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Natural Products Solution against Superbugs: A Challenge of Biodiversity in a Public Health Issue

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Introduction

Antimicrobial resistance is currently one of the greatest challenges and threats to the health of populations, in which two fundamental problems come together, such as the inappropriate use of antibiotics as well as the implementation of deficient measures for the control of infections [1]. Because the use of an antimicrobial inevitably leads to the emergence of resistance, a constant search for new molecules is required with which to deal with outbreaks and decrease the infection rate [2]. This indiscriminate use of anti-infectives both in humans and in agriculture makes possible the appearance of multidrug-resistant strains (MDR). Between them the most reported MDR microorganisms are methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), *Escherichia coli* and *Pseudomonas aeruginosa* resistant to fluoroquinolones, *Klebsiella pneumonia* resistant to ceftazidime, *Acinetobacter baumannii*, and isoniazid-rifampicin resistant *Mycobacterium tuberculosis* [3]. Additionally, this very serious public health problem is complicated by the lack of availability and research into new active medicines against MDR microorganisms [4]. So several initiatives have been proposed as 10 × 20 initiative from Infectious Disease Society of America that propose the global union of several leading institutions in order to develop 10 new antimicrobial drugs by 2020 [5,6]. In this order of ideas, to assume this great challenge makes it necessary to overcome the mechanisms of microbial defense that induce resistance as biofilms that allows the survival of microorganisms in their interior through chemically induced environmental changes that favor their adaptation [7-9]. Also, research into new antibiotics has decreased because they have a lower rate of return than drugs used to treat chronic diseases [10,11].

In this way, the largest source of new novel chemical entities has been natural products, because the production of secondary metabolites evolves through the interaction and communication between the different species, which increases chemical diversity and makes promising the study of new compounds with novel mechanisms of action [12,13]. Thanks to this, natural products were the architects of the golden age of antibiotics, which under a suitable platform of rational bio prospecting makes them again the center of a new pharmaceutical industry in order to obtain new formulations capable of inhibiting the mechanisms of resistance [14,15], searching for the development of new antimicrobial adjuvants [16,17]. Therefore, the objective of this is to point out a correlation between antimicrobial activity against superbugs and rational screening in a new line of antimicrobial drug discovery with the end of to reinforce a new search for medicines obtained from natural products.

Natural products the source of chemical diversity

The research and development of new antibacterial have some bottlenecks identified by So et al. (2011) [18]:

Identification of bioactive compounds: At present, the performance of screening protocols based on high throughput has been low for the discovery of new antimicrobial drugs [19].

Medicinal chemistry: The search for new compounds based on the inhibition of therapeutic targets has shown little correlation in contrast to the old methods that evaluated *in vitro* antimicrobial activity on whole cells [20]. This effort to identify a therapeutic target slows the process to reach clinical trials.

Translational science versus basic science: When trying to apply the results obtained under the methods of basic science process known as translational science, it has been possible to observe a reproducibility bump known as the valley of death, which prevents discoveries from being applied to patients [21]. For to get out of this pothole is only possible through the disciplinary integration that controls the associated risks (Scientific, Intellectual Property, Market, and Regulatory) [22]. This is how, in the process of discovering new antimicrobials, it is necessary to optimize medicinal chemistry methods in conjunction with the costs [21,23].

Policies and regulations: Likewise, the change in drug evaluation policies both *in vitro*, *in vivo* and in clinical studies has made the development of new products difficult for an increasingly demanding market. [21,22].

Reimbursement satisfaction: Perhaps this is the most controversial aspect of antibiotic research where the low rate of return for an average treatment of 10-14 days does not make the investment profitable compared to chronic diseases [18].

The evaluation of natural products has drastically decreased in recent years due to the rise of combinatorial chemistry and methods of high throughput screening [24]. Limiting research on antibacterial, because despite the availability of a material with greater chemical diversity requires structural isolation and elucidation [25-27]. In this way the soil has been the most researched environment with the largest number of products isolated from the organisms that inhabit it [28]. Among them the species with the highest production of secondary antimicrobial metabolites are streptomyces, bacillus, and myxococcus species [26]. Also microorganisms represent the largest source of natural products to date in where 45% are produced by actinomycetes, 38% by fungi and 17% by unicellular bacteria [29,30]. Evaluating the causes of the decrease in the isolation of new chemical entities Berdy (2012), has determined the following factors [31]:

1. Use of chemical libraries instead of microbial products.

2. Scientific failure for insisting on evaluating material that is not chemically diverse with methods with low clinical prediction.
3. Likewise, the investment and return costs do not match for the financing entities [31].

