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Review Article

## REVIEW ON A POTENTIAL OF ANTIBIOTICS

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### ABSTRACT

Observations about the growth of some microorganisms inhibiting the growth of other microorganisms have been reported since the late 1800s. These observations of antibiosis between microorganisms led to the discovery of natural antibacterial. This paper deliberates important findings of the educations conducted by numerous national and international combined organizations on a brief indication of the antibacterial agents' detection in recent years. In India especially the developing antibiotics, need to institute methods for the suitable choice of drug conduct a compound problem involving prescribers, dispensers, and consumers.

**Keywords:** Antibiotic, Antibiotic resistance, bacterial Infection

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## INTRODUCTION

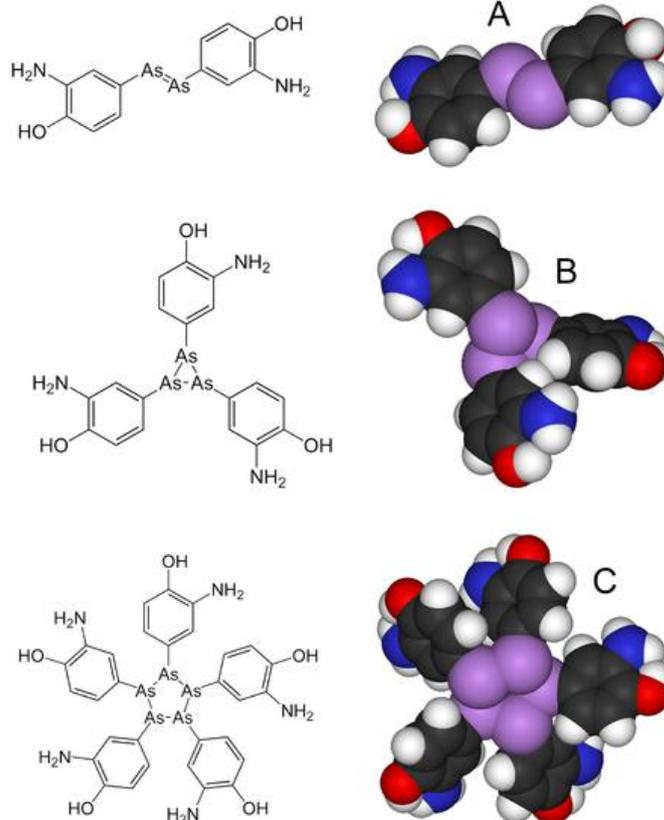
### a) History

Before the early 20th century, treatments for infections were based primarily on medicinal folklore. Mixtures with antimicrobial properties that were used in treatments of infections were described over 2000 years ago.<sup>1</sup> Many ancient cultures, including the ancient Egyptians and ancient Greeks, used a specially selected mold and plant materials and extracts to treat infections.

Synthetic antibiotic chemotherapy as a science and development of antibacterial began in Germany with Paul Ehrlich in the late 1880s. He then proposed the idea that it might be possible to create chemicals that would act as a selective drug that would bind to and kill bacteria without harming the human host. After screening hundreds of dyes against various organisms, in 1907, he discovered a medicinally useful drug, the first synthetic antibacterial salvarsan now called arsphenamine.<sup>2</sup>

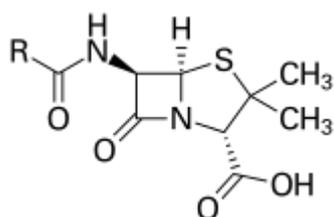
The Hoechst company began to market the compound toward the end of 1910 under the name Salvarsan. This drug is now known as arsphenamine. The drug was used to treat syphilis in the first half of the 20th century. In 1908, Ehrlich received the Nobel Prize in Physiology or Medicine for his contributions to immunology.<sup>3</sup>

The first sulfonamide and the first systemically active antibacterial drug, Prontosil, was developed by a research team led by Gerhard Domagk in 1932 or 1933 at the Bayer Laboratories of the IG Farben conglomerate in Germany, for which Domagk received the 1939 Nobel Prize in Physiology or Medicine.<sup>4</sup> Sulfanilamide, the active drug of Prontosil, was not patentable as it had already been in use in the dye industry for some years. Prontosil had a relatively broad effect against Gram-positive cocci, but not against enterobacteria. The research was stimulated apace by its success. The discovery and development of this sulfonamide drug opened the era of antibacterial.<sup>5</sup>



Arsphenamine, also known as salvarsan, discovered in 1907 by Paul Ehrlich.

#### b) Penicillin and other natural antibiotics



Penicillin, discovered by Alexander Fleming in 1928

In 1874, physician Sir William Roberts noted that cultures of the mold *Penicillium glaucum* that is used in the making of some types of cheese did not display bacterial contamination. In 1876,<sup>6</sup> physicist John Tyndall also contributed to this field. Pasteur conducted research showing that *Bacillus anthracis* would not grow in the presence of the related mold *Penicillium notatum*.

