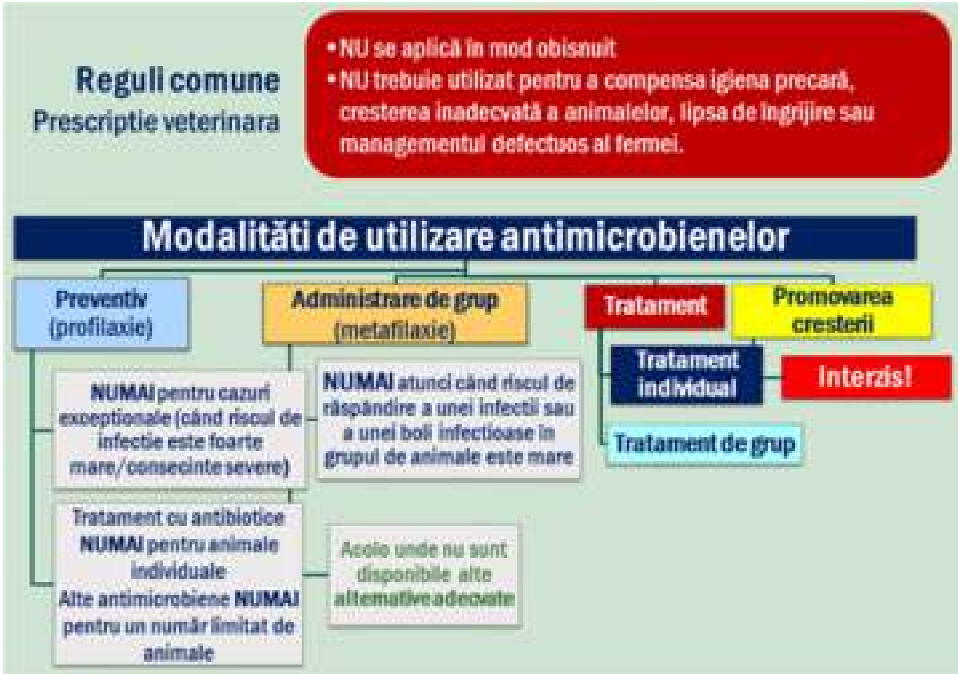






Statele membre vor furniza orientări pentru a promova înțelegerea factorilor de risc asociate cu metafilaxia si vor include criterii pentru implementarea.

Categorii AMEG	Clasa antimicrobiene, subclase, substanțe
A (Evită) EMA-AMEG *Antimicrobial Advice ad hoc Expert Group	Carbapeneme și alte peneme Amidinopeniciline Cefalosporine: Alte cefalosporine și peneme (ATC J01DI) Glicopeptide Glicilcicline Lipopeptide Monobactami Oxazolidinone Peniciline: combinații de carboxi-peniciline și ureido-peniciline cu inhibitori de β-lactamaze Derivați acidului fosfonic (de exemplu fosfomicină) Acid pseudomonic Riminofenazine Streptogramine Sulfone Medicamente utilizate exclusiv pentru tratarea tuberculozei sau a altor mico-bacterioze
B (Restricționat)	Cefalosporinele din, a 3-a și a 4-a generație Polimixinele (de exemplu, colistina) Chinolonele (fluorochinolone și alte chinolone)
C ("Prudență")	Aminoglicozide și aminociclitol Aminopeniciline în combinație cu inhibitori de β-lactamază (de exemplu, amoxicilină-acid clavulanic) Amfenicoli (florfenicol și tiamfenicol) Cefalosporine, de generația I și II, și cefamicine Macrolide Lincosamide Pleuromutiline Rifamicine
D ("Prudență")	Aminopeniciline, fără inhibitori de β-lactamaza Polipeptide ciclice (bacitracin) Derivați de nitrofuran (de exemplu, nitrofurantoină) Nitroimidazoli* Peniciline: Anti-stafilococice (peniciline rezistente la β-lactamază) - Răspuns la solicitarea Comisiei Europene pentru actualizarea avizului științific cu privire la impactul asupra sănătății publice și sănătății animalelor al utilizării antibioticelor la animale - Categorizarea antimicrobianelor EMA/CVMP/CHMP/682198/2017, pp. 6-67 Clasa antimicrobiană, subclase, substanțe Peniciline: Naturale, peniciline cu spectru îngust (sensibile la β-lactamază) Antibacteriene steroidiene (acid fusidic)* Sulfamide, inhibitori ai dihidrofolat-reductazei și combinațiile.


Reguli comune
Prescriptie veterinara
•NU se aplică în mod obișnuit
•NU trebuie utilizat pentru a compensa igiena precară, cresterea inadecvată a animalelor, lipsa de îngrijire sau managementul defectuos al fermei.
Modalități de utilizare antimicrobienelor
Preventiv (profilaxie)
Administrare de grup (metafilaxie)
Tratament
Promovarea cresterii
Tratament individual
Interzis!
Tratament de grup
NUMAI pentru cazuri exceptionale (când riscul de infectie este foarte mare/consecinte severe)
NUMAI atunci când riscul de răspândire a unei infectii sau a unei boli infectioase în grupul de animale este mare
Tratament cu antibiotice NUMAI pentru animale individuale
Alte antimicrobiene NUMAI pentru un număr limitat de animale
Acolo unde nu sunt disponibile alte alternative adecvate


Reguli comune – Prescriptie veterinară
Medicație prin furaje sau apă
Se aplică reguli diferite
Furaj medicamentat
(furaj amestecat cu medicamente într-o fabrică de furaje sau de către un producător de amestecuri de furaje mobil sau într-un vehicul echipat special de către operatorul din sectorul hranei pentru animale)
Reg. (UE) 2019/4 (FM)
Medicație orală
(amestecare în exploatatie în furaje sau în apă de către detinătorul animalelor)
prin furaj
prin apă
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Reguli comune – Prescriptie veterinară
Prescriptii veterinare în legătură cu furajele medicamentate (2/2)
1 prescriptie = 1 tratament veterinar


Părțile componente ale noului model de rețetă

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The importance of antibiotics and the evolution of resistance to antimicrobial substances

Importanţa antibioticelor şi evoluţia rezistenţei de substanţele antimicrobiene

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Keywords: *antibiotic resistance, antibacterial substances, public health*
Cuvinte cheie: *antibiorezistenţă, substanţe antibacteriene, sănătate publică*

Abstract

By exploring the history of antibiotic discovery and how antimicrobial resistance has become a global problem, this study aims to provide a comprehensive perspective on the impact of these factors on public health. At the same time, we will analyze the strategies proposed to counter this worrying development and to ensure a future in which antibiotics remain effective tools in the treatment of bacterial infections. The purpose of this paper is to review proposed strategies for countering antimicrobial resistance, including the development of new antibiotics, improved prescribing practices, and public awareness of the responsible use of these drugs. In an era where treatment-resistant infections are becoming more common, it is crucial that we engage in concerted efforts to maintain the effectiveness of antibiotics and ensure the future health of the global population.

Rezumat

Prin explorarea istoriei descoperirii antibioticelor și a modului în care rezistența la antimicrobiene a devenit o problemă globală, această lucrare oferă o perspectivă comprehensivă asupra impactului acestor factori asupra sănătății publice. Totodată, se vor analiza strategiile propuse pentru a contracara această evoluție preocupantă și pentru a asigura un viitor în care antibioticele rămân instrumente eficiente în tratarea infecțiilor bacteriene. Scopul acestei lucrări este de a analiza strategiile propuse pentru contracararea rezistenței la antimicrobiene, inclusiv dezvoltarea de noi antibiotice, îmbunătățirea practicilor de prescriere și conștientizarea publicului cu privire la utilizarea responsabilă a acestor medicamente. Într-o eră în care infecțiile rezistente la tratament devin din ce în ce mai frecvente, este crucial să ne angajăm în eforturi concertate pentru a menține eficacitatea antibioticelor și a asigura sănătatea viitoare a populației globale.

Introduction

The discovery of antibiotics marked a crucial moment in the history of medicine, offering effective solutions for the treatment of bacterial infections.

At the center of this revolution stands the emblematic figure of Alexander Fleming, whose observations on the effects of penicillin opened new therapeutic horizons.

Over the decades, antibiotics such as streptomycin and tetracycline have become essential tools in the treatment of infections, saving millions of lives.

However, the apparent success of antibiotics has been overshadowed by the emergence and spread of antimicrobial resistance, a phenomenon fueled by reckless practices such as the excessive and inappropriate use of these drugs.

The evolution of antibiotic discovery has been a complex and fascinating process, from Fleming's accidental discovery of penicillin in 1928 to the subsequent development of a wide range of broad-spectrum antibiotics.

These medications have had a significant impact on improving the survival rate of patients affected by bacterial infections, revolutionizing medical practice and reducing mortality associated with these diseases.

However, the success of antibiotics has come with unexpected challenges.

The intensive and often inappropriate use of these drugs has paved the way for the evolution of antimicrobial resistance.

Bacteria have developed defense mechanisms against the action of antibiotics, thus compromising the effectiveness of these treatments and posing a global threat to public health (13,17).

The phenomenon of antimicrobial resistance is fueled by several factors, including the pressure exerted by extensive use in medicine and agriculture, the lack of compliance with antibiotic administration rules, and even self-medication.

This vicious cycle has created a conducive environment for the natural selection of resistant bacterial strains, thereby accelerating their spread in communities and worldwide (16,18).

Faced with this growing threat, the medical community and researchers have sought innovative solutions to counteract antimicrobial resistance.

Their efforts have included the development of new classes of antibiotics, improving prescribing practices to reduce inappropriate use, and promoting public awareness of the importance of responsible antibiotic use.

History of antibiotics

The discovery of penicillin represented a crucial moment in the evolution of medicine, marking the significant contribution of British microbiologist Sir Alexander Fleming.

At a time when bacterial infections posed a major challenge in medical practice, Fleming's research had profound consequences for the treatment of these conditions. Alexander Fleming's observations on bacterial cultures, especially those of the genus *Staphylococcus*, revealed that a fungus, later identified as *Penicillium notatum*, released a substance that inhibited bacterial growth (14).

The initial impact of the discovery of penicillin was profound, leading to a significant change in the paradigm of bacterial infection treatment.

The scientific and medical community quickly recognized the therapeutic potential of penicillin, paving the way for further research and the development of other classes of antibiotics.

Alexander Fleming's contribution to the discovery of penicillin was recognized with numerous awards and honors, consolidating his status as a pioneer in the field of medicine. His legacy remained fundamental to the progress of modern medicine, with penicillin continuing to be "one of the essential tools in the fight against bacterial infections" (11).

Penicillin was successfully used in the treatment of conditions such as pneumonia, septicemia, and endocarditis, significantly contributing to the reduction of mortality associated with these diseases.

The application of penicillin in surgery also had a major impact, allowing for more extensive surgical interventions and reducing the risk of postoperative complications caused by bacterial infections.

Over time, the use of penicillin expanded to other conditions, including sexually transmitted infections such as syphilis and gonorrhea.

The positive impact of penicillin in treating these conditions was notable, substantially changing perspectives on the control and treatment of infectious diseases (8,14).

As penicillin solidified its place in the medical arsenal, its multiple applications and benefits became evident. Penicillin treatment quickly became a reference point in medicine, marking a significant transition from previous approaches with limited effectiveness.

The main contribution of penicillin manifested in the treatment of severe and often fatal bacterial infections, restoring hope for affected patients. In surgical interventions, the use of penicillin reduced the risk of postoperative infectious complications, thus expanding the range of possible surgical procedures and improving patient prognosis (19).

However, as penicillin became increasingly prevalent in medical practice, challenges began to emerge.

