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Molecular Entities of Antimicrobial Drugs and Resistance Mechanism Underlying: Bioaccessibility, Bioavailability and Bioaccumulation

Rajiv Kumar

NIET, National Institute of Medical Science, India

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ABSTRACT

The three major groups of antifungal agents are there that are used in clinical use, azoles, polyenes, and allylamine/thiocarbamates, all own their antifungal activities to inhibit the reactivity of microbial or stop direct interaction of microbial with healthy cells.[3] Microbial organometallic assimilation, the bioaccessibility, bioavailability, and bioaccumulation properties of inorganic metals in different antimicrobial moieties that are interrelated and classified as abiotic (e.g., organic carbon) and biotic (e.g., uptake and metabolism).[4]

*Corresponding author. e-mail: chemistry_rajiv@hotmail.com

Introduction

The development of antifungal and antibacterial agents is different because of unpredictable consequences of the cellular events and features of the organisms. Hence, substantial attention has been focused on developing a more detailed understanding of the mechanisms of antimicrobial resistance, improved methods to detect resistance when it occurs search new antimicrobial options in treating infections caused by resistant organisms, and methods to prevent the emergence and spread of resistance in the first place since such efforts initiated.[1] Most of the attention has devoted to the study of antibiotic resistance in bacteria for several reasons: (i) bacterial infections are responsible for the bulk of community-acquired and nosocomial infections; (ii) the large and expanding number of antibacterial classes offers a more diverse range of resistance mechanisms to study; and (iii) the ability to move bacterial resistance determinants into standard well-characterized bacterial strains facilitates the detailed study of molecular mechanisms of resistance in bacterial species.[2] Moreover, the three major groups of antifungal agents are there that are used in clinical use, azoles, polyenes, and allylamine/thiocarbamates, all own their antifungal activities to inhibit the reactivity of microbial or stop direct interaction of microbial with healthy cells.[3] Microbial organometallic assimilation, the bioaccessibility, bioavailability, and bioaccumulation properties of inorganic metals in different antimicrobial moieties that are interrelated and classified as abiotic (e.g., organic carbon) and biotic (e.g., uptake and metabolism).[4]

Modifying factors determine the amount of an inorganic metal that interacts at biological surfaces and binds it and finally was absorbed across the membranes.[5] A major challenge is to consistently and accurately measure quantitative differences in bioavailability between multiple forms of inorganic metals in the environment. Microbes interact with metals and minerals in natural and synthetic environments, altering their physical and chemical state, with metals and minerals also able to affect microbial growth, activity, and survival. Additionally, many minerals are biogenic in origin, and the formation of such biominerals is of global geological and industrial significance, as well as provides important structural components for many organisms, including important microbial groups i.e. diatoms, foraminifera, and radiolarian. The current article summarizes each category of antimicrobial agents in order to illustrate the diverse modes of coordination/association of the ligands having different donor atoms (N. S. and O. etc.).

This phenomenon is usually achieved by increasing asymmetry in the mode of coordination of these ligands as a donor of electrons. Wherever it was found appropriate, the comments relating to the physiological role, biochemical mechanism, environmental significance, and bioremediation potential of the microbial biotransformation are included (Fig. 1).[6]

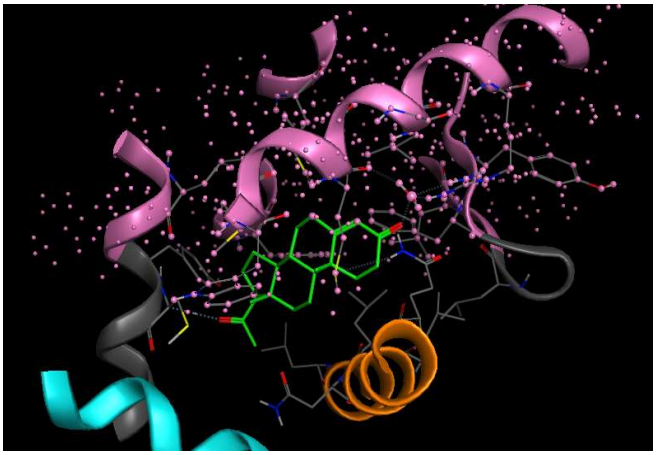

Figure 1. Illustrate the phenomenon of antimicrobial drugs and resistance mechanism underlying: bioaccessibility, bioavailability, and bioaccumulation.

