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Modification of Gemifloxacin Drug Antibacterial to Promising Anti-Prostate Cancer PC3 Azomethine Compounds: Synthesis and *in Vitro* Studies

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Abstract. *In this study, we report a novel azomethine derivatives synthesis (H and G) by reacting pure Gemifloxacin drugs with 2-aminobenzaldehyde and 2-methylbenzaldehyde. Spectroscopic techniques, such as FT-IR spectroscopy, characterized the derivatives (G and H). All the synthesized derivatives (G and H) were evaluated in vitro against microorganisms such as Bacillus subtilis and E. coli by zone inhibition method and screened for antimicrobial activities and anti-Prostate cancer PC3 cell viability cell lines.*

Keywords: *Antibacterial, Antibiotic, Gemifloxacin, Cancer.*

1. INTRODUCTION

Prostate cancer PC3 begins in the prostate, a little gland like a walnut situated behind the bladder and in front of the rectum in males and individuals assigned male at birth (AMAB). The prostate gland produces fluid that combines with semen, ensuring the vitality of sperm for fertilization and gestation.

Prostate cancer is a grave illness. Fortunately, the majority of individuals with prostate cancer get a diagnosis prior to the disease spreading beyond the confines of their prostate gland. At this point, medication often reduces the tumor.

The PSA screening measures the level of antigen specific for the prostate (PSA), a protein found in the bloodstream. PSA is generated only by the prostate gland and prostate tumors. The conventional approach for presenting the findings of this test is by expressing the results in nanograms of prostate-specific antigen per milliliter (ng/mL) of blood. The PSA test is used to detect alterations in the prostate's PSA production. It is used for cancer staging, therapy planning, and monitoring treatment progress. An abrupt increase in PSA levels may indicate an underlying issue. Furthermore, your physician may assess the testosterone concentration in your bloodstream.

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Before the oxazolidinones were introduced, the quinolones were the first really novel group of antibacterial drugs to be found in three decades. The β-lactam-based compounds, together with its related derivatives such as cephalosporins, cephamycins, carbapenems, and monobactams, were thoroughly studied and developed from the 1960s to the 1980s and are still being researched. Furthermore, the macrolide and its related chemicals were further refined as improvements to erythromycin. The introduction of quinolones marked a significant breakthrough in the field of antimicrobial medicine. The quinolones, which were successfully marketed, provided a wide range of activity, effectiveness, safety, and tolerance. They were available in both oral and intravenous forms, with minimal or no decrease in effectiveness when taken orally. The oral formulations were suitable for use both in hospitals and in the community.

Most bacterial species are non-pathogenic. Some of them have positive effects on your health. The beneficial bacteria are mainly located on the skin and in the gastrointestinal system. The collections of bacteria that live in and colonize your body are known as resident flora or your microbiome. The gut microbiota plays a crucial role in preserving health by facilitating nutrient absorption, metabolizing food, and inhibiting the proliferation of pathogenic bacteria.

Gemifloxacin is a quinolone antibiotic used to treat acute bacterial aggravation of chronic bronchitis and mild to severe community-acquired pneumonia caused by sensitive bacteria. Gemifloxacin treats bronchitis and pneumonia caused by bacterial infections. Gemifloxacin is classified as a quinolone antibiotic. It functions by eradicating germs or inhibiting their proliferation. Nevertheless, this medication is ineffective against colds, flu, or other viral diseases.

This study synthesized new azomethine derivatives (Gand H), characterized FTIR, and screened for antimicrobial activities and anti-breast cancer PC3 cell lines.

2. MATERIAL AND METHODS

Materials

All chemicals used in this study were obtained from Sigma Aldrich and Merch companies.

Methods

Synthesis of azomethine-gemifloxacin

Dissolve (0.389 g, 1.0 mmol) of gemifloxacin in 10 ml of absolute ethanol and added 1.0 mole of 2-aminobenzaldehyde and 2-methylbenzaldehyde to solution with refluxed for 3 hours. The precipitates were cooled, collected, and dried at room temperature.

A evaluation of the antibacterial properties of Azomethine compounds (G and H)

The antibacterial characteristics of the synthesized derivatives (G and H) were assessed using the cup-plate agar diffusion method, and the inhibition zone was quantified in millimeters. The synthesized compounds were evaluated for their antibacterial activity compared to gemifloxacin, using concentrations (0.1, 0.001, and 0.00001 M). The derivatives assessed for their antibacterial efficacy against four microorganisms: *Bacillus subtili*, *Staphylococcus aureus*, and *Escherichia coli*. The germs were obtained from infected wounds, nasal swabs, urinary tract infections, and surgical operating rooms. The experimentation was carried out utilizing Muller Hinton agar. The aseptic agar media was poured onto Petri plates and let to harden. The microbial suspensions were uniformly dispersed throughout the press surface using a sterilized triangular loop.