The development of penicillin resistance in certain bacterial strains underscored the need for ongoing approaches in researching and developing new antibiotics to counteract bacterial evolution.

After the discovery of penicillin, the development of antibiotics saw a significant stage with the isolation and characterization of streptomycin.

This substance, initially identified in *Streptomyces* strains, represented a major advance in antimicrobial therapy (14).

Streptomycin, discovered in 1943 by Waksman and Schatz, marked a new era in the fight against infections.

This broad-spectrum antibiotic was initially successfully used in the treatment of tuberculosis, representing a significant progress compared to previous treatment options (23,24).

Through further development, streptomycin was identified as an example of a new class of antibiotics, aminoglycosides. This discovery stimulated research in the field, contributing to the identification and isolation of other classes of antibiotics with diverse chemical structures and specific mechanisms of action.

As new antibiotics were discovered and developed, it became evident that their diversity could cover a wide range of bacterial infections.

Tetracyclines, macrolides, and cephalosporins, among others, became essential components of the medical arsenal, offering alternatives and tailored solutions for various clinical contexts (23).

With progress in antibiotic development, a window of opportunities opened in the treatment of various bacterial conditions.

Tetracyclines were introduced into the medical arsenal with an extended spectrum of action, addressing various infections such as respiratory, urinary, and dermatological.

This diversity of medications allowed doctors to tailor treatments according to the specificity of each infection, contributing to the optimization of therapeutic outcomes.

Macrolides, such as erythromycin, were successfully used in the treatment of upper respiratory infections, while cephalosporins became essential in surgical interventions and the treatment of more severe bacterial infections (6,14).

However, the extensive and often uncontrolled use of antibiotics raised concerns about the emergence and spread of antimicrobial resistance. The phenomenon of antibiotic resistance became a global issue, significantly impacting the ability to treat bacterial infections and public health outcomes (7).

Addressing antibiotic resistance became a priority, and research focused on developing innovative strategies.

Efforts included identifying new classes of antibiotics, improving prescribing practices by adopting more precise protocols, and promoting awareness of the rational use of these medications among healthcare professionals and the general public (5).

The benefits of antimicrobial substances

The significant beneficial effects of antibiotics on the treatment of bacterial infections indeed mark remarkable progress in the field of medicine.

These effects have positively influenced the course of patients affected by various infections, bringing tangible benefits both at the individual and public health levels. Thus, antimicrobial pharmacological agents have contributed to:

- **Eradicating bacterial infections:** antibiotics have had a major impact on the treatment of bacterial infections, successfully destroying or inhibiting the growth of pathogenic bacteria. This direct effect on the causative agent of the infection allows for faster recovery and prevents the progression of the disease to more severe stages.
- **Reducing morbidity and mortality:** the use of antibiotics has led to a significant decrease in the morbidity and mortality rates associated with bacterial infections. Through early and effective interventions, antibiotics have saved lives and contributed to improving the quality of life for those affected.

- **Preventing postoperative complications:** in surgery, antibiotics are used to prevent postoperative infections. This has allowed for the expansion of surgical procedures, increased success rates of interventions, and reduced the risk of complications associated with infections.

- **Controlling sexually transmitted diseases:** Antibiotics have had a significant impact on controlling and treating sexually transmitted diseases, offering effective solutions in cases such as syphilis and gonorrhea (13).

- **Improving quality of life:** by rapidly and efficiently treating bacterial infections, antibiotics have contributed to reducing convalescence periods, facilitating the return to a normal and active life for patients.

However, it is essential to emphasize that responsible use of antibiotics is crucial to prevent the development of antimicrobial resistance and ensure their long-term effectiveness.

The considerable benefits of antibiotics are accompanied by responsibilities in the proper management of these medications to protect public health and maintain treatment efficacy in the future (1, 7, 20).

The evolution of antimicrobial resistance

The evolution of resistance in the context of extensive use has been determined by a series of interconnected factors, reflecting the complex relationship between microorganisms and their environment.

Globally, the widespread use of antibiotics in medicine and agriculture has significantly contributed to the natural selection of resistant bacterial strains.

The frequent and uncontrolled administration of these medications has created a favorable environment for resistance development.

As antibiotics are used excessively or inappropriately, bacteria exhibiting resistance capabilities to them become predominantly selected, leading to an increase in the frequency of these strains in the community (3,10).

In the medical field, pressure on antibiotics through self-medication, inappropriate prescriptions, and their use in preventive treatments or clinically unjustified situations contribute to the emergence and spread of resistance.

Additionally, the increasing use of antibiotics in agricultural practices, both for treating animals and promoting their growth, has raised additional concerns in the evolution of antimicrobial resistance.

The process of transferring resistance genes between different environments, such as medical and agricultural, adds a level of complexity. Resistance genes can be transferred between various types of bacteria and between bacteria and other microorganisms, contributing to the rapid and global spread of resistance capabilities (17).

One of the significant challenges in the evolution of antimicrobial resistance is the phenomenon of "selective pressure."

The more frequently antibiotics are used, the greater the pressure exerted on bacteria to develop resistance.

This phenomenon is exacerbated by the inappropriate use of antibiotics, such as administering them at suboptimal doses or for viral conditions where they are ineffective (2,15).

Another important aspect of resistance evolution is the transfer of resistance genes between different bacterial species (Figure 1).

This ability to transfer genetic material between them allows bacteria to rapidly and efficiently acquire resistance characteristics to multiple antibiotics.

The transfer of resistance can occur not only between bacteria of the same type but also between bacteria of different species and even between bacteria and other microorganisms, such as plasmids or transposons (16).

Antimicrobial resistance is not limited to the medical field but has serious consequences for animal health and ecosystems as well. The intensive use of antibiotics in agricultural practices can contribute to the emergence and spread of antimicrobial resistance among animals and the surrounding environment, potentially affecting human health indirectly through food chains or direct contact (1,5).

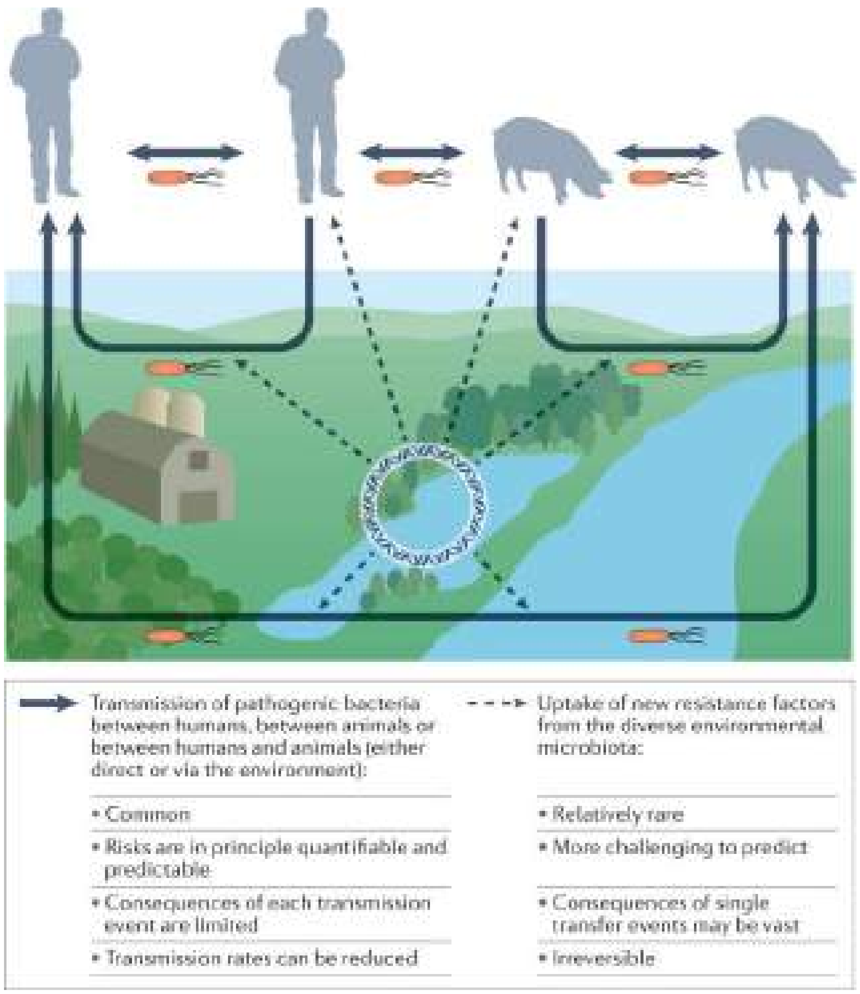

Figure 1. Routes of transmission of bacterial pathogens.
The dominant routes of transmission of (resistant) pathogens (arrows) are between humans, between domestic animals, and sometimes between animals and humans. These routes of transmission can be direct or indirect through the external environment, often through faecal contamination. (Source: Larsson D.G.J., Flach C.F., 2022)

The factors that contribute to the appearance of antibiotic resistance

The emergence of antimicrobial resistance is a complex and multifactorial phenomenon, influenced by a series of elements that interact synergistically. Understanding these contributing factors is essential for developing effective strategies for prevention and control of resistance (26).

• **Excessive and Inappropriate use of antibiotics:** one of the most significant causes of antimicrobial resistance is the excessive and inappropriate use of antibiotics. This practice includes administering antibiotics in the absence of a clear diagnosis, using them in suboptimal doses, and not adhering to the recommended treatment duration.

• **Self-medication and self-prescription:**
Self-treatment with antibiotics without the supervision of a medical professional and self-prescription of these medications contribute to the emergence of resistance. These practices can lead to the unjustified use of antibiotics and incorrect administration of these medications.

• **Inappropriate practices in agriculture:** the use of antibiotics in agricultural practices, such as promoting animal growth or disease prevention, contributes to the development of antimicrobial resistance. The transfer of resistance genes between bacteria in the agricultural environment and those in the medical environment represents an additional threat (4).

• **Lack of monitoring and control:** in some regions, there is a lack of monitoring and control regarding the use of antibiotics and resistance to them. This can facilitate the uncontrolled increase of resistance in communities and healthcare institutions.

• **Transfer of resistance genes:** the ability of bacteria to transfer resistance genes between them is an important mechanism in the evolution of antimicrobial resistance. This phenomenon can occur not only between bacteria of the same type but also between different species and in various environments.

• **Use of antibiotics in food and aquaculture industries:** in addition to agricultural practices, the use of antibiotics in the food and aquaculture industries can contribute to the spread of antimicrobial resistance, with potential consequences for human health through the consumption of contaminated food.

Overall, combating antimicrobial resistance requires an integrated approach that addresses all these contributing factors.

This involves improving antibiotic use practices, public education, promoting research for the development of new antibiotics, and strengthening global efforts to monitor and control resistance (25, 26).

The impact of antimicrobial resistance

The impact of antimicrobial resistance on public health is complex and manifests in various ways, with a global spread of resistant bacteria posing a series of threats to the effectiveness of medical treatments.

1. Global spread of resistant bacteria: antimicrobial resistance knows no national borders and is a problem that affects the entire world. Resistant bacteria can travel widely, either through traveling individuals or through the export of food or other goods.

This contributes to the increasing prevalence of resistant bacteria worldwide, posing a cross-border threat to public health.

2. Spread of multidrug-resistant infections: resistant bacteria can cause multidrug-resistant infections, meaning infections that no longer respond to multiple classes of antibiotics.

This makes treating these infections more difficult and sometimes impossible.

Multidrug-resistant infections are associated with higher rates of morbidity and mortality, higher treatment costs, and the need for more complex medical interventions.

3. Complication of treating common diseases: antimicrobial resistance affects the treatment of common diseases such as respiratory, urinary, and skin infections.

