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A review of rise of modern pharmaceutical biotechnology in antibiotic drug discovery and development from natural sources and future implications

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Background: In the context of antibiotic research and development (R&D), Biotechnology is the exploitation of biological processes for industrial production. Early antibiotic biotechnology relied on empirical research whereas modern biotechnology is regarded as having started in 1973 with the discovery of recombinant DNA technology. Currently, two thirds of antibiotics in clinical use globally are of natural microbial origin, and were developed through these same empirically derived techniques. Empirical antibiotic R&D from natural sources (NS) was, however, not sustainable. No new classes of antibiotics were discovered until after 2000 when there was renewed interest in antibiotic R&D from NS, this time powered by advances in biotechnology. Unfortunately, there are currently no comprehensive systematic reviews of the technologies, focus areas of antibiotic R&D and outcomes thereof over the years. This review aims to highlight the most important developments, and contributions in antibiotic discovery and development from natural sources (NS).

Methods: A systematic literature review design was adopted for the review. Publications on R&D on antibiotics and biotechnology were retrieved from research databases including science direct, PubMed, Medline and open source databases like google scholar. The search terms included "antibiotics and biotechnology, research and development, methods and production." The main outcome variables were trends, advances and contributions of biotechnology used for R&D of novel antibiotic classes/types. The study included publications that are peer reviewed and that give antibiotic outcomes with market authorization. Data was analyzed thematically and results are descriptively reported. Antibiotic innovations were ranked using a criteria assessing the significance of contribution to clinical practice and future applicability to R&D of novel antibiotics from NS as well as applicability to other biomedical sciences.

Results: Out of the 126 articles retrieved from the literature (1928 – 2017), 47 studies met the inclusion criteria. Fifteen (15) articles were excluded due overlap of information. Out of the 32 articles reviewed, 25 innovations in biotechnology had impact on R&D of novel antibiotics in clinical use. The main trends in antibiotic R & D were in four eras: 1928-mid 1940s – the primordial era, an initial phase when the first antibiotics were discovered without clinical use and no mass production; 1944 - 1962 is era when most antibiotics currently in clinical use were discovered and when mass production started. Twenty (20) new classes of antibiotics were discovered and are still used in clinical practice; 1962 – 2000 there were no innovations in new classes of antibiotics but rather synthetic modifications of existing compounds. The era of high discoveries of antibiotics was referred to as the golden era 1944-1970; the rise in antimicrobial resistance due to over use of antibiotics led to combinatorial techniques for novel synthetic antibiotics in the 1980s with no new classes; in 1990's genomic era – the biotechnological advances in genome sequencing led to innovations of antibiotics discovery based on high throughput screens of existing compound libraries to identify targets as well as the genes encoding. Unfortunately the yield for antibiotics based on genomic sequencing remained poor and because of these disappointments, interest in antibiotics from NS was revitalized in the 2000's renascence era, using advanced biotechnology. This led to two new classes of novel antibiotics being marketed by 2010 and two more were still in phase I of the pipeline. A small number were in the preclinical phases.

Conclusion: A combination of advanced biotechnology applied on NS alongside synthetic modifications has the highest potential for R&D of novel antibiotics. The future focus areas for antibiotic R&D from NS will focus on the 99% non-culturable microorganism that have not been exploited, on R&D all microbes with silent genes with potential, R&D on microbes from unexplored environments and R&D on non-multiplying microorganisms.

Biography

Daniel Mavu is a Pharmacist by profession registered in Namibia and Zambia. He is currently working as a Pharmaceutics Lecturer at the School of Pharmacy, University of Namibia. Prior to this, he has worked as a Lecturer and Coordinator of the Pharmacist Assistant training program at the National Health Training Centre, Windhoek, Namibia from 2013. From 2005-2013, he was the Pharmacist-In-Charge at the Livingstone General Hospital, Zambia. He has taught Chemistry at Hillcrest National School in Livingstone, Zambia for three years and was also a Lecturer of Chemistry at the Natural Resources Development College in Lusaka, Zambia. He holds a Master of Pharmacy degree (Pharmaceutics) from the University of the Western Cape, Bachelor of Pharmacy degree and BSc degree both from the University of Zambia. He is currently a PhD candidate working on characterization and pharmaceutical development of antimicrobial compounds from microorganisms growing in selected soil types in Namibia.

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