The first known scholarly work to consider the therapeutic capabilities of molds resulting from their anti-microbial activity. In his thesis, Duchesne proposed that bacteria and molds engage in a perpetual battle for survival.<sup>7</sup> Duchesne observed that *E. coli* were eliminated by *Penicillium glaucum* when they were both grown in the same culture. He also observed that when he inoculated laboratory animals with lethal doses of typhoid bacilli together with *Penicillium glaucum*, the animals did not contract typhoid.<sup>8</sup> Unfortunately, Duchesne's army service after getting his degree

prevented him from doing any further research. Duchesne died of tuberculosis, a disease now treated with antibiotics.

In 1928, Sir Alexander Fleming postulated the existence of penicillin, a molecule produced by certain molds that kill or stops the growth of certain kinds of bacteria. Fleming was working on a culture of disease-causing bacteria when he noticed the spores of a green mold, *Penicillium chrysogenum*, in one of his culture plates.<sup>9</sup> He observed that the presence of the mold killed or prevented the growth of the bacteria. Fleming postulated that the mold must secrete an antibacterial substance, which he named penicillin in 1928. Fleming believed that its antibacterial properties could be exploited for chemotherapy. He initially characterized some of its biological properties and attempted to use a crude preparation to treat some infections, but he was unable to pursue its further development without the aid of trained chemists.

Later, Norman Healthy developed the back-extraction technique for efficiently purifying penicillin in bulk. The chemical structure of penicillin was first proposed by Abraham.<sup>10</sup> Purified penicillin displayed potent antibacterial activity against a wide range of bacteria and had low toxicity in humans. Furthermore, its activity was not inhibited by biological constituents such as pus, unlike the synthetic sulfonamides.<sup>11</sup> The development of penicillin led to renewed interest in the search for antibiotic compounds with similar efficacy and safety. For their successful development of

penicillin, which Fleming had accidentally discovered but could not develop him, as a therapeutic drug, Chain, and Florey shared the 1945 Nobel Prize in Medicine with Fleming.<sup>12</sup> World War II. Gramicidin, however, could not be used systemically because of toxicity. Tyrocidine also proved too toxic for systemic usage. Research results obtained during that period were not shared between the Axis and the Allied powers during World War II and limited access during the Cold War. .

### Antibiotics

The term *antibiotic* was first used in 1942 by Selman Waksman and his collaborators in journal articles to describe any substance produced by a microorganism that is antagonistic to the growth of other microorganisms in high dilution.<sup>13</sup> This definition excluded substances that kill bacteria but that are not produced by microorganisms (hydrogen peroxide). It also excluded synthetic antibacterial compounds such as the sulfonamides. In current usage, the term "antibiotic" is applied to any medication that kills bacteria or inhibits their growth, regardless of whether that medication is produced by a microorganism or not. An antimicrobial drug used in the treatment and prevention of bacterial infections.<sup>14</sup> They may either kill or inhibit the growth of bacteria. Sometimes the term antibiotic (which means "opposing life") is used to refer to any substance used against microbes, synonymous with an antimicrobial. Some sources distinguish between antibacterial and antibiotic; antibacterial is used in soaps and disinfectants, while antibiotics are used as medicine. Antibiotics revolutionized medicine in the 20th century. This has led to widespread problems, so much as to prompt the World Health Organization to classify antimicrobial resistance as a "serious threat is no longer a prediction for the future, it is happening right now in every region of the world and has the potential to affect anyone, of any age, in any country."<sup>15</sup>

### Medical Uses

Antibiotics are used to treat or prevent bacterial infections, and sometimes protozoan infections. When an infection is suspected of being responsible for an illness, but the responsible pathogen has not been identified, an empiric therapy is adopted.<sup>16</sup> This involves the administration of a broad-spectrum antibiotic based on the signs and symptoms presented and are initiated pending laboratory results that can take several days.

When the responsible pathogenic microorganism is already known or has been identified, definitive therapy can be started. This will usually involve the use of a narrow-spectrum antibiotic. The choice of antibiotic given will also be based on its cost. Identification is critically important as it can reduce the cost and toxicity of the antibiotic therapy and reduce the possibility of the emergence of antimicrobial resistance.<sup>17</sup> To avoid surgery, antibiotics may be given for non-complicated acute appendicitis.