What would have been treatable conditions with common antibiotics in the past can now become a significant challenge, with serious implications for population health (11).

4. Prolonged hospital stays: patients infected with resistant bacteria often require longer hospital stays and more intensive treatments. This not only puts an additional burden on healthcare systems but also increases the risk of transmitting resistant bacteria in the hospital environment.

5. Limitation of therapeutic options: as antimicrobial resistance spreads, available therapeutic options become limited.

This can lead to situations where doctors are forced to use stronger or more toxic antibiotics, with potential negative side effects.

6. Global health issues: Antimicrobial resistance poses a serious threat to global public health efforts, affecting the ability to manage pandemics, complex surgical interventions, and the treatment of chronic infectious diseases.

Overall, the global spread of resistant bacteria has significant consequences for public health, necessitating the need for global and collaborative strategies to combat antimicrobial resistance (12, 21).

Consequences of antimicrobial resistance

Antimicrobial resistance generates significant consequences for the treatment and management of infections, introducing substantial challenges and limitations in the medical approach to these conditions.

These consequences affect both the individual level, through the impact on patients, and the healthcare system as a whole (4).

1. Treatment failure: antibiotic-resistant bacteria can lead to the failure of standard treatment, as they no longer respond to common antibiotics.

This complicates the management of infections, allowing them to persist or worsen, putting patients at increased risk of complications and requiring more intensive medical interventions.

2. Increased morbidity and mortality: infections caused by bacteria resistant to treatment may be associated with higher rates of morbidity and mortality.

Difficulty in treating these infections increases the risk of complications and reduces the effectiveness of treatment, thus contributing to the negative impact on the health status of patients.

3. Prolonged hospitalization: patients infected with antibiotic-resistant bacteria often require longer hospital stays and more complex treatments, contributing to the increased costs of the healthcare system and limiting the availability of hospital beds for other patients.

4. Use of stronger antibiotics: antibiotic resistance forces doctors to resort to the use of stronger antibiotics or combinations of antibiotics, with potential side effects and risks for patients. The choice of these options may be limited and may be associated with higher treatment costs.

5. Postoperative complications: in surgery, postoperative infections with antibiotic-resistant bacteria can lead to significant complications, including soft tissue infections, sepsis, and surgical failure. These complications can affect the recovery and long-term outcomes of patients.

6. Limitation of therapeutic options: as antimicrobial resistance spreads, available therapeutic options become limited, affecting the ability to treat infections effectively and properly manage associated diseases.

Challenges and opportunities in managing antimicrobial resistance

Managing antimicrobial resistance faces numerous challenges and, at the same time, offers opportunities for innovation and improvement in medical and public health practices (22).

Challenges:

- Excessive and inappropriate use of antibiotics: Inappropriate prescribing practices and excessive use of antibiotics in medical treatments or agricultural practices constitute a major challenge, generating selective pressure for the development of bacterial resistance.
- Global transfer of resistant bacteria: antimicrobial resistance knows no boundaries, and the global movement of people and goods can contribute to the rapid spread of resistant bacteria worldwide.
- Lack of rapid and accurate diagnostics: Limited availability of rapid and accurate diagnostics for identifying pathogens and their antibiotic resistance may delay the prescription of appropriate treatments and contribute to the inefficient use of antibiotics.
- Pharmaceutical industry and the economic incentives: The lack of sustainable economic models for the development of new antibiotics is a challenge. The pharmaceutical industry often faces economic uncertainties and profitability challenges compared to other types of medications.

Opportunities:

- Development of new diagnostic technologies: innovations in diagnostic technologies can improve the speed and accuracy of identifying bacteria and their sensitivity to antibiotics, allowing for the prescription of personalized treatments.
- Global collaboration: collaboration among countries, research institutions, the pharmaceutical industry, and international organizations provides opportunities for the exchange of knowledge, resources, and joint initiatives to combat antimicrobial resistance.
- Education and public awareness: continuous education and public awareness can contribute to changing behaviors regarding antibiotic use, thereby reducing pressure on resistance development.
- Promotion of research and innovation: Supporting research and innovation in the development of new antibiotics, including providing financial incentives and encouraging collaboration across sectors, can be essential opportunities in combating antimicrobial resistance (22, 25).

Managing antimicrobial resistance involves addressing both challenges and opportunities with an integrated and collaborative framework to promote sustainable and effective medical practices globally (9,22).

Conclusions

The evolution of antibiotic discovery and antimicrobial resistance represents a complex process, influenced by significant scientific discoveries as well as medical and socioeconomic practices, with substantial implications for public health and the medical approach to bacterial infections.

Antimicrobial resistance is now a serious threat to public health, making it essential to recognize the shared responsibility in preventing resistance progression.

Promoting responsible use of antibiotics becomes crucial for maintaining the effectiveness of these medications and ensuring effective treatments in the future.

Implementing rational medical practices and appropriate usage protocols are important steps in addressing antimicrobial resistance and protecting public health.

Continuous education of healthcare professionals and the general public is essential in this regard.

Looking to the future, addressing antimicrobial resistance involves integrating efforts globally, including promoting responsible antibiotic prescribing practices, developing new antibiotics and innovative diagnostic technologies, and stimulating research to deeply understand resistance mechanisms and identify innovative therapeutic strategies.

Thus, in the context of medical evolution and antibiotic discovery, the future depends on the responsible use of these medications, promoting continuous research for the development of new antibiotics, and strengthening global collaboration.

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Antibiotic resistance dynamics of the most frequently isolated potentially pathogenic bacteria from the food sector

Dinamica antibiorezistenței celor mai frecvent izolate bacterii cu potențial patogen din sectorul alimentar

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Keywords: *antibiotic resistance, antibacterial substances, public health, pathogenic bacteria, bacterial isolates*

Cuvinte cheie: *antibiorezistenţă, substanţe antibacteriene, sănătate publică, bacterii patogene, izolate bacteriene*

Abstract

Antibiotic resistance is a significant threat to human health, and the food sector often serves as an important reservoir of potentially pathogenic bacteria. In this context, it is important to investigate and know the dynamics of antibiotic resistance at the level of the most frequently isolated bacteria from the food sector. The aim of this study was to highlight the implication of antibiotic resistance in the food sector to protect public health and to counter the emerging threats generated by bioresistance in the food sector. Thus, we presented the role of the food sector in the spread of bioresistance, the methodology necessary to investigate antibiotic resistance in the food sector and the importance of identifying antibiotic resistance in bacteria isolated from food.

Rezumat

Antibiorezistența reprezintă o amenințare semnificativă la adresa sănătății umane, iar sectorul alimentar servește adesea ca un important rezervor de bacterii cu potențial patogen. În acest context, este importantă investigarea şi cunoaşterea dinamicii antibiorezistenței la nivelul celor mai frecvente izolate bacterii din sectorul alimentar. Scopul acestui studiu a fost de a evidenţia implicarea antibiorezistenţei în sectorul alimentar pentru a proteja sănătatea publică și pentru a contracara amenințările emergente generate de biorezistență în sectorul alimentar. Astfel, am prezentat rolul sectorului alimentar în răspândirea biorezistenţei, metolodogia necesară investigării antibiorezisteţei în sectorul alimentar şi importanţa indentificării rezistenței la antibiotice în bacteriile izolate din alimente.

Introduction

Antimicrobial resistance, defined as the ability of bacteria to survive exposure to drugs, poses a major challenge to human health and the effectiveness of medical treatments.

The food sector, due to its complex and diverse nature, can serve as an important reservoir for potentially pathogenic bacteria and, consequently, for the development and spread of antibiotic resistance (2, 7).

This paper presents the dynamics of antimicrobial resistance in the case of the most commonly isolated bacteria from the food sector (Figure 1).

The main objective is to highlight the sensitivity of these bacteria to various antibiotics and identify potential resistance mechanisms.

By understanding these aspects, we aim to contribute to the development of effective strategies for managing antimicrobial resistance in the food industry.

Through the collection and analysis of samples from various food sources, we aim to provide a detailed perspective on the current status of antibiotic resistance in this critical domain.

Identifying and presenting these issues could serve as a basis for implementing more responsible agricultural and food practices, thereby reducing the risk of antimicrobial resistance spread and protecting public health (10, 13).

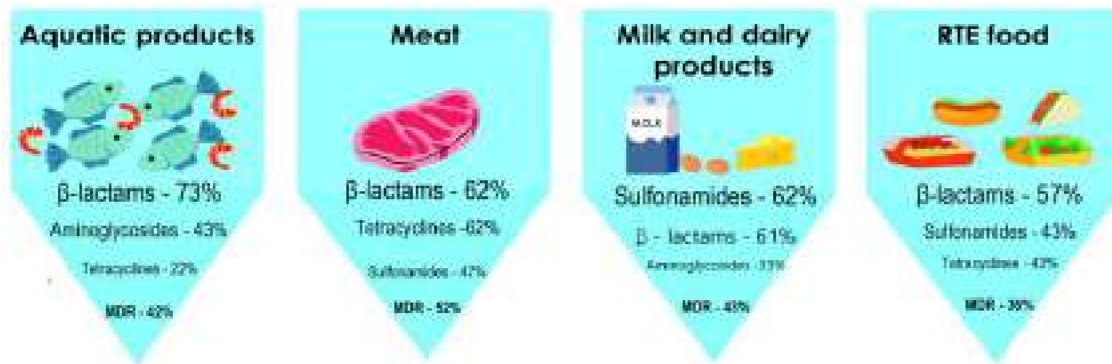

Figure 1. The most common types of antibiotic resistance by type of food product (**Source:** Grudlewska-Buda, K. şi col., 2023)

This work is based on the belief that understanding the mechanisms and patterns of antibiotic resistance in foodborne bacteria is essential for implementing effective management measures.

By analyzing antibiotic sensitivity profiles, we will be able to identify antibiotics that are still effective and, at the same time, highlight areas where resistance is growing (9, 1,15).

This information is crucial for adapting and optimizing treatment regimens.

Additionally, the significant variability among different food sources draws attention to possible influences of environmental, technological, or geographical factors on the development of antibiotic resistance (11,16,18,28).

Another key aspect of this work is highlighting the importance of responsible agricultural practices.

The excessive and inappropriate use of antibiotics in agriculture can significantly contribute to the growth of antibiotic-resistant foodborne bacteria.

By identifying the links between agricultural practices and resistance levels, we can develop guidelines and regulations to promote a balance between agricultural needs and the need to protect human health.

Promoting responsible antibiotic use and implementing sustainable practices in the food sector are essential to ensure that this global public health issue is addressed effectively and sustainably (17,24,26).

In the context of an increasing threat to the effectiveness of medical treatments, understanding the dynamics of antibiotic resistance in the food sector is essential, providing valuable information for the development of effective intervention and control strategies.

Antibiotic resistance and its implications for human health

Antibiotic resistance, as a biological phenomenon, has evolved in recent decades as a complex and pressing issue in human health.

The concept of antibiotic resistance refers to the ability of microorganisms to resist the action of medicinal substances, especially antibiotics, which generates significant difficulties in the treatment of infections (2,3).

The implications of antibiotic resistance for human health are multiple and deeply concerning.

First, the ability of bacteria to evolve and develop resistance to antibiotics reduces the effectiveness of medical treatments, exposing patients to increased risks of complications and even death.

Additionally, antibiotic resistance has a negative impact on the duration and costs associated with medical care.

The spread of antibiotic resistance in the medical community underscores the need for a global and coordinated approach to manage this problem and ensure the availability of effective therapy against bacterial infections (4,5,8).

Furthermore, antibiotic resistance has direct implications for global public health.

The phenomenon is susceptible to facilitating the spread of resistant infections worldwide, due to increased population mobility and international contacts.

