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Research paper

Plant-Based Bioactive Compounds for Combating Antibiotic Resistance

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Abstract

Current antibiotic resistance is one of the most enduring dangers to rigorous antimicrobial stewardship. Even while medications that target bacterial viability have historically delivered outstanding results, the selection pressure that different modes of action exert on the bacteria leads to the production of antibiotic-resistant strains. Finding new antibiotics has been the main focus of most research and exciting advancements, but the gap between the growing number of bacteria that are resistant to drugs and the decreasing number of novel medicines has not yet been closed. Additionally, P. aeruginosa infections are difficult to treat because it can produce new resistance mechanisms to several antibiotic families, including aminoglycosides, fluoroquinolones, and βlactams. As one of the primary causes of nosocomial infections, Pseudomonas aeruginosa can occasionally produce a serious situation in medical facilities. The pathogen can avoid the effects of contemporary antibiotics thanks to its protective outer membrane and efflux pumps, which serve as essential survival tools. As a result, the World Health Organization has designated P. aeruginosa as a priority pathogen because of the growing number of multidrug-resistant (MDR) strains that urgently need new medications.

Keywords: *Antibiotics; Lactamases; Overlapping; Development; Bacterial.*

1. Introduction

Most human needs, including food, shelter, clothes, transportation, fertilizers, tastes, and medications, have been derived either directly or indirectly from natural resources for thousands of years [1]. Early man sought treatment in his immediate natural environment to alleviate pain and discomfort in his daily life. This led to the use of various plants, animals, minerals, and other materials, as well as the development of a variety of healing catalysts [7] [17]. There have been numerous reasons to switch from synthetic to herbal medicines, which are a gift of life, particularly in the current scenario where people are suffering from numerous health hazards because of their lifestyle [2]. Natural products have drawn the interest of several researchers over the years and are highly valued worldwide as a successful foundation for therapeutic sources for the treatment of nearly all metabolic problems. Although the therapeutic potential of medicines has been known for a long time, there are currently numerous beneficial developments in healthcare approval; as a result, new research on plants that contain bioactive chemicals is booming on a global scale [5] [15].

The most important sources of life-saving medications worldwide are natural ingredients. Therefore, it is essential for producing therapeutic plant genotypes in large quantities [3] [11]. The integrated methods of cultural systems will provide the groundwork for the near-term manufacturing of novel, less hazardous, and superior substances for human use. Antimicrobial resistance is still a major problem for world health. New antibiotic discovery has lagged behind the rise of multidrug-resistant bacteria like Pseudomonas aeruginosa [16]. The need for novel therapeutic strategies is urgent, and plant-based antimicrobials offer promising alternatives [18]. Natural products, including plant-derived bioactive compounds, have long been recognized for their therapeutic potential and are being increasingly explored as sources of new antibiotics [19] [20]. Furthermore, natural habitats for medicinal vegetation are rapidly disappearing, and it is getting harder and

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harder to obtain vegetation-consequent compounds because of the abandoned assortment and trade of large amounts of vegetation, as well as demographic pressure, environmental instability, and geopolitical unrest. Researchers must consider the potential avenues of inquiry to find an alternative to the production of herbal medications [4]. Studies on herbal medications that offer a thorough comprehension of the processes, mode of action, and biosynthesis of significant bioactive compounds and nutraceuticals [9].

2. Materials and Methods

Antibiotics are fascinating compounds, whether they're derived from nature or created in a lab, and they play a crucial role in fighting off pesky microorganisms [14]. Organizations such as the World Health Organization have taken notice of this expanding issue, which has grown to be a significant challenge for the global medical community.

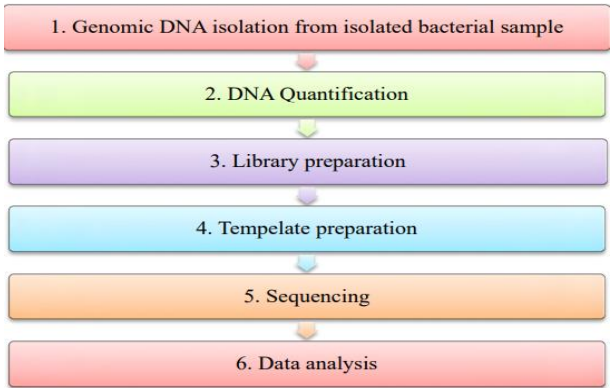


Fig. 1: Flow Chart of Whole Genome Sequencing Process.