Antibiotics may be given as a preventive measure (prophylactic) and this is usually limited to at-risk

populations such as those with a weakened immune system (particularly in HIV cases to prevent pneumonia), those taking immune suppressive drugs, cancer patients and those having surgery. Their use in surgical procedures is to help prevent infection of incisions.<sup>18</sup> They have an important role in dental antibiotic prophylaxis where their use may prevent bacteremia and consequent infective endocarditis. Antibiotics are also used to prevent infection in cases of neutropenia particularly cancer-related.<sup>19</sup> There are many different routes of administration for antibiotic treatment. Antibiotics are usually taken by mouth. In more severe cases, particularly deep-seated systemic infections, antibiotics can be given intravenously or by injection. Topical use is also one of the treatment options for some skin conditions including acne and cellulitis.<sup>20</sup> Advantages of topical application include achieving a high and sustained concentration of antibiotic at the site of infection; reducing the potential for systemic absorption and toxicity, and total volumes of antibiotic required are reduced, thereby also reducing the risk of antibiotic misuse.<sup>21</sup> Topical antibiotics applied to certain types of surgical wounds have been reported to reduce the risk of surgical site infections. However, there are certain general causes for concern with topical administration of antibiotics. Some systemic absorption of the antibiotic may occur; the quantity of antibiotic applied is difficult to accurately dose, and there is also the possibility of local hypersensitivity reactions or contact dermatitis occurring.<sup>22</sup>

### Side-effects

Antibiotics are screened for any negative effects before their approval for clinical use and are usually considered safe and well tolerated. Some antibiotics have been associated with a wide extent of adverse side effects ranging from mild to very severe depending on the type of antibiotic used, the microbes targeted, and the individual patient.<sup>23</sup> Side effects may reflect the pharmacological or toxicological properties of the antibiotic or may involve hypersensitivity or allergic reactions. Safety profiles of newer drugs are often not as well established as for those that have a long history of use. Common side-effects include diarrhea, resulting from disruption of the species composition in the intestinal flora, resulting, for example, an overgrowth of pathogenic bacteria, such as *Clostridium difficile*.<sup>24</sup> Antibacterial can also affect the vaginal flora and may lead to overgrowth of yeast species of the genus.

### Correlation with obesity

It is unclear whether antibiotics cause obesity in humans. Studies have found a correlation between early exposure of antibiotics (<6 months) and increased body mass (at 10 and 20 months). Another study found that the type of antibiotic exposure was also significant with the highest risk of being overweight in those given macrolides compared to penicillin and cephalosporin.<sup>25</sup> Therefore, there is a correlation between antibiotic exposure in early life and obesity in humans, but whether there is a causal relationship remains unclear. Although there is a correlation between antibiotic use in early life and obesity, the effect of

antibiotics on obesity in humans needs to be weighed against the beneficial effects of clinically indicated treatment with antibiotics in infancy.<sup>26</sup>

## INTERACTIONS

### Birth control pills

Well controlled studies on the effect of oral contraceptive failure and antibiotics are very limited. The majority of studies indicate antibiotics do not interfere with birth control pills, such as clinical studies that suggest the failure rate of contraceptive pills caused by antibiotics is very low (about 1%). Situations that may increase the risk of oral contraceptive failure include non-compliance (missing taking the pill), vomiting or diarrhea.<sup>27</sup> Gastrointestinal disorders or interpatient variability in oral contraceptive absorption affecting ethynyl estradiol serum levels in the blood. Women with menstrual irregularities may be at higher risk of failure and should be advised to use backup contraception during antibiotic treatment and for one week after its completion.<sup>28</sup> If patient-specific risk factors for reduced oral contraceptive efficacy are suspected, backup contraception is recommended.

Clinicians have recommended that extra contraceptive measures be applied during therapies using antibiotics that are suspected to interact with oral contraceptives. More studies on the possible interactions between antibiotics and birth control pills (oral contraceptives) are required as well as a careful assessment of patient-specific risk factors for potential oral contraceptive pill failure prior to dismissing the need for backup contraception.<sup>29</sup>

### Alcohol

Interactions between alcohol and certain antibiotics may occur and may cause side-effects and decreased effectiveness of antibiotic therapy. While moderate alcohol consumption is unlikely to interfere with many common antibiotics, there are specific types of antibiotics, with which alcohol consumption may cause serious side-effects.<sup>30</sup> Therefore, potential risks of side-effects and effectiveness depend on the type of antibiotic administered. In addition, the efficacy of doxycycline and erythromycin succinate may be reduced by alcohol consumption. Other effects of alcohol on antibiotic activity include the altered activity of the liver enzymes that break down the antibiotic compound.<sup>31</sup> A bactericidal activity of antibacterial may depend on the bacterial growth phase, and it often requires ongoing metabolic activity and division of bacterial cells. These findings are based on laboratory studies, and in clinical settings have also been shown to eliminate bacterial infection. Since the activity of antibacterial depends frequently on its concentration, *in vitro* characterization of antibacterial activity commonly includes the determination of the minimum inhibitory concentration and minimum bactericidal concentration of an antibacterial.<sup>32</sup>