This perspective underscores the need for consolidated international cooperation to develop effective strategies for controlling and preventing antibiotic resistance (1,10,14).

The role of the food sector in the spread of antibiotic resistance

The food sector plays a significant role in the spread of antibiotic resistance, providing a conducive environment for the development and transmission of antibiotic resistance genes in different environments and organisms.

This complex phenomenon involves multiple interactions between microorganisms present in food, the surrounding environment, and agricultural and food practices (22,26).

The most important aspects influencing the spread of antibiotic resistance in the food sector are:

- **Excessive use of antibiotics in agriculture:** antibiotics are often used in agricultural practices to promote animal growth and prevent infections. This extensive use can create a conducive environment for the development and selection of antibiotic-resistant bacteria.

- **Transfer of resistance genes through the food chain:** antibiotic-resistant bacteria and resistance genes can be transferred from antibiotic-treated animals to humans through the consumption of contaminated food products. This phenomenon contributes to the increased incidence of antibiotic resistance at the human level.

- **Environmental surroundings and food contamination:** the environment in which animals are raised and food production processes can facilitate contamination with resistant bacteria. This may include contamination of irrigation water, soil, and other natural resources used in food production.

- **International trade of food products:** In the context of globalization, food products can travel between countries and continents. This trade exchange can contribute to the spread of antibiotic-resistant bacteria and associated genes globally.

- **Inadequate food hygiene practices:** Inadequate hygiene practices in food processing and handling can facilitate contamination with resistant bacteria. This may include failure to comply with hygiene standards on farms, slaughterhouses, or in the food production process.

The food sector is an environment where antibiotic resistance can thrive and spread.

Addressing this issue requires special attention to agricultural and food practices, promoting responsible antibiotic use, improving food hygiene, and developing control strategies globally (12, 23).

Methodology for investigating antibiotic resistance

Investigating the dynamics of antibiotic resistance in the food sector requires a rigorous methodology for collecting samples and evaluating the sensitivity of identified bacteria.

Selection of food sources: identification and selection of food sources are based on their relevance in terms of the potential transmission of pathogenic bacteria to consumers.

This includes animal and plant products, processed and raw products, covering a wide range of commonly consumed foods.

Sampling process: sampling is carried out randomly at different geographical locations and food production units to ensure adequate representativeness.

Samples must be collected by specialized personnel using laboratory-approved techniques.

Each sample must be properly identified and recorded according to the type of food and the place of collection. Sample collection is done with sterile instruments to minimize the risk of contamination.

For packaged foods, the integrity of the packaging is ensured to avoid subsequent contamination.

For raw food products, sampling is done at multiple points to cover the bacterial diversity in different regions of the product.

Transport and storage of samples: after collection, samples must be transported to the laboratory under controlled temperature conditions to maintain the bacteriological integrity.

Upon arrival, they are stored according to laboratory standards to avoid contamination and degradation of biological material.

Identification and documentation of samples: in the laboratory, each sample must undergo a rigorous process of identification and documentation.

Relevant data, such as the type of food, date, and place of collection, are recorded to ensure precise and correlated tracking of results with specific sources.

Analysis of antibiotic sensitivity profiles

Analysis of antibiotic sensitivity profiles is carried out to obtain a detailed understanding of the resistance of bacteria isolated from food samples.

The procedure involves several well-defined steps to ensure the accuracy and relevance of the results:

Isolation and identification of bacteria: before performing antibiotic sensitivity tests, bacteria must be isolated and properly identified at the species level.

This step involves the use of molecular and biochemical technologies to confirm the presence of pathogenic bacteria and ensure the uniformity of the sample batch.

Establishing antibiotic concentrations: the exact concentrations of antibiotics used in tests must be established according to CLSI (Clinical and Laboratory Standards Institute) guidelines or other relevant international standards.

Antibiotic susceptibility techniques: antibiotic susceptibility tests are performed using standardized methods such as agar diffusion, dilution in liquid media, or automated methods, depending on the specific bacteria and antibiotics tested.

Special attention must be paid to CLSI standards to ensure the comparability of results.

Interpretation and documentation of results: Test results are interpreted according to reference values established by international organizations.

Detailed analysis of antibiotic sensitivity profiles provides essential data for understanding the extent and diversity of resistance among bacteria in the food sector and can serve as a basis for recommendations regarding responsible antibiotic use in agricultural and food practices (25,27).

Identification of resistance genes and mechanisms involved

To better understand antibiotic resistance at the molecular level and to identify resistance genes and mechanisms involved in bacteria isolated from the food sector, the following steps can be taken:

Extraction of bacterial DNA: bacterial DNA is extracted from isolated samples using specialized extraction techniques, ensuring the purity and integrity of the genetic material. This process is essential to obtain reliable and representative genetic sequences.

Genomic sequencing: the extracted DNA undergoes genomic sequencing to obtain a complete picture of the genetic material of bacteria.

Bioinformatic analysis: sequence data is analyzed using bioinformatic software to identify antibiotic resistance genes and determine any associated mutations.

This analysis includes comparison with reference databases to confirm gene identification.

Experimental validation: To validate the results of bioinformatic analysis, experimental tests such as PCR (Polymerase Chain Reaction) are performed to amplify and identify specific genes. This step is essential to confirm the presence of resistance genes identified by genomic sequencing.

Characterization of resistance mechanisms: based on the information obtained from bioinformatic analysis and experimental validation, specific mechanisms of antibiotic resistance are characterized.

This includes identifying the type of resistance (efflux, enzymatic modifications, etc.) and evaluating the expression level of the respective genes.

Interpretation and correlation with sensitivity profiles: the results obtained in identifying resistance genes and mechanisms involved are correlated with antibiotic sensitivity profiles.

This data integration provides a comprehensive understanding of the genomic and phenotypic characteristics of isolated bacteria.

This integrated approach to identifying resistance genes and mechanisms involved makes a significant contribution to understanding antibiotic resistance at the molecular level and can provide crucial information for developing precise and targeted strategies in managing antibiotic resistance in the food sector (25).

The expansion of antibiotic resistance in foodborne bacteria

The expansion of antibiotic resistance in foodborne bacteria indicates persistent pressure on these microorganisms, highlighting the need for a comprehensive and in-depth approach to managing this phenomenon.

The identified resistance mechanisms provide a detailed picture of how bacteria adapt to antibiotic pressure, facilitating the development of effective combating strategies (26).

The expansion of antibiotic resistance in foodborne bacteria represents a major threat to human health, with the potential to affect the effectiveness of treatments and increase the risk of complications.

Close monitoring and regulation are necessary to reduce unjustified antibiotic use in agriculture and to promote responsible food practices (21, 24).

The analysis of variability in resistance among food sources has identified important contributing factors to this phenomenon.

Agricultural practices, including antibiotic use in animal husbandry, have been identified as significant factors.

Additionally, differences in production processes and food hygiene have contributed to variation in resistance between food categories.

This detailed understanding of contributing factors provides the necessary basis for developing effective intervention strategies aimed at reducing resistance in the food sector (14,26,19).

Implications for public health and food practices

Antibiotic resistance in the food sector has significant implications for public health and food practices.

The expansion of antibiotic resistance in foodborne bacteria represents a major threat to human health, with the potential to affect the effectiveness of treatments and increase the risk of complications.

Close monitoring and regulation are necessary to reduce unjustified antibiotic use in agriculture and to promote responsible food practices (9, 15).

Numerous previous studies have made significant contributions to understanding antibiotic resistance in the food sector.

These researches have examined various aspects, including antibiotic resistance profiles of bacteria isolated from foods, the impact of agricultural practices on resistance development, and the implications of this resistance for human health.

The study conducted by Elder et al. in 2016 explores antibiotic resistance in foodborne pathogens, emphasizing the need for a global approach to managing this issue.

The authors highlight the links between antibiotic use in agriculture and the spread of resistance worldwide (9).

Additionally, Mukherjee et al. (2020) investigate the impact of agricultural practices, particularly soil irrigation, on the development of antibiotic resistance in *Escherichia coli*, exploring connections between irrigation water use and resistance emergence (20).

Research on antibiotic resistance in *E. coli* is complemented by Caruso in 2018, who analyzes antibiotic resistance in *Escherichia coli* isolated from farm animals, examining the evolution of resistance to various classes of antibiotics and highlighting the importance of constant monitoring in the agricultural sector (6).

Another study that contributed to understanding antibiotic resistance in the food sector is "*Antibiotic Resistance in Foodborne Bacteria - An Emerging Public Health Problem*," in which author Komolafe examines antibiotic resistance in foodborne bacteria and highlights the magnitude of the problem as an emerging threat to public health, emphasizing the need for an interdisciplinary approach to counteract this problem (17).

Conclusions

Understanding the dynamics of antibiotic resistance in the food sector is essential for implementing new strategies for managing antibiotic resistance.

The adoption of responsible agricultural practices and rational antibiotic use is necessary to reduce selective pressure on bacteria, thereby minimizing the risk of resistance expansion.

These measures are imperative for protecting public health and for effectively managing a phenomenon evolving in a continuously changing food context.

Continuous monitoring of antibiotic resistance in the food sector is a key element in our efforts to anticipate and manage these emerging threats to human health.

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Utilizarea și eficacitatea implantului cu deslorelină la animalele de companie

The use and effectiveness of deslorelin implant in companion animals

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Keywords: *deslorelin, GnRH agonist, chemical sterilization*
Cuvinte cheie: *deslorelină, GnRH agonist, sterilizarea chimică*

Abstract

Control of reproduction in companion animals is ensured both by surgical sterilization and by the administration of contraceptive medication. Since most progestogens have frequent severe adverse effects, long-acting gonadotropin-releasing hormone (GnRH) agonists, such as deslorelin, are now more commonly used. The advantages of the deslorelin implant are easy administration, increased efficiency over a long period of time, safety of use and reversibility of sterilization. Apart from using the implant as a contraceptive method, it can be administered in the therapy of conditions such as benign prostatic hyperplasia or in the treatment of behavioral disorders (aggression, excessive marking). The purpose of this short review is to present the advantages of using the deslorelin implant in pets and to highlight its effectiveness in controlling thier reproduction.

Rezumat

Controlul reproducerii la animalele de companie este asigurat atât prin sterilizarea chirugicală, cât şi prin administrarea medicaţiei contraceptive. Intrucât majoritatea progestativelor prezintă frecvente efecte adverse severe, în prezent sunt mai des utilizaţi agoniştii cu acţiune prelungită ai hormonului de eliberare a gonadotropinei (GnRH), precum deslorelina. Avantajele implantului cu deslorelină sunt administrarea uşoară, eficienţa crescută pe o perioadă îndelungată, siguranţa utilizării şi reversibilitatea sterilizării. În afara utilizării implantului ca metodă contraceptivă, acesta poate fi administrat în terapia unor afecţiuni precum hiperplazia benignă a prostatei sau în tratamentul tulburărilor de comportament (agresivitate, marcare excesivă). Scopul acestui scurt review este de a prezenta avantajele utilizării implantului cu deslorelină la animalele de companie şi de a evidenţia eficienţei acestuia în controlul reproducerii acestora.

Introduction

Reproductive control in companion animals is becoming increasingly important today and is an active concern for owners.

Sterilization / castration is primarily resorted to in order to reduce or eliminate a series of conditions that may arise over time, such as mammary cancer, ovarian cancer, pyometra in females; testicular cancer, prostatic hyperplasia in males, or the spread of TVT (transmissible venereal tumors), but also to significantly reduce the rate of abandonment of companion animals (12).

Over the years, several contraceptive medications have been developed for companion animals, but the frequency and severity of secondary adverse effects have limited their use.