During the following steps of metal usage, the acquired metal is transferred through intracellular trafficking pathways, which may include diverse storage compartments to be directed to cofactor assembly systems and final microorganism targeting can be achieved.[7] Several of these used metals, organic moieties and related channeling routes, which have been described recently since their evolution, provide first insights into the later steps of metal assimilation and help in the characterization of an essential part of the cellular metal homeostasis network.

Overall, so many challenges existed in this concept of antimicrobial drugs, and a few of them are related to the molecular entities of antimicrobial drugs. But, others have been concerned with the emergence of microbial resistance to the drugs applied and gradually limiting the efficiency of these antimicrobial remedies.[8] But in the current, no solution is available, although the innovation of effective antimicrobial drugs is continuing. Several efforts have done for increasing the life of current drugs and designing of new antimicrobial drugs that will have to solve the problem of short life expectancy through scientific or adopting new strategies such as vaccination and other approaches for disease resistors are being tracked. The main causes of the resistance investigated and a few of them are as follows: innate features of the microbial, multiplying abilities of microbial, non-multiplying state, mutation, or gene transfer.[9] In accordance with scientific evidence reported, it is easy to destroy the multiplying microbial quickly by existing antimicrobial drugs, but in the case of non-multiplying or slowly multiplying microbial, it is not quite easy. These findings elaborate on the need for highly effective antimicrobial drugs and conventional prolonged courses of drugs.[10] One of the solutions that can be applied for it is; by applying the combination of antimicrobial drugs of both the categories, one class of drugs that target non-multiplying and other types of drugs that treat multiplying microbial.[11] Sometimes these simple strategies can work and be an effective solution for the problem that can into existence because of the emergence of antimicrobial resistance.[12] The other option is to develop a new class of antimicrobial agents that could remain effective for extended periods comparatively than presently existing antimicrobial drugs.

The phenomenon of resistance especially emerged in the microbial impact and specific needs are there to deal it by applying antibacterial drugs and during treatment also, it can become a severe problem for the health of human beings. Therefore, the concern to have potential antimicrobial drugs is good whys and wherefores for it and is at the top of the current priority that is in demand. Antimicrobial drugs were developed by following a concept, which can induce new features to the organic moiety of the proposed drug to empower the central metal atom as well.[13] Then, the developed antimicrobial drugs will have more potential to inhibit the multiplication processes of the microbial, and that is why it is considered a key concept in the discovery of antibacterial drugs. Among them, several other options are available that can be adopted for developing antimicrobial drugs, an alternative novel strategy is one of them.[14] According to this concept, the primarily alleviate the current need, and after that incorporates new functional and many required features required for drug resistance, that are generated by interacting the potential moieties and effective metal combinations. These predetermined abilities were developed for targeting the non-multiplying latent.[15] These strategies are helpful in the development of antimicrobial drugs that can prolong the duration of antimicrobial impact and enhanced the abilities that can break the microbialresistance. These routes of discovery are also helpful against prolonged suboptimal bactericidal growth, which is considered the main cause for the emergence of resistance.[16] These settings of resistance and unhealthy biological features exist not only in the target pathogen, but also presented a different class of tissues and organs i.e. the gut, and throat. These pathogens can initiate fatal diseases in healthy tissues. The proper analysis of these strategies proved that long-term use of antimicrobial drugs can deal with microbial resistance in a better way comparatively than a shorter period. These results encourage researchers in dealing with the emergence of resistance initiated by the microbial.[17] But, in some cases, the approach of a long course can develop more complications in the patients and as a result, it will enhance the power of resistance. In the current situation, the use of drug libraries can be applied to avoid such situations. Newly developed antimicrobial drugs should be screened against non-multiplying bacteria for the discovery of potential antimicrobial drugs that can destroy the microbial and originated resistance responsible for initiating the disease too. This opinion covers the approaches useful in the discovery of novel antimicrobial drugs by applying classic screening, by the analysis of structural changes done in drugs, by genome hunting; and by adopting a novel route that targets non-multiplying, latent microbial.[18] The author tried his best to correlate all the original facts and concerning the chemistry of drug resistance with a special focus on antimicrobial drugs and concerned resistance mechanism underlying in the context of bioaccessibility, bioavailability, and bioaccumulation.[19]

In the end, it is a better way to adopt the latest scientific approach available, recently discovered tools and theories. By doing so, greater chances and much hope are there to be successful in the discovery of novel antimicrobial drugs that will reduce the emergence of resistance caused by the antimicrobial agents and treat the diseases in a better way.