## Resistances

The emergence of resistance of bacteria to antibiotics is a common phenomenon. The emergence of resistance often reflects evolutionary processes that take place during antibiotic therapy. The antibiotic treatment may select for bacterial strains with physiologically or genetically enhanced capacity to survive high doses of antibiotics.<sup>33</sup> Under certain conditions, it may result in the preferential growth of resistant bacteria, while the growth of susceptible bacteria is inhibited by the drug. Resistance may take the form of biodegradation of pharmaceuticals, such as sulfamethazine-degrading soil bacteria introduced to sulfamethazine through medicated pig feces. The survival of bacteria often results from an inheritable resistance, but the growth of resistance to antibacterial also occurs through horizontal gene transfer.<sup>34</sup> Antibacterial resistance may impose a biological cost, thereby reducing the fitness of resistant strains, which can limit the spread of antibacterial-resistant bacteria, for example, in the absence of antibacterial compounds.<sup>35</sup> Additional mutations, however, may compensate for this fitness cost and can aid the survival of these bacteria. Paleontological data show that both antibiotics and antibiotic resistance are ancient compounds and mechanisms. Useful antibiotic targets are those for which mutations negatively impact bacterial reproduction or viability. Acquired resistance results from a mutation in the bacterial chromosome or the acquisition of extra-chromosomal DNA. Antibacterial-producing bacteria have evolved resistance mechanisms that have been shown to be like and may have been transferred to, antibacterial-resistant strains.<sup>36</sup> The spread of antibacterial resistance often occurs through vertical transmission of mutations during growth and by genetic recombination of DNA by the horizontal genetic exchange. For instance, antibacterial resistance genes can be exchanged between different bacterial strains or species via plasmids that carry these resistance genes.

Antibacterial-resistant strains and species sometimes referred to as "superbugs", now contribute to the emergence of diseases that were for a while well controlled. For example, emergent bacterial strains causing tuberculosis that are resistant to previously effective antibacterial treatment pose many therapeutic challenges.<sup>37</sup> Every year, nearly half a million new cases of multidrug-resistant tuberculosis (MDR-TB) are estimated to occur worldwide. Many antibiotics are frequently prescribed to treat symptoms or diseases that do not respond to antibiotics or that are likely to resolve without treatment. Also, incorrect or suboptimal antibiotics are prescribed for certain bacterial infections. The overuse of antibiotics, like penicillin and erythromycin, has been associated with emerging antibiotic resistance since the 1950s. Widespread usage of antibiotics in hospitals has also been associated with increases in bacterial strains and species that no longer respond to treatment with the most common antibiotics.<sup>38</sup>

## Research

The increase in bacterial strains that are resistant to conventional antibacterial therapies together with decreasing number of new antibiotics currently being developed in the drug pipeline has prompted the development of bacterial disease treatment strategies that are alternatives to conventional antibacterial.<sup>39</sup> Non-compound approaches (that is, products other than classical antibacterial agents) that target bacteria or approaches that target the host including phage therapy and vaccines are also being investigated to combat the problem.

## Vaccines

Vaccines rely on immune modulation or augmentation. Vaccination either excites or reinforces the immune competence of a host to ward off infection, leading to the activation of macrophages, the production of antibodies, inflammation, and other classic immune reactions.<sup>40</sup> Antibacterial vaccines have been responsible for a drastic reduction in global bacterial diseases. Vaccines made from attenuated whole cells or lysates have been replaced largely by less erectogenic, cell-free vaccines consisting of purified components, including capsular polysaccharides and their conjugates, to protein carriers, as well as inactivated toxins (toxoids) and proteins.<sup>41</sup>

## Phytochemicals

Some antioxidant dietary supplements also contain phytochemicals (polyphenols), such as grape seed extract, and demonstrate *in vitro* anti-bacterial properties. Phytochemicals can inhibit peptidoglycan synthesis, damage microbial membrane structures modify bacterial membrane surface hydrophobicity and modulate quorum-sensing.<sup>42</sup> With increasing antibiotic resistance in recent years, the potential of new plant-derived antibiotics is under investigation.

## CONCLUSION

Antibiotics have protected millions of exists and changed modern medicine, but they are becoming less actual. The Essential Elements of Antibiotic healthcare workers, health systems, hospitals, clinics, and nursing homes can participate as active forces in serving to advance antibiotic custom. Antibiotics are used to treat, stop, and regulator disease among food creatures and in some cases to improve feed utilization. Antimicrobial agents enable decontamination or sanitization of animal creation premises, transport facility equipment, and effective hygiene during food processing, and confirm food excellence and protection. Many hospitals have already better-quality their antibiotic recommending by following the Fundamental Elements. When antibiotic programs and follows are accepted, patients obtain the best antibiotic treatment.

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