Beta-lactam antibiotics are among the most significant classes of antibiotics used to treat bacterial infections. Throughout human history, infectious diseases have continued to be a leading cause of death. Infectious diseases such as cholera, influenza, cryptosporidiosis, hepatitis, HIV/AIDS, meningitis, and others are also prevalent today and cause nearly one-third of all fatalities worldwide [10] [12]. Viruses, fungi, and bacteria are the causative microbes. When we look at the history of antibiotics, we can see that up to the 19th century, medicines made from different materials were used to treat wounds. One of the main obstacles in the fight against infectious diseases brought on by bacterial and fungal pathogens is the emergence of antibiotic resistance. The microorganisms carry genes for resistance and can be passed on to other microbes by various natural mechanisms (conjugation, transformation, etc).

Bioactivity-guided fractionation was performed to isolate bioactive compounds. The process began with crude plant extracts being screened for antibacterial activity. To guarantee correct compound separation, the fractions were subsequently separated using silica gel column chromatography and observed using thin-layer chromatography. The disc diffusion method was used to assess each fraction's antibacterial efficacy against Pseudomonas aeruginosa. This method ensures that the most potent bioactive compounds are isolated for further characterization.

3. Analysis

A gradual increase in antibiotic resistance and a reduction in the availability of new medications have made treating illnesses increasingly difficult. In fact, after using penicillin consistently for four years, resistant infections were reported. However, during the 1950s and 1960s, resistant bacterial species were rare. This was a significant advancement in the modification of authorized antibiotics to reduce toxicity and develop drugs to which bacteria have developed resistance.



Fig. 2: Collection of Selected Plants.

Hybrid medications and other next-generation approaches are outperforming the present treatment regimens [6]. The "Trojan horse" tactic of covalently bonding a siderophore (Greek for iron carrier) pharmacophore to a biocidal pharmacophore tricked bacteria into delivering the antibiotic aggressively inside the cell. Iron in the form of ferric ions is necessary for bacterial development, especially in low-iron settings like the mammalian host. By producing siderophores, which are tiny molecules that effectively mix with iron to form compounds, bacteria can scavenge iron from their surroundings. Active transport systems, like Ton-dependent transporters, then absorb these siderophore-iron complexes. One approach to the delivery of antibiotics into bacterial cells has been the siderophore-based Trojan horse strategy in which the siderophores (iron carriers) are covalently attached to antibiotics. This method has proved to be more effective when used

against multidrug-resistant bacteria. The siderophore-iron complexes take advantage of bacterial transport systems, which include the TonB-dependent transporters, and enter the bacterial membrane through them. The approach improves not only the delivery of antibiotics but also minimizes the resistance mechanisms of bacteria, hence providing a promising alternative to the usual antibiotic treatments.

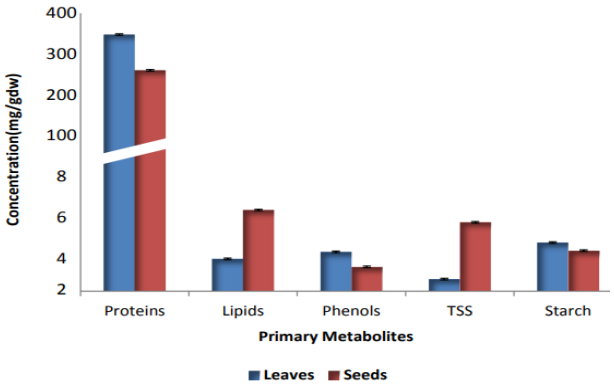


Fig. 3: Primary Metabolites.