Also in order to decrease the weaknesses of the search for new microbial metabolites and increase the rate of discovery it is important to take into consideration:

1. Perform rational bio prospecting of promising new sources of natural products (endophytes) [32].
2. Develop new screening methods with high clinical predictability [33].
3. Implement innovative models of evaluation of therapeutic targets on the pathogenesis of infectious diseases [34].

It is also important to focus efforts towards the development of a personalized therapy that prevents the emergence of resistance in the different environments where it occurs [35,36].

In this order of ideas we must transcend the merely economic aspect to obtain new drugs with which to address the public health problems of our time [37]. Under the aforementioned three trends must be taken into consideration for the discovery of new antibiotics:

1. Look for new chemical entities with novel mechanisms of action
2. Develop new compounds from chemical entities with proven mechanism of action
3. Develop new formulations with chemical entities that have demonstrated activity in order to enhance it [38].

However, antibiotic discovery is a process that involves risks. For that reason pharmaceutical companies obtain new antibiotics from chemical variations of existing [39].

Natural products are a fundamental part of drug discovery and contributed to obtaining the most available antimicrobial agents. Such rational methods in discovery of new antibiotics should be applied to existing multitargets and those still to be defined by bioinformatic techniques. Finally, natural products should not be discards. Because provided the innovation and the power of chemical diversity for to realize a necessary impact in public health in the golden age of antibiotic resistance.

