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Searching for Antimicrobials in the Unlikeliest of Places

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Introduction

The biggest challenge facing the world's population is the shortage of antimicrobial compounds. This has arisen due to the overprescribing of antibiotics and other antimicrobials; as a consequence of bacterial resistance, arising from evolutionary mechanisms or plasmid transfer, to one or more antimicrobial compound [1]; to add to this the threat of newly emerging pathogens remains ever-present. From the discovery of penicillin and tetracycline in the 1940s through to the late 1990s, people have been able to be treated when infected against wide-range of pathogens. The rate of people dying due to a lack of effective antimicrobials is growing and some experts predicts that 10 million could die each year by 2050 if no new types of antimicrobials are developed [2]. As part of the surveillance, the U.S. Centers for Disease Control (CDC) recently released an interactive online tool, termed the National Antimicrobial Resistance Monitoring System [3], to allow medics to track the trajectory of drug-resistant food borne bacteria.

The drive for the pharmaceutical sector to develop new antimicrobials is hampered by the long development time and the predicted low returns on investment; for new compounds much of the incentive is stemming from the university sector and governments [4]. A few antimicrobials have emerged in recent years; included here is teixobactin, which is the first new type of antibiotic to be discovered since the late 1980s. Teixobactin was isolated from *Eleftheriaterrae*, a soil related bacterium and it has proved effective in animal models against Methicillin-Resistant *Staphylococcus aureus* (MRSA) and *Mycobacterium tuberculosis*, where it inhibits bacterial growth [5].

Even if more resources could be harnessed, the identification of new and effective antimicrobials is not straightforward. In order to accelerate the process, microbiologists are examining more unusual sources. In this editorial, some of the more novel approaches are highlighted.

Searching for Antimicrobials

The most tried place to find antimicrobials is through the studying of soil samples. The difficulty with soil microorganisms is that only a few can be cultured in the laboratory and most of those that offered target compounds were exploited during the 1960s and 1970s. Given the scarcity today, researchers have returned to screening soil samples from previously unexamined parts of the planet in the hope of finding more compounds like teixobactins.

The marine environment is one area being targeted for new antimicrobials. With this University of Exeter Medical School's European Centre for Environment and Human Health is screening seaweed. For the exercise, researchers have been examining samples of seaweed gathered from rock pools around Cornwall, England. Extracts from compounds isolated from the seaweed have been trialed against resistant and problematic bacteria, with effectiveness against some types of multi-drug resistant *Staphylococcus aureus* recorded [6].

Taking a different tract, University of Queensland, Australia has discovered what appears to be a potential new class of antibiotics based on the sugar molecules produced by bacteria. The new molecules disrupt the linkages that hold bacterial cell walls together. The reasoning behind this is that bacteria are unlikely to develop resistant to an antibiotic formulated similarly to modified version of their own sugar [7].

One difficulty in processing the potential compounds detected by universities is the scale of the task and the need for additional resources, laboratory equipment and computer processing power. To overcome this, an initiative called 'Community for Open Antimicrobial Drug Discovery' has been put together. This is a not-for-profit initiative created in 2015. The aim is to screen different compounds for antimicrobial activity against the so-called ESKAPE bacterial pathogens: *Escherichia coli*, *Klebsiellapneumoniae*, *Acinetobacterbaumannii*, *Pseudomonas aeruginosa*, *S. aureus*;

and the fungi *Cryptococcus neoformans* and *Candida albicans* [8]. Tapping into community science, the organization is willing to receive potential compounds from around the world from any academic research group.

New technologies are also making the screening task easier. A device called the iChip ('isolation chip'), for example, was used for the identification of teixobactin. The iChip is an assembly of hydrophobic plastic polyoxymethylene layers. The device allows single microbial cells to be captured within individual agar gel matrices. Incubation occurs in bacterial cell's original environmental habitat, along with naturally occurring nutrients and growth factors, meaning that screening can be conducted on organisms that would otherwise be uncultivable on standard laboratory media [9].

Other research groups are using chemical platforms to synthesize candidate antimicrobial molecules to evaluate their potential for combating multi-drug-resistant bacterial infections. Relatedly robotics are being used to develop peptoids, which are synthetic peptides designed to help the body fight infections [10].

A different approach is with finding novel ways to boost the properties of existing antimicrobials. This is through "resistance breakers", compounds that function to boost the effectiveness of existing antibiotics. One candidate compound is coded HT61. This is a small quinolone-derived compound, active against non-multiplying bacteria. The molecule disrupts the bacterial cell membrane and cell wall [11].

Testing

As part of the screening process, antimicrobials need to be effectively screened. The effectiveness of antibiotics can be measured through minimum inhibitory concentration or minimum bactericidal concentration testing *in vitro*. As an alternative, more sophisticated pharmacokinetic profiling techniques to measure a range of pharmacological parameters can be deployed [12,13]. The process of screening is complex and takes a long period of time. Once complete, this must be followed up by animal studies and eventual clinical trials (phases I, II and III). One reason for the need for prolonged testing has emerged in a University of California (Santa Barbara) study a conditional resistance mechanism occurs when bacteria enter variable chemical environments (such as in the human body). This additional mechanism may explain why antimicrobials successful in laboratory trials are not effective against pathogens when they come into contact with human tissues

Summary

The positive news from this review is that progress is being made in search for new antimicrobials. However, the time required for clinical trials and to gain regulatory approval is necessarily lengthy. In the meantime, tighter controls are required on medical staff not to prescribe antimicrobials unnecessarily and to educate the public that antimicrobials should only be sought in cases of serious diseases.

References

1 Sandle T (2014) Novel Methods to Address Antimicrobial Resistance. SOJ Microbiol Infect Dis 2: 2-3.

2 Jim ON (2014) Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations-2014, Review on Antimicrobial Resistance, London : Department of Health.

3 http://www.cdc.gov/narms/

4 Sandle T (2014) The Antibiotic Crisis and the Need for New Forms of Antibiotics. EC Microbiology 1: 1-3.

5 Sandle T (2015) Teixobactin: A New Class of Antibiotic. SOJ Microbiology & Infectious Diseases 3: 1-2.

6 Anon (2015) Researchers turn to seaweeds in quest for new drugs. Exeter : University of Exeter Medical School.

7 Matt C (2015) Sweet Revenge Against Superbugs, University of Queensland 1-2.

8 Copper MA (2015) A community-based approach to new antibiotic discovery. Nature Reviews Drug Discovery 14: 587-588.

9 Nichols D, Cahoon N, Trakhtenberg N (2010) Use of ichip for high-throughput in situ cultivation of “uncultivable” microbial species. Appl Environ Microbiol 76: 2445-2450.

10 Mojsoska B, Zuckermann RN, Jenssen H (2015) Structure-activity relationship study of novel peptoids that mimic the structure of antimicrobial peptides. Antimicrob Agents Chemother 59: 4112-4120.

11 Sandle T (2015) Taking on bacterial resistance with 'resistance breakers'. Toronto : Digital Journal 1.

12 Sandle T (2012) Introducing Antimicrobials. Arab Medical Hygiene 5: 37-41.

13 Kubicek-Sutherland JZ, Heithoff DM, Ersoy SC, William RS, John KH, et al. Host-dependent Induction of Transient Antibiotic Resistance: A Prelude to Treatment Failure.EBioMedicine 2: 1169-1178.