Most types of progestives, oral or injectable, have been avoided both by owners and veterinarians, so surgical sterilization has been the most widely used method, being safe and permanent (12, 25).

When surgical intervention was not possible, reproductive control was achieved using progestogens, until now, when new and challenging options have become available, such as long-acting agonists of gonadotropin-releasing hormone (GnRH).

A new therapeutic approach has been the development of analogs of gonadotropin-releasing hormone (GnRH). GnRH is a hypothalamic decapeptide hormone which has the same amino acid sequence in all mammals (12).

Modifications of the decapeptide structure of a GnRH agonist provide two types of analogs: GnRH antagonists and GnRH agonists. GnRH antagonists bind to the GnRH receptor (GnRHr) and completely block the secretion of LH/FSH and downstream signaling pathway activation that stimulates gonadotropin biosynthesis.

After cessation of GnRH agonist treatment, the animal becomes fertile, but the time period is unpredictable (12, 25, 26, 27).

The development of efficient implants with low doses, slow release, potent GnRH agonists such as deslorelin (Suprelorin, Virbac) (Figure 1) has allowed their use to become widespread in companion animals (12).

Figure 1. Deslorelin implant

The use of the deslorelin implant in dogs

The first study involving the administration of deslorelin to male dogs was conducted in 2001 by Trigg et al., using a 6 mg implant. Subsequently, several studies were conducted (12, 25, 26, 27) using different concentrations (2.1, 4.7, 6, 9.4, and 12 mg/implant).

These studies reported that deslorelin implants represent a safe and well-tolerated sterilization method in dogs (12).

Moreover, repeated implantation is possible, and regardless of the concentration of deslorelin implant, following the loss of efficacy of these implants, all treated dogs reached physiological testosterone levels within 7-9 weeks, and semen quality returned completely.

Complete resumption of sexual function is a huge advantage in the case of valuable dogs used for breeding (9,10,11,17,18,19,22,25,26).

Typically, a rise in plasma levels can be detected as soon as 20 minutes following the implantation of deslorelin (10).

These levels drop to baseline values after 3 days and are not detectable at approximately 12 days post-implantation.

Regardless of size, all dogs treated with a 4.7 mg deslorelin implant show testosterone levels of <0.4 ng/ml from 22 to 33 days for at least 180 days (25).

Reduced levels of gonadotropins and plasma concentrations of testosterone explain the significant reduction in testicular volume and azoospermia in dogs treated with deslorelin (12).

The dose-response relationship is not expressed in the degree of suppression of reproductive function but in the duration of suppression, with a slow-release 6 mg or 9.4 mg implant reducing testosterone and sperm production for up to a year (26).

Decreased testosterone levels are usually accompanied by a decrease in testicular volume (10, 12, 25, 26).

Complete recovery of semen quality was obtained for all dogs at all tested doses.

The recovery time of steroidogenesis has been reported to be variable, with smaller dogs (<10 kg) taking longer to recover than medium or large dogs (25).

Dogs are expected to remain sexually incompetent for up to an additional 9 weeks after discontinuing deslorelin treatment (21, 22, 24, 25).

In addition to contraception, GnRH agonists also cause significant contraction of the prostate gland (11,16), which is clinically advantageous for dogs with benign prostatic hyperplasia (BPH), a common condition in intact male dogs (11, 16).

The effects of deslorelin on prostate volume in healthy dogs and clinically affected dogs with BPH have been evaluated by several authors (12), indicating the efficacy of deslorelin in BPH therapy.

A study by Niżański et al. in 2020 demonstrated that deslorelin acetate administration has longer-lasting efficacy compared to osaterone acetate in BPH (14).

According to a study by De Gier and Vinke (2010), another indication for using deslorelin in male dogs is the control of certain unacceptable behaviors related to testosterone action, such as aggression, fear/uncertainty, and sexual behavior in dogs (3).

Deslorelin implants are also used to delay puberty without affecting ovarian function and body development in both male and female dogs.

A study by Schäfer-Somi et al. in 2022 showed that in prepubertal bitches, both 4.7 mg and 9.4 mg implants delayed puberty until >2 years of age.

The local impact of deslorelin on ovarian suppression and resumption of ovarian activity has been highlighted, with no negative effects found on ovarian function after cyclicity recurrence (23).

Long-term reproductive data (up to two years after the first estrus) collected by Gontier et al. in 2022 support the hypothesis that females implanted with deslorelin have returned to fertility, exhibited regular heat cycles, were able to reproduce, and continued to conceive and give birth without major safety issues (8).

Thus, this implant offers a safe and highly effective alternative for reversible sterilization, with studies showing no evident side effects or health problems induced by repeated use of implants (8).

Initially, deslorelin implants were intended only for male contraception, being approved in the European Union only for administration to male dogs.

However, they are now being tested for use in females as well (2).

The use of the deslorelin implant in cats

In feline reproductive control, GnRH agonists are increasingly used.

The first study on chemical sterilization of male cats by administering deslorelin (4.7 mg implant) was conducted by Goericke-Pesch et al. (2010).

Just like in dogs,, the effect of chemical sterilization occurs through a decrease in testosterone levels (after an initial increase); however, in cats, the initial increase in testosterone was not significant, unlike findings in dogs.

Researchers found that testosterone levels rapidly decreased on day 20 post-implantation (<0.1 ng/ml) and remained at baseline concentrations for 11 weeks in most treated cats (6,7).

Similar to dogs, repeated implantation is possible, and after discontinuation of deslorelin implants, sexual function is resumed (4, 6, 7).

The main effect in male cats is on sexual behavior, and there is also a noticeable change in testicular size.

However, there is limited information about the effect of deslorelin on sperm quality and the return of sperm production in this species.

Histological studies have confirmed a rapid restoration of spermatogenesis at 1 month after implant removal, but more studies are needed on the return of sexual activity (5, 15).

A study by Amaral et al. in 2023 highlighted the effectiveness of deslorelin implants in reducing sexual behaviors in male cats, including reducing vocalization, urine marking, and aggression (1).

In female cats, the main use of deslorelin implants is to inhibit estrus.

A study by Munson et al. (2001) confirmed that deslorelin can be used to effectively suppress ovarian activity, but the duration of inhibition was highly variable (average of 14 months) (13, 20).

Conclusion

Chemical sterilization by administering deslorelin implants is a reliable option, offering a safe and effective reduction in fertility in males.

The main advantage of this implant is its reversibility, with full sexual function being resumed upon discontinuation.

At the same time, deslorelin helps decrease sexual behavior, providing an alternative therapy for behavioral disorders in pets due to testosterone. In males, deslorelin also represents a highly effective therapy option for benign prostatic hyperplasia.

Although deslorelin implants are currently widely administered only in males, more and more studies support their use in females.

The easy administration, long-lasting effectiveness of the implant, and its reversibility are just a few of the qualities supporting its use in pet reproductive control.

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A Decade of Data: *E. coli* Presence in Europe's Wild Bird Species – an epidemiological study

Un deceniu de date: Prezența *E. coli* la speciile de păsări sălbatice din Europa - un studiu epidemiologic

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Key words: *Escherichia coli, wild birds, Europe, epidemiology*
Cuvinte cheie: *Escherichia coli, păsări sălbatice, Europa, epidemiologie.*

Abstract

Over the past decade, understanding the presence and dynamics of *Escherichia coli* in Europe's wild bird species has emerged as a critical area of research. This article synthesizes a comprehensive analysis of *E. coli* prevalence among wild bird populations across Europe from 2011 to 2022. Beginning with an overview of *E. coli* research in wild birds from 1997 to 2024, the review explores the evolution of scientific interest in this topic and highlights trends in publication frequency. A focused examination of publications reveals a surge in research activity, reflecting growing concerns about antimicrobial resistance and environmental health. Furthermore, the review presents a detailed analysis of *E. coli* isolates from wild birds, examining the annual distribution of cases and identifying patterns across different European countries. Additionally, the review identifies the top five bird species most frequently studied in relation to *E. coli* presence, providing insights into the focal points of research efforts. By synthesizing a decade's worth of data, this review contributes to a comprehensive understanding of the epidemiology and dynamics of *E. coli* infections in Europe's wild bird populations.

Rezumat

În ultimul deceniu, înțelegerea prezenței și a dinamicii *Escherichiei coli* la speciile de păsări sălbatice din Europa a devenit un domeniu de cercetare esențial. Acest articol sintetizează o analiză cuprinzătoare a prevalenței *E. coli* în rândul populațiilor de păsări sălbatice din Europa în perioada 2011-2022. Începând cu o prezentare generală a cercetărilor privind *E. coli* la păsările sălbatice din 1997 până în 2024, analiza explorează evoluția interesului științific pentru acest subiect și evidențiază tendințele în ceea ce privește frecvența publicațiilor. O examinare concentrată a publicațiilor relevă o creștere bruscă a activității de cercetare, reflectând preocupările crescânde privind rezistența antimicrobiană și sănătatea mediului. Se prezintă o analiză detaliată a izolatelor de *E. coli* de la păsările sălbatice, examinând distribuția anuală a cazurilor și identificând modele în diferite țări europene. În plus, analiza identifică primele cinci specii de păsări cel mai frecvent studiate în ceea ce privește prezența *E. coli*, oferind o perspectivă asupra punctelor centrale ale eforturilor de cercetare. Prin sintetizarea unui deceniu de date, această analiză contribuie la o înțelegere cuprinzătoare a epidemiologiei și dinamicii infecțiilor cu *E. coli* în populațiile de păsări sălbatice din Europa.

Introduction

Compared to 2021, the total number of reported isolates increased from 366 794 to 392 602.

The most commonly reported bacterial species in 2022 were:

- *Escherichia coli* (39.2%), followed by
- *Staphylococcus aureus* (22.1%),
- *Klebsiella pneumoniae* (12.3%),
- *Enterococcus faecal*is (8.2%),
- *Pseudomonas aeruginosa* (6.1%),
- *Enterococcus faecium* (5.9%),
- *Streptococcus pneumoniae* (3.7%) and
- *Acinetobacter spp*. (2.5%).

This ranking differed from 2021, with *P. aeruginosa* and *S. pneumoniae* one rank higher in 2022 [10].

The genus *Escherichia* contains five species: albertii, coli, fergusonii, hermannii, and vulneris; the species blattae has recently been moved into the Shimwellia genus. Escherichia is the type genus of the Enterobacteriaceae family, with coli the type species of the genus. *Escherichia coli* is the only species that includes important pathogens of animals.

Many *E. coli* are commensals of the intestinal tract, especially the large intestine; however, many are opportunistic or primary pathogens too. Pathogenic *E. coli* are broadly divided into diarrheagenic and extraintestinal strains. Diarrheagenic *E. coli* are economically important pathogens of neonatal piglets, calves, and lambs.

In avian species, *E. coli* is an important cause of air sacculitis, pneumonia, septicemia, and omphalitis. Zoonotic infections with Shiga toxin-producing *E. coli* (STEC) and host-specific diarrheagenic and extraintestinal infections are of major importance in human medicine.

Reservoir and Transmission: Strains of *E. coli* capable of producing disease reside in the lower gastrointestinal tract and are abundant in environments inhabited by animals. Transmission is through the fecal-oral route. The lower intestinal tract has been termed the “primary habitat” and the environment outside the animal, the “secondary habitat” of *E. coli*.

This reflects the importance of the lower intestine in providing the necessary nutrients and warm temperatures for *E. coli* (a mesophile) to be in a positive growth state, and also the need for it to exit one host in order to enter a new one to complete its “life cycle” [22].

The primary objective of this study was to determine the prevalence of *E. coli* in the feces of wild birds across Europe in the last decade.