References

1. Vernet G, Mary C, Altmann DM, Doumbo O, Morpeth S, et al. (2014) Surveillance for antimicrobial drug resistance in under-resourced countries. Emerg Infect Dis 20: 434-441.
2. Clardy J, Fischbach MA, Walsh CT (2006) New antibiotics from bacterial natural products. Nat Biotechnol 24: 1541-1550.
3. Kon KV, Rai MK (2012) Plant essential oils and their constituents in coping with multidrug-resistant bacteria. Expert Rev Anti Infect Ther 10: 775-90.
4. Fair RJ, Tor Y (2014) Antibiotics and bacterial resistance in the 21st century. Perspect Medicin Chem 6: 25-64.
5. Infectious Diseases Society of America (2010) The 10 x '20 Initiative: pursuing a global commitment to develop 10 new antibacterial drugs by 2020. Clin Infect Dis 50: 1081-1083.
6. Boucher HW, Talbot GH, Bradley JS, Edwards JE, Gilbert D, et al. (2009) Bad bugs, no drugs: no ESKAPE! An update from the infectious diseases society of America. Clin Infect Dis 48: 1-12.
7. Boire NA, Riedel S, Parrish NM (2013) Essential Oils and Future Antibiotics: New weapons against emerging "Superbugs". J Anc Dis Prev Rem 1.
8. Costerton JW, Stewart PS, Greenberg EP (1999) Bacterial biofilms: A common cause of persistent infections. Science 284: 1318-1322.
9. Hoiby N, Bjarnsholt T, Givskov M, Molin S, Ciofu O, et al. (2010) Antibiotic resistance of bacterial biofilms. Int J Antimicrob Agents 35: 322-332.
10. Fischbach MA, Walsh CT (2009) Antibiotics for emerging pathogens. Science 325: 1089-1093.
11. Shlaes DM (2010) Antibiotics: The perfect storm. Heidelberg: Springer pp: 15-28.
12. Butler MS, Buss AD (2006) Natural products--the future scaffolds for novel antibiotics?. Biochem Pharmacol 71: 919-929.
13. Hadacek F, Bachmann G, Engelmeier D, Chobot V (2011) Hormesis and a chemical raison d'etre for secondary plant metabolites. Dose Response 9: 79-116.
14. Dougherty TJ, Pucci MJE (2012) Antibiotic discovery and development. Heidelberg: Springer pp: 10-12.
15. Livermore DM (2011) Discovery research: The scientific challenge of finding new antibiotics. J Antimicrob Chemother 66: 1941-1944.
16. Liu S, Hou Y, Chen X, Gao Y, Li H, et al. (2014) Combination of fluconazole with non-antifungal agents: A promising approach to cope with resistant Candida albicans infections and insight into new antifungal agent discovery. Int J Antimicrob Agents 43: 395-402.
17. Musiol R, Mrozek-Wilczkiewicz A, Polanski J (2014) Synergy against fungal pathogens: Working together is better than working alone. Curr Med Chem 21: 870-893.
18. So AD, Gupta N, Brahmachari SK, Chopra I, Munos B, et al. (2011) Towards new business models for R&D for novel antibiotics. Drug Resist Updat 14: 88-94.
19. Moy TI, Conery AL, Larkins-Ford J, Wu G, Mazitschek R, et al. (2009) High-throughput screen for novel antimicrobials using a whole animal infection model. ACS Chem Biol 4: 527-533.
20. Silver LL (2011) Challenges of antibacterial discovery. Clin Microbiol Rev 24: 71-109.
21. Butler D (2008) Crossing the valley of death. Nature 453: 840-842.
22. Pienta KJ (2010) Successfully accelerating translational research at an academic medical center: The University of Michigan-Coulter translational research partnership program. Clin Transl Sci 3: 316-318.
23. Pan SY, Pan S, Yu Z, Ma DL, Chen SB, et al. (2010) New perspectives on innovative drug discovery: An overview. J Pharm Pharm Sci 13: 450-471.
24. Macarron R, Banks MN, Bojanic D, Burns DJ, Cirovic DA, et al. (2011) Impact of high-throughput screening in biomedical research. Nat Rev Drug Discov 10: 188-195.
25. Kingston DGI (2011) Modern natural products drug discovery and its relevance to biodiversity conservation. J Nat Prod 74: 496-511.
26. Singh SB, Pelaez F (2008) Biodiversity, chemical diversity and drug discovery. Prog Drug Res 65: 143-174.
27. Zakeri B, Lu TK (2013) Synthetic biology of antimicrobial discovery. ACS Synth Biol 2: 358-372.
28. De Castro AP, Fernandes GDR, Franco OL (2014) Insights into novel antimicrobial compounds and antibiotic resistance genes from soil metagenomes. Front Microbiol 5: 489.
29. Liu X, Ashforth E, Ren B, Song F, Dai H, et al. (2010) Bioprospecting microbial natural product libraries from the marine environment for drug discovery. J Antibiot (Tokyo) 63: 415-422.
30. Rahman MA, Islam MZ, Islam MAU (2011) Antibacterial activities of actinomycete isolates collected from soils of Rajshahi, Bangladesh. Biotechnol Res Int 2011: 6.
31. Berdy J (2012) Thoughts and facts about antibiotics: Where we are now and where we are heading. J Antibiot (Tokyo) 65: 385-395.
32. Joseph B, Priya RM (2011) Bioactive compounds from endophytes and their potential in pharmaceutical effect: A review. Am J Biochem Mol Biol 1: 291-309.

33. Bueno J (2012) In vitro antimicrobial activity of natural products using minimum inhibitory concentrations, looking for new chemical entities or predicting clinical response. Med Aromat Plants 1: 113.
34. Peleg AY, Jara S, Monga D, Eliopoulos GM, Moellering RC Jr, et al. (2009) Galleria mellonella as a model system to study Acinetobacter baumannii pathogenesis and therapeutics. Antimicrob Agents Chemother 53: 2605-2609.
35. Baquero F, Coque TM, De la Cruz F (2011) Ecology and evolution as targets: the need for novel eco-evo drugs and strategies to fight antibiotic resistance. Antimicrob Agents Chemother 55: 3649-3660.
36. Sengupta S, Chattopadhyay MK, Grossart H (2013) The multifaceted roles of antibiotics and antibiotic resistance in nature. Front Microbiol 4: 47.
37. Lionakis MS (2011) Drosophila and Galleria insect model hosts: New tools for the study of fungal virulence, pharmacology and immunology. Virulence 2: 521-527.
38. Fabbretti A, Gualerzi CO, Brandi L (2011) How to cope with the quest for new antibiotics. FEBS Lett 585: 1673-1681.
39. De Souza Mendes CD, De Souza Antunes AM (2013) Pipeline of known chemical classes of antibiotics. Antibiotics 2: 500-534.