Innovative linker chemistry, which is sometimes overlooked in traditional synthetic chemistry, is a critical success element in the hybrid drug approach. Proper linker selection is crucial to balancing conjugate stability and antibiotic release at the site of action, particularly if cytosolic targets are being targeted [13]. Triazoles are being used more and more in drug design as linkers to boost the effectiveness of the medications and as bioisosteres with various functions. Furthermore, triazoles are inherently aromatic with a pi electron shortage, have a strong dipole moment, and can form hydrogen bonds.

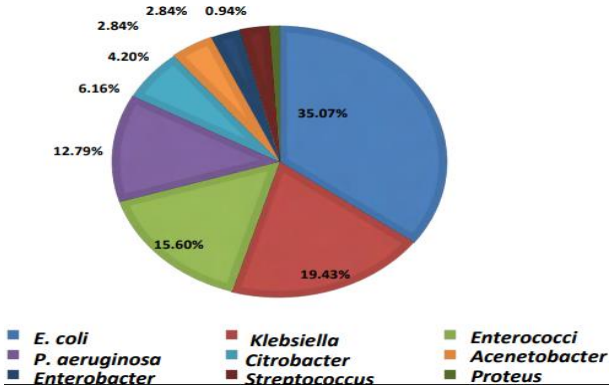


Fig. 4: Distribution Pattern of Uropathogens.

Researchers can explore completely described, unique natural products by screening these libraries to evaluate the bioactivities of different molecules [8].

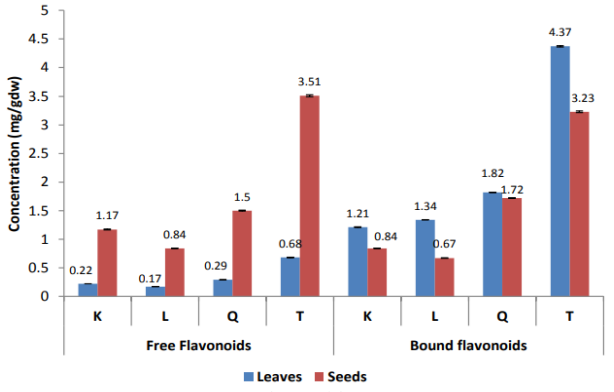


Fig. 5: Flavonoid Content.

Another method, known as bioactivity-guided fractionation, employs bioassays to monitor the fractionation process [9-10]. This approach employs continuous fractionation cycles to evaluate bioactive extracts, making sure that the pure and active principal compounds are separated. It's the go-to method for pinpointing bioactive substances. Even though there has been a significant rise in studies reporting bioactive compounds through this method, many botanicals and their preparations are still used without a clear understanding of their bioactive properties.

4. Results and Discussion

When choosing plant materials, we look at how plants typically interact with their surroundings, keeping in mind that some of the secondary metabolites they produce might offer valuable health benefits for us humans. The process of screening plant-derived substances for potential drugs involves a mix of random sampling, traditional knowledge from ethnopharmacology, and computational methods.

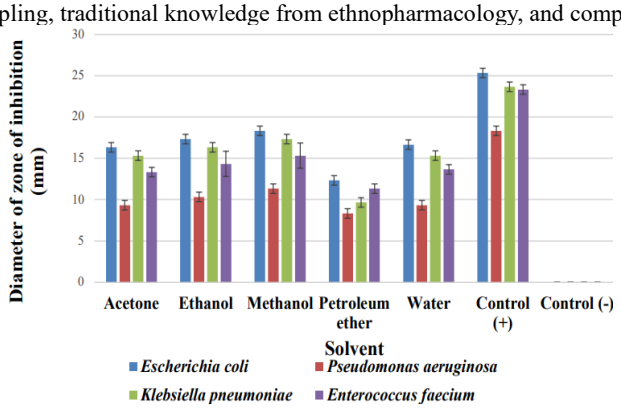


Fig. 6: Antibacterial Activity of Stevia Rebaudiana.

Effective antimicrobial capabilities against Pseudomonas aeruginosa are indicated by an inhibitory zone surrounding the extract disc in Figure 6, which illustrates the antibacterial activity of Stevia rebaudiana. This result confirms the potential of Stevia as an antimicrobial agent, particularly in combating multidrug-resistant pathogens. The size of the inhibition zone correlates with the potency of the extract, showcasing the efficacy of the plant's bioactive compounds in preventing bacterial growth.