Materials and Methods

A systematic literature review of the available publications describing the presence of *Escherichia coli* in wildlife was performed using a rigorous search strategy in the online version of the PubMed (https://pubmed.ncbi.nlm.nih.gov) [29], where we searched from 2013 until 2024 for articles using the combination of terms ‘*E. coli*’, ‘wild birds’ and ‘Europe’.

The last search was done in March 2024. We made no restrictions regarding language or types of articles. All available titles and abstracts were reviewed. The focus of this search was to find publications that contained *Escherichia* isolates from wild birds in the last decade in Europe.

All the publications from literature search were analysed in two steps: (i) firstly, titles and abstracts were analysed and the publications which did not fill the inclusion criteria (e.g., focus on *E. coli*, wild birds, Europe countries) were excluded; and (ii) secondly, the full text was analysed and the relevant information was extracted. All query results were verified manually before excluding duplicates.

Finally, results for all articles were imported into a bibliographic referencing tool (Zotero Desktop 6.0.23). All publications were included with the following variables extracted: year of publication, location of analysed samples, animal data, bacterial data and citation.

Results and Discussion

From the literature search, a total of 54 publications were obtained.

This number was reduced to 34 after the first step of analysis (title and abstract) and, after the second step of analysis (full text), only 22 publications remained.

Publications focusing on *Escherichia coli* from wildlife are relatively recent and date from 1997. The first publication, in 1997, with the title ”Enteropathogenic Bacteria in Migrating Birds Arriving in Sweden”, reported that they did not isolate *Escherichia coli* in any of the bird stools examined from 151 wild birds (50 gulls and 101 passerines) in Sweden, but their data do not exclude the possible existence of a bird reservoir of this bacteria in that year [25].

From a different perspective, Guenther et al. reported in 2010 that a total of 201 putative *E. coli* isolates were cultured from 275 samples collected from 226 birds. These samples were obtained from various sources including feces (n=160), heart (n=6), liver (n=9), lung (n=13), spleen (n=6), and kidney (n=7).

Furthermore, they identified *E. coli* in 40 out of 55 avian species tested at the individual bird species level [14].

The number of publications on this topic has grown since 1997 until now, but the largest number of publications is concentrated in 2010–2019.

These datas represents the number of publications about the studied subject over the years.

There is a fluctuating pattern in the number of publications over time, with varying counts from year to year.

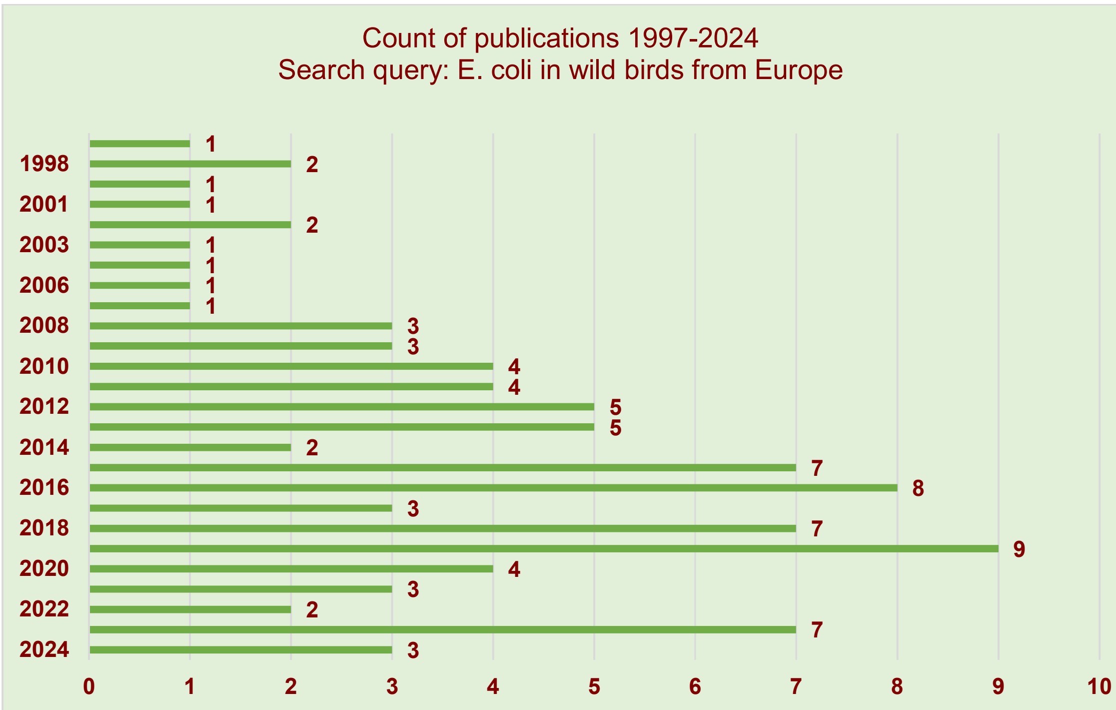

Figure 1. Publications *E. coli* reported in wildbirds since 1997 [PubMed]

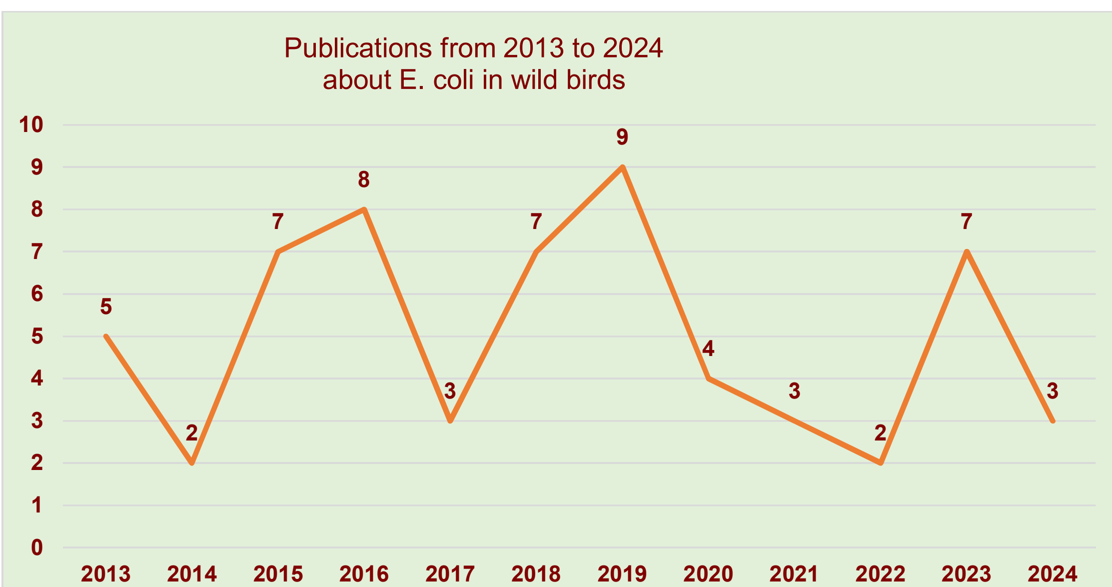

Figure 2. Trends of publication *E. coli* reported in wildbirds 2013-2024 [PubMed]

The highest number of publications was recorded in 2019, with 9 publications, followed by 2016 and 2018, with 8 and 7 publications, respectively.

From 2007 to 2015, there seems to be a relatively stable number of publications, with counts ranging from 1 to 7.

There are fewer publications in the earlier years (before 2000), with counts mostly ranging from 1 to 3.

The lowest counts are observed in 2004, 2006, 1999, 1997, and 2001, with only 1 publication each.

Overall, the data suggests fluctuating interest or research activity in the studied subject over the years, with some years experiencing higher publication rates than others.

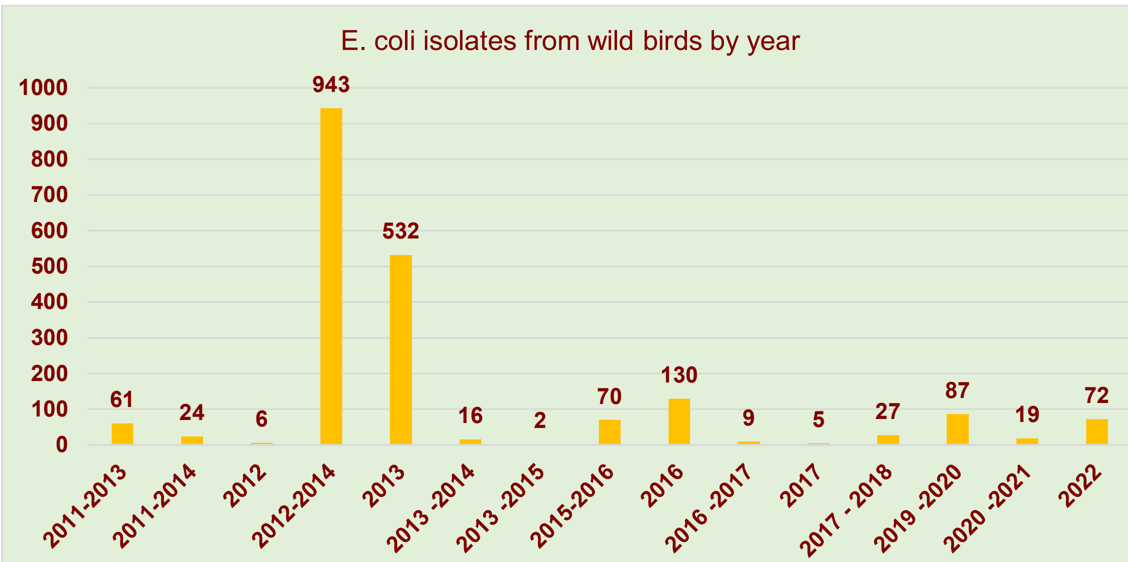

Figure 3. *E. coli* isolates by year from Europe 2011-2022.

The data suggests variations in the reported number of *E. coli* isolates from wild birds over the years, indicating fluctuating prevalence rates.

Some years exhibit higher prevalence than others.

- Between 2012 and 2014, there was a significant increase to 943 isolates [19].
- In 2013, there were 532 reported isolates, indicating a high prevalence [4, 8, 13, 18].
- From 2013 to 2014, the number decreased to 16 isolates [1, 16].
- From 2013 to 2015, only 2 isolates were reported [3].
- In 2015-2016, there was a slight increase to 70 isolates [12, 24].
- In 2016, the number increased significantly to 130 isolates [5, 7, 23].
- From 2016 to 2017, there were 9 isolates reported [9].
- In 2017, the number decreased to 5 isolates [17].
- From 2017 to 2018, there was a slight increase to 27 isolates [21].
- From 2019 to 2020, there was a notable increase to 87 isolates [15].
- From 2020 to 2021, the number decreased to 19 isolates [11].
- In 2022, there were 72 reported isolates [6].

Austria and the Czech Republic have the highest number of reported *E. coli* cases in wild birds between 2013 and 2023, with 473 and 470 cases, respectively.

This indicates a relatively high prevalence of *E. coli* infections among wild bird populations in these countries during the specified period.

Sweden follows closely behind, with 415 reported cases, suggesting a significant presence of *E. coli* infections in wild birds within the country. Spain has a lower but still notable number of reported cases, with 300 instances of *E. coli* infections in wild birds.

Ireland and Hungary have fewer reported cases compared to the previously mentioned countries, with 87 and 72 cases, respectively.

Poland, Italy, Germany, the Netherlands, and Ukraine have even fewer reported cases, ranging from 55 to 19 cases each.

Switzerland and France have the lowest number of reported cases, with only 6 instances of *E. coli* infections in wild birds each.

Eastern Slovakia has reported 5 cases during the specified period (Table 1).