References:

1. Ghannoum, M. A. & Rice, L. B. Antifungal agents: Mode of action, mechanisms of resistance, and correlation of these mechanisms with bacterial resistance. *Clinical Microbiology Reviews* vol. 12 501–517 **(1999)**.
2. Miotto, P., Zhang, Y., Cirillo, D. M. & Yam, W. C. Drug resistance mechanisms and drug susceptibility testing for tuberculosis. *Respirology* vol. 23 1098–1113 **(2018)**.
3. Weersma, R. K., Zhernakova, A. & Fu, J. Interaction between drugs and the gut microbiome. *Gut* vol. 69 1510–1519 **(2020)**.
4. Kumar, R. & Chhikara, B. S. Organometallic assemblies: π-electron delocalization, μ-bridging spacers, flexibility, lipophilic nature, bio-accessibility, bioavailability, intracellular trafficking pathways and antimicrobial assimilation. *J. Organomet. Chem.*776, **(2015)**.
5. McGeer, J. *et al.* Issue paper on the bioavailability and bioaccumulation of metals. in *US Environmental Protection Agency risk assessment forum (Vol. 1200)* 122 **(2004).**
6. Orazi, G. & O'Toole, G. A. 'It takes a village': Mechanisms underlying antimicrobial recalcitrance of polymicrobial biofilms. *Journal of Bacteriology* vol. 202 **(2020)**.
7. Claudel, M., Schwarte, J. V. & Fromm, K. M. New Antimicrobial Strategies Based on Metal Complexes. *Chemistry (Easton).***2**, 849–899 **(2020).**
8. Cascioferro, S. *et al.* Thiazoles, Their Benzofused Systems, and Thiazolidinone Derivatives: Versatile and Promising Tools to Combat Antibiotic Resistance. *Journal of Medicinal Chemistry* vol. 63 7923–7956 **(2020)**.
9. Tyson, G. H., Sabo, J. L., Rice-Trujillo, C., Hernandez, J. & McDermott, P. F. Whole-genome sequencing based characterization of antimicrobial resistance in Enterococcus. *Pathog. Dis.***76**, **(2018)**.
10. Yoo, H. H., Kim, I. S., Yoo, D. H. & Kim, D. H. Effects of orally administered antibiotics on the bioavailability of amlodipine: Gut microbiota-mediated drug interaction. *J. Hypertens.***34**, 156–162 **(2016)**.
11. Du, D. *et al.* Multidrug efflux pumps: structure, function and regulation. *Nature Reviews Microbiology* vol. 16 523–539 (2018).
12. Luthra, S., Rominski, A. & Sander, P. The role of antibiotic-target-modifying and antibiotic-modifying enzymes in mycobacterium abscessusdrug resistance. *Frontiers in Microbiology* vol. 9 **(2018)**.
13. Abd-El-Aziz, A. S., Abdelghani, A. A. & Mishra, A. K. Optical and Biological Properties of Metal-Containing Macromolecules. *Journal of Inorganic and Organometallic Polymers and Materials* vol. 30 3–41 **(2020)**.
14. Alamino, R. C. An agent-based lattice model for the emergence of anti-microbial resistance. *J. Theor. Biol.***486**, (2020).
15. Serban, G., Stanasel, O., Serban, E. & Bota, S. 2-Amino-1,3,4-thiadiazole as a potential scaffold for promising antimicrobial agents. *Drug Design, Development and Therapy* vol. 12 1545–1566 **(2018)**.
16. Levy, S. B. & Bonnie, M. Antibacterial resistance worldwide: Causes, challenges and responses. *Nature Medicine* vol. 10 S122–S129 **(2004)**.
17. Kumar S., S. B. R. An Overview of Mechanisms and Emergence of Antimicrobials Drug Resistance. *Adv. Anim. Vet. Sci.***1**, 7 – 14 **(2013)**.
18. Fairlamb, A. H., Gow, N. A. R., Matthews, K. R. & Waters, A. P. Drug resistance in eukaryotic microorganisms. *Nature Microbiology* vol. 1 **(2016)**.
19. Rhouma, M., Beaudry, F., Thériault, W. & Letellier, A. Colistin in pig production: Chemistry, mechanism of antibacterial action, microbial resistance emergence, and one health perspectives. *Frontiers in Microbiology* vol. 7 **(2016)**.