The throughput of pharmacological experiments is typically medium to small. This limits the number of bioassays we can do because the initial test samples, such as extracts, fractions, or pure chemicals, are frequently available in limited quantities.

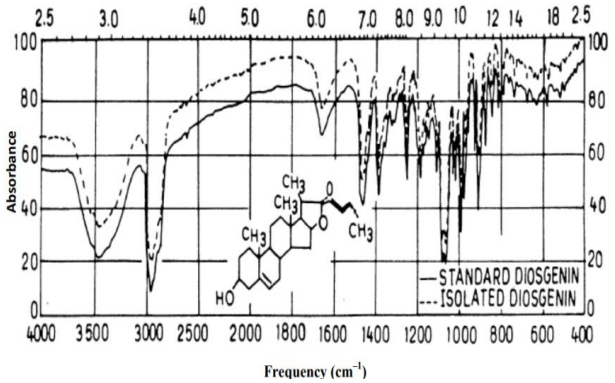


Fig. 7: GC-MS of Flavonoids Isolated from Seeds.

The GC-MS profile of the flavonoids that were separated from Stevia rebaudiana is shown in Fig. 7, which also highlights the chemical makeup of the bioactive substances that give Stevia its antibacterial properties. The chromatogram shows the retention times of the various flavonoids, with distinct peaks corresponding to different compounds. These findings provide insight into the specific chemical components that contribute to the antimicrobial activity observed in Fig. 6, offering a deeper understanding of the mechanisms by which Stevia combats bacterial pathogens.

Because they share a high degree of genetic similarity with humans, these models offer significant insights into the pathophysiological relevance of findings in a whole organism. However, there are some drawbacks to this approach, such as slow processing speeds, the need for ethical approvals, and the requirement for specialized animal facilities. It often takes quite a bit of time to dive deep into research until we can identify the targets at a molecular level.

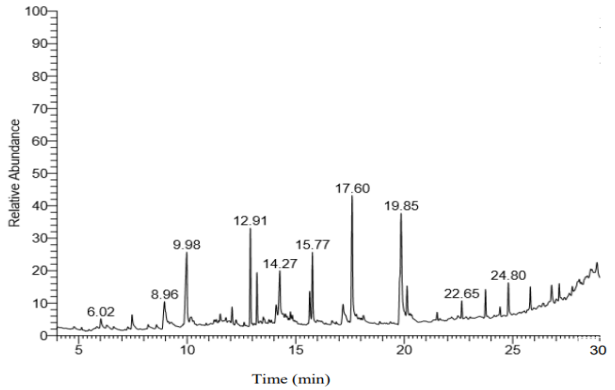


Fig. 8: Functional Screening of Steroids.

Non-mammalian models, such as Caenorhabditis elegans and zebrafish, are gaining traction because they're readily available and come with tools that make high-throughput screening a breeze. Plus, their value as disease models has really been boosted by the latest breakthroughs in gene editing techniques.

5. Conclusion

The issue of antibiotic resistance isn't just a recent development; it's a long-standing and complex challenge that arises when bacteria are exposed to antibiotics. Unfortunately, it hasn't received the attention it deserves, even though it's become a significant concern for human health. This troubling trend is on the rise, yet it still hasn't made its way into the strategic planning of health professionals, scientists, or researchers. The current surge in multidrug-resistant bacteria poses a global threat, highlighting the urgent need for new solutions. Given the obvious lack of novel antimicrobials reaching the market, the pharmaceutical industry's largely untapped potential—particularly in medicinal herbs—may offer a viable route for developing medications to address the escalating problem of antibiotic resistance. Antimicrobials derived from plants are exhibiting significant potential for medication development.

The synergistic effects of plant-derived substances and currently available antibiotics should be investigated in future studies. Investigating combination therapies, particularly with plant-based bioactive compounds, could improve the efficacy of treatments against multidrug-resistant pathogens like Pseudomonas aeruginosa. Additionally, scalability challenges in producing these compounds for clinical use must be addressed, with an emphasis on developing cost-effective extraction methods and ensuring their stability in pharmaceutical formulations.

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