Overall, these data suggest variations in the prevalence of *E. coli* infections among wild bird populations across different countries.

Factors such as habitat, environmental conditions, and human activities may contribute to these differences.

Further investigation may be needed to understand the underlying factors influencing the occurrence of *E. coli* infections in wild birds in each country.

Table 1.
Number of reporting *E. coli* in wildbirds per country.

Country	*E. coli* cases 2013-2023
Austria	473
Czech Republic	470
Sweden	415
Spain	300
Ireland	87
Hungary	72
Poland	55
Italy	40
Germany	24
Netherlands	23
Ukraine	19
Switzerland	6
France	6
Slovakia	5

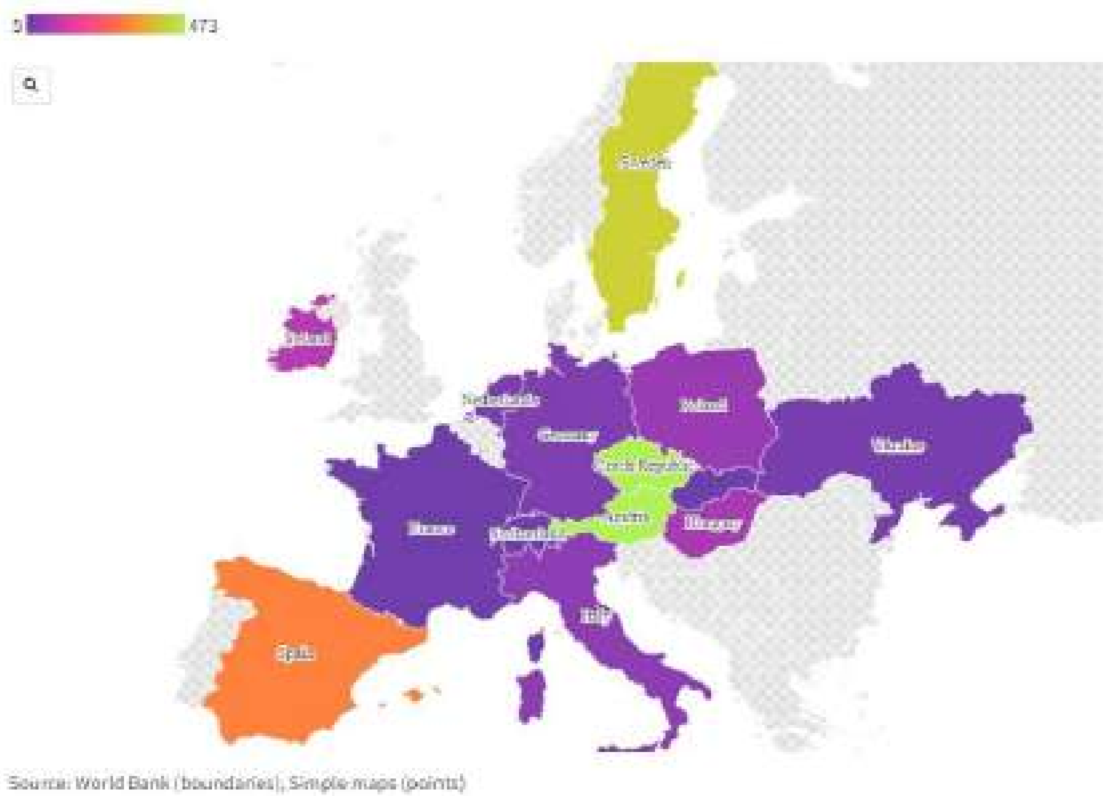

Figure 4. Europe map (made it with Flourish) representing the number of *E. coli* positive isolates from wild birds per country. The number of publications per country are color-coded as per the index and the top left of the figure [28].

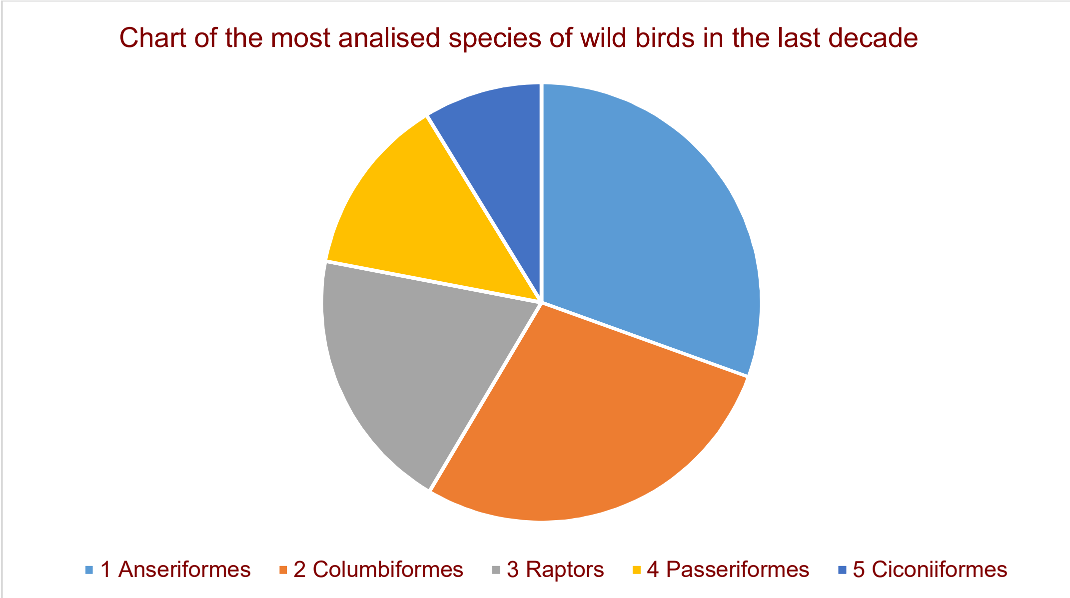

Figure 5. Top 5 wild birds species with reported *E. coli* occurrence.

Wildlife of Birds

Anseriformes, including wild ducks and waterfowl birds are the most commonly mentioned species in scientific articles related to the isolation of *E. coli* from wild birds, with a total of 491 mentions in the last decade. Pigeons (*Columbiformes*) rank second in terms of frequency, with 451 mentions in these articles. Birds of prey (*Accipitriformes*, *Strigiformes* and *Falconiformes*) follow in third place, with 314 mentions. *Passeriformes*, which include a variety of birds, are in fourth place with 213 mentions. Storks (*Ciconia Ciconia*) are at the bottom of the short list of the most frequently mentioned species in these articles, with 141 mentions.

Diurnal birds of prey identified in the reviewed studies included Griffon vulture (*Gyps fulvus*), Black kite (*Milvus migrans*), Red kite (*Milvus milvus*), Golden eagle (*Aquila chrysaetos*), Eurasian sparrowhawk (*Accipiter nisus*), Northern goshawk (*Accipiter gentilis*), Common buzzard (*Buteo buteo*), Common kestrel (*Falco tinnunculus*), European honey buzzard (*Pernis apivorus*), Booted eagle, Black vulture, Bonelli's eagle and Egyptian vultures, with a total of 302 mentions.

Nocturnal birds of prey - the owls – including Barn owl (*Tyto alba*), Long-eared owl (*Asio otus*), Eurasian scops owl (*Otus scops*), Tawny owl (*Strix aluco*) and Eurasian eagle-owl (*Bubo Bubo*), were mentioned 12 times collectively.

These findings indicate that *Anas platyrhynchos* (Mallard) are the most studied and observed species in studies focusing on the isolation of *E. coli*, followed by Pigeons, Raptors, and Passerines. Storks are less frequently mentioned in these studies compared to other bird species.

Among gulls such as *Larus marinus*, *Larus argentatus*, *Larus canus* and *Croicocephalus ridibundus*, Herring gulls, Lesser black-back gulls, *Larus michahellis* - yellow-legged gull, were next in terms of the number of positive isolates, totaling 127 cases.

Conclusions

In conclusion, our analysis reveals a comprehensive overview of the distribution of *E. coli* isolates among various wild bird species in research conducted over the past years.

The analysis of publication counts from 1997 to 2024 reveals a growing interest in the study of *E. coli* in wild bird populations over time.

This reflects the recognition of *E. coli* as a significant pathogen in avian ecology and highlights the importance of continued research in this area.

A focused examination of publications from 2013 to 2024 indicates a significant surge in research activity during this period. This heightened interest may be attributed to concerns about antimicrobial resistance, environmental health, and the potential zoonotic transmission of *E. coli* from wild birds to humans.

Analysis of yearly isolate counts reveals fluctuations in the number of *E. coli* cases isolated from wild birds over the past decade. These variations may be influenced by factors such as changes in environmental conditions, migratory patterns, and surveillance efforts.

Mallards, pigeons, raptors, and passerines emerge as the most frequently studied and observed species in relation to *E. coli* isolation, highlighting their significance in research efforts.

Overall, these conclusions highlight the diverse roles of various bird species in *E. coli* research and underscore the importance of understanding their contributions to the epidemiology of *E. coli* infections in wild bird populations.

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Prezentare de carte

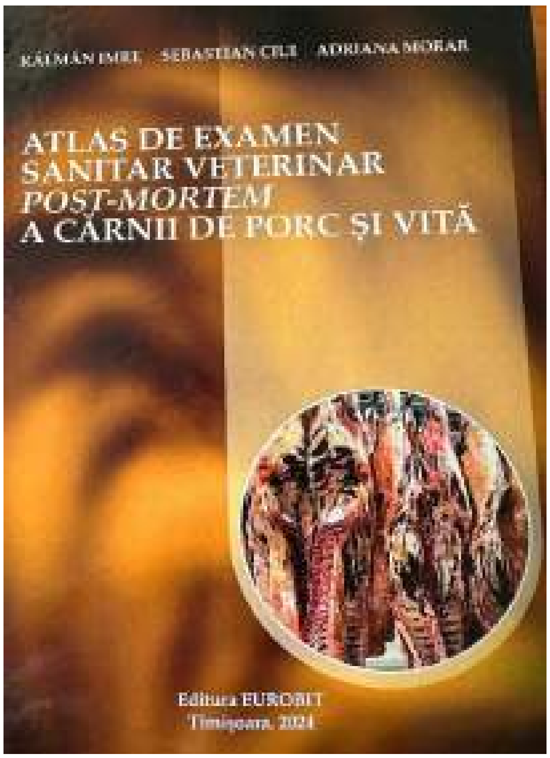
Atlas de examen sanitar veterinar post-mortem a cărnii de porc și vită

Autori: Kalman Imre, Sebastian Ciui, Adriana Morar, Eurobit Timișoara, 2024

Book presentation

Atlas of post-mortem veterinary sanitary examination of pork and beef

Authors: Kalman Imre, Sebastian Ciui, Adriana Morar, Eurobit Timișoara, 2024



Lucrarea *Atlas de examen sanitar veterinar post-mortem a cărnii de porc și vită,* autori: Kalman Imre, Sebastian Ciui, Adriana Morar, Editura Eurobit Timișoara, 2024, ISBN 978-630-326-073-0, 479 pp., este un ghid excelent și o premieră în România, care vine în întâmpinarea cerințelor medicilor veterinar de abator, în protejarea sănătății consumatorului, în una din sarcinile esențiale ale activității lor în inspecția *post-mortem* fiind identificarea unor modificări în organele și carcasele destinate consumului.

Atlasul este o lucrare originală, rodul unei activități de mai mulți ani unde autorii au dat dovada probității lor profesionale. Ilustrațiile originale și de foarte bună calitate, surprind cele mai sugestive modificări structurale determinate de patologia diverselor boli la suine și bovine.

Concepută ca un vademecum, Atlasul este un instrument util mediclor veterinar și va contribui cu certitudine la finisarea competențelor în importantul domeniu al siguranței alimentelor.

Sunt convins că vor mai urma și alte frumoase lucrări!

Felicitări autorilor!

The work Atlas of post-mortem veterinary sanitary examination of pork and beef, authors: Kalman Imre, Sebastian Ciui, Adriana Morar, Editure Eurobit Timișoara, 2024, ISBN 978-630-326-073-0, 479 pp., is an excellent guide and a premiere in Romania, which meets the requirements of the slaughterhouse veterinarians, in protecting the health of the consumer, in one of the essential tasks of their activity in the post-mortem inspection being the identification of changes in the organs and carcasses intended for consumption.

The atlas is an original work, the fruit of many years of effort where the authors have proven their professional probity. Original and very good quality illustrations capture the most suggestive structural changes determined by the pathology of various diseases in pigs and cattle.

Designed as a vademecum, the Atlas is a useful tool for veterinarians and will certainly contribute to the refinement of skills in the important field of food safety.

I am sure that there will be other beautiful works to come!

Congratulations to the authors!

Romeo T. Cristina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▼*Necrolog*

Dr. Aurel Mihai GHERDAN
(24.05.1933 - 26.06.2024)

Aurel Mihai Gherdan a văzut lumina zilei la 24 Mai 1933, în Târnăveni, Mureș

Este absolventul Facultății de Medicină Veterinară din Arad, în promoția anului 1957.

Evoluție: Medic veterinar circumscripţia Timişoara, 1957-1964; Medic veterinar şef al municipiului Timişoara. Specializare în domeniul Farmacologiei la UMV Budapesta. Din 1968 asistent la FMV Timişoara; șef lucrări, titularul cursului de „Boli de nutriţie şi toxicoze", 1972.

Din anul 1972 până în 1981, domnul dr. Gherdan a fost titularul cursului la disciplina „Toxicologie şi toxicoze", iar din anul 1974, domnul dr. Gherdan a preluat disciplina de „Farmacologie veterinară" unde a activat până în 1997, la pensionarea sa.

Activitatea publicistică

Domnul Dr. Gherdan a fost unic autor al „Caietului de lucrări practice de farmacologie veterinară" (1977, 1981, 1992, Lito IAT) și colaborator la: manualul unic „Toxicologie şi toxicoze" (1977), Ed. Didactică şi Pedagogică Bucureşti, E. Şuţeanu, A. Gherdan, S. Ghergariu, O. Popescu. și respectiv colaborator la „Îndrumător de lucrări practice de toxicologie", A. Trif, A. Gherdan, Lito IAT, 1984. În cursul carierei sale Domnul dr. Gherdan a publicat peste 200 lucrări ştiinţifice ca prim autor sau colaborator și a îndrumat cu competență peste 50 lucrări de diplomă ale studenților de la secția medicină veterinară.

Activitatea de cercetare științifică

Din activitatea la disciplină este de remarcat aplecarea domnului dr. Gherdan către cercetarea științifică, domnia sa fiind unul dintre cadrele didactice cu numeroase granturi multianuale câştigate și aplicate din cele 70 de teme și subteme contractuale câștigate. Dr. Aurel Gherdan a desfăşurat o fructuoasă colaborare cu ICCF Bucureşti, cu intreprinderile de medicamente de uz veterinar din țară şi din străinătate, contribuind, prin cercetările efectuate, la introducerea în terapia veterinară a numeroase produse medicamentoase noi. Dr. Aurel Gherdan a fost mulți ani membru în Comisia medicamentului de uz veterinar precum și un expert național recunoscut în domeniu.

Un lucru care trebuie spus despre domnul dr. Aurel Gherdan – omul, este acela că, a fost o persoană populară, comunicativă, accesibilă, și de o fină jovialitate. Ținuta, comportamentul, manierele, vocabularul adecvat conjuncturii, eleganța și frumusețea fizică (dublată de frumusețea sufletească), făceau din el prototipul adevăratului "domn" pe care eu l-am admirat întotdeauna!.

Dumnezeu să-l odihnească în pace!
Cu adâncă recunoștiința,
Romeo T. Cristina

▼ *Instructiuni pentru autori*

Instrucţiuni pentru autori

Revista *Medicamentul veterinar / Veterinary Drug* (*Med. Vet. / Vet. Drug*) este publicaţia oficială a *Asociaţiei Naţionale a Fabricanţilor de Produse de Uz Veterinar din România* **(ANFPUVR)** cu apariţie semestrială în lunile Mai – Iunie și Decembrie.

Sunt aşteptate spre publicare lucrări din domenii conexe topicului acestei reviste, care să fie asimilabile următoarelor:

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- autorii vor fi citati in text intre paranteze simple, numele autorului fiind urmat de anul aparitiei lucrării.
- ex.: (Paştea, 1990)[..].
- dacă sunt doi autori, vor fi citaţi ambii: ex. (Teuşdea şi Mitrănescu, 1999)[..].
- dacă sunt mai mulţi de doi: ex. (Taylor şi col., 2004).
- dacă se face referire la un autor, care la rândul lui este citat de către alt autor: (Trif şi col. cit. de Oros, 2006)[..].
- verificaţi ca toţi autorii din bibliografie să fie citaţi în text şi viceversa, toţi autorii din text să apară la bibliografie.
- citarea lucrărilor se face înscriind numărul de ordine al lucrării (lucrărilor) în paranteze drepte, de regula, la sfârşitul frazei. ex.:„Aceste aspecte au fost relevate de

numeroşi autori din literatura de specialitate [1, 3, 15, 33]".

Italicele*:* se scriu obligatoriu cu italice:
- cuvintele în limba latină: *ad libitum, in vitro, in vivo, et al., per se, ad hoc, inter alia, inter se* etc.
- denumirile stiinţifice ale speciilor: *Haemonchus contortus, Brachyspira spp., Datura stramonium, Candida albicans* etc.
- constante şi necunoscute matematice,
- prima folosire în text a unui termen special,
- denumirile anatomice în limba latina: muşchiul *latissimus dorsi,* osul *humerus*, vena *cava caudalis.*

nu se scriu obligatoriu cu italice: corpus luteum, via, N.B., i.m., i.v., s.c., post mortem, post partum etc.;

Liniuţa de unire:
- nu se recomandă despărţirea în silabe la capătul rândului, ci scrierea cuvântului întreg.
- poate fi utilizată după prefixe: anti-estrogenic, pre-tratament, non-activ, post-partum,

Nerecomandabil
- nu se admite limbajul echivoc, neştiinţific şi imprecis.
- nu sunt recomandate expresii ca: „Un bine cunoscut cercetător ...”„de la 10 la 12 ore” etc.

Parantezele:
- se pot utiliza toate cele trei tipuri, fără să existe o regulă generală.

Se scriu cu majusculă:
- toate denumirile ştiintifice ale speciilor, numele claselor, ordinelor şi familiilor (bacteriene, virale, parazitare etc).
- numele proprii ale persoanelor, instituţiilor,
- abrevierile.
- numele bolilor nu vor fi capitalizate.

Numeralele:
- se folosesc litere pentru numeralele de la unu la nouă (ex.: doi, cinci, şapte) şi cifre peste nouă (ex.: 10, 11, 231 etc.);
- separarea zecimalelor: prin virgula în cazul redactării în limba romană şi prin punct, în cazul limbii engleze;
- pentru numerele mari din text se vor adopta formulări cât mai scurte, ex.: 10.000.000 / 10^7;
- pentru înmulţire se foloseste semnul **x**; ex. 129 x 236,
- pentru împărţire, semnul ***/***. Exemplu: 129/236.

Unităţile de măsură:
- se vor exprima conform standardelor intenaţionale agreate şi utilizate în literatura de specialitate.
- exprimarea concentraţiei şi a compoziţiei: se preferă exprimarea în moli (M sau mM) sau echivalenţi (Eq sau mEq) (cu excepţiile legate de procentul de mortalitate, exprimarea procentuală (%) a soluţiilor sau alte valori simple care se pretează la această formă de prezentare fiind folosită recomandabil în aceste situaţii).

Simbolurile:
- conform standardelor matematice: ex. >,< ,=,±,≡,≥, ≤, ≠, ≈, ∞, ♂, ♀ etc.
- semnele statistice: ex.*P<0,05,**P>0,01,***P<0,001 etc.

Abrevierile:
- vor fi cele standard ex: FSH, LH, ACTH, DNA, RNA, approx., I.U.- internaţional units; vs – versus etc.

Redactarea tabelelor:
- tabelele vor fi concepute astfel încât să ocupe toată lăţimea oglinzii paginii, fără să o depăşească.
- dacă un tabel trece pe pagina următoare, el va fi precedat de o linie care să cuprindă repetarea capătului de tabel sau daca este de mari dimensiuni, acesta va fi inserat fără cap de tabel pe fiecare pagină.
- corpul de literă la tabele poate fi de 8 sau 9.
- numerotarea tabelelor se face aliniat dreapta, italic,astfel: **Tabelul 1**
- titlul tabelului va fi redactat în limba romană şi în limba engleză, bold, centrat.
- numerotarea şi titlul tabelelor vor fi redactate cu corpul de litera **10**.
- textul tabelului, în interiorul acestuia, va fi redactat de asemenea bilingv.
- titlurile tabelelor să fie suficient de detaliate, fără prescurtări.
- tabelele (ca şi figurile) vor fi obligatoriu citate în text şi comentate.
- dacă există tabele care conţin note, acestea, ca şi legenda, se vor scrie imediat sub tabel.

Materialul ilustrativ:
- este reprezenat de figuri (noţiunea incluzând fotografii, desene, scheme, grafice etc.).
- toate figurile vor fi prezentate în alb-negru sau color, cu un contrast cât mai bun.
- dimensiunea acestora să nu depăşească ¼ din lăţimea oglinzii paginii.
- numerotarea figurilor se face centrat, sub figură, cu bold: **Fig. 1**.
- titlul, urmează după numerotare, simplu, centrat, **10 pt.,** adnotările din cadrul figurilor se vor face cu corpul **literă 8**.
- numerotarea şi textul figurilor vor fi redactate în limba română.
- toate figurile vor fi citate în text (şi comentate).

Notele de subsol (footnotes)
- acestea se vor marca cu cifre, mărimea fontului **8**.
- notele de pe o pagina trebuie să se regăsească în subsolul paginii respective.

Head Editor
Prof. Dr. Romeo T. Cristina


ROMAVERMECTIN B, 1%
Soluție injectabilă
Bovine: 1ml / 50 kg g.v.
Ovine: 0,5 ml / 25 kg g.v.
ROMAVERMECTIN B, 1% PLUS
Soluție injectabilă
Bovine: 1ml / 50 kg g.v.
ROMIVERMECTIN 1%
Soluție injectabilă
Bovine, ovine, caprine: 1 ml / 50 kg g.v.
Porcine: 1 ml / 35 kg g.v.
ANTIHELMINTIC CU SPECTRU LARG, ACARICID
TREMATODOCID NEMATODICID ACARICID INSECTICID
ANTIHELMINTIC CU SPECTRU LARG, ACARICID
PRODUSE RECOMANDATE ÎN COMBATEREA ENDO- ŞI ECTOPARAZIȚILOR
Asigură sănătatea animalelor
Cresc producția de lapte & carne printr-o bună conversie a furajului
Reduc morbiditatea & a mortalitatea
ROMVAC
COMPANY S.A.
Producător de vaccinuri şi medicamente de uz veterinar, cu o experiență de peste 30 de ani în domeniu este partenerul de încredere în asigurarea sănătății animalelor dumneavoastră.
CU NOI SUNTEȚI ÎN SIGURANȚĂ!