3. RESULTS AND DISCUSSION

The spectroscopic result of the azomethine group appeared in FTIR and disappeared the amine group of the gemifloxacin drug.

Azomethine derivative (A): Yield: 71%, M.p.: 222-225 °C, Color: Yellow. FTIR: 3388 cm^{-1} (OH), 3029 cm^{-1} (C-H of Ar ring), 1717 cm^{-1} (carbonyl carboxylic acid), 1632 cm^{-1} (azomethine group), 1564 cm^{-1} (C=C of aromatic ring).

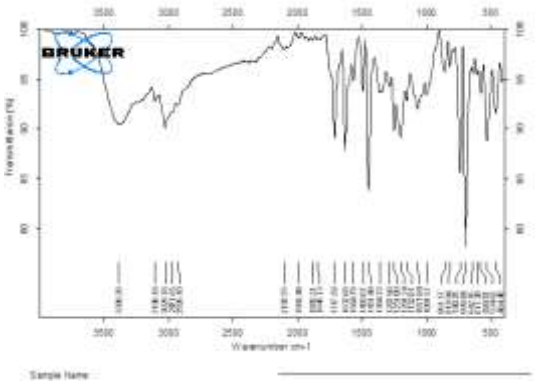

Figure 1: FTIR spectrum of azomethine derivative G.

Azomethine derivative (B): Yield: 78%, powder, M.p.: 189-191 °C, Color: Dark yellow. FTIR: 3398 cm^{-1} (OH), 3035 cm^{-1} (C-H of Ar ring), 1728 cm^{-1} (carbonyl carboxylic acid), 1666 cm^{-1} (azomethine group), 1588 cm^{-1} (C=C of aromatic ring).

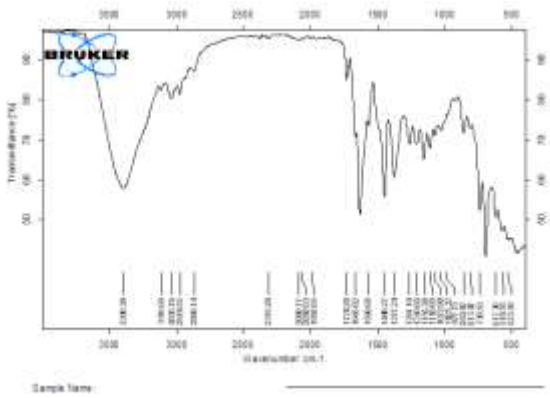

Figure 2: FTIR spectrum of azomethine derivative H.

Bioactivity: The in vitro antimicrobial or antibacterial aspects of a new group of azomethine derivatives (G and H) were screened, and the findings were obtained. After evaluating the data on the inhibitory zones of *Bacillus subtilis, Streptococcus pneumonia*, and *E. coli*, it is clear that most of the new Azomethine derivatives demonstrated better antibacterial effectiveness than the original gemifloxacin substance. There is a direct relationship between the concentration and the amount of bioactivity. The microorganisms *Bacillus subtilis* and *E. coli* were most significantly affected by derivative G. Nevertheless, the normal medication exhibits greater efficacy against *Streptococcus pneumonia* than derivatives G and H, as seen in Figures 3, 4, and 5. The derivative G has a solitary pair of electrons on the amino group's nitrogen atom, which may influence bacterial cells and establish contact with the target enzyme via hydrogen bonding.

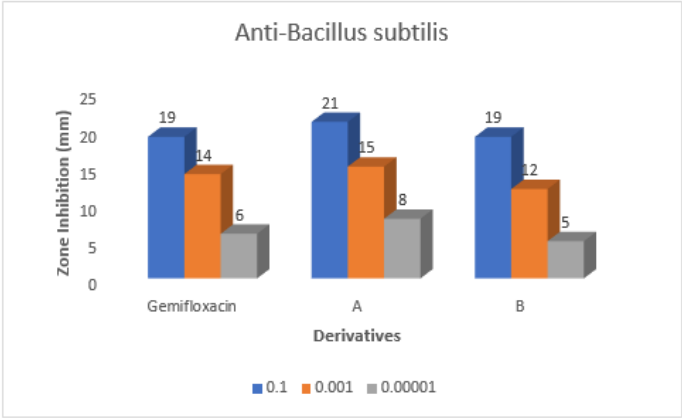

Figure 3: Role of gemifloxacin and azomethine compounds against *Bacillus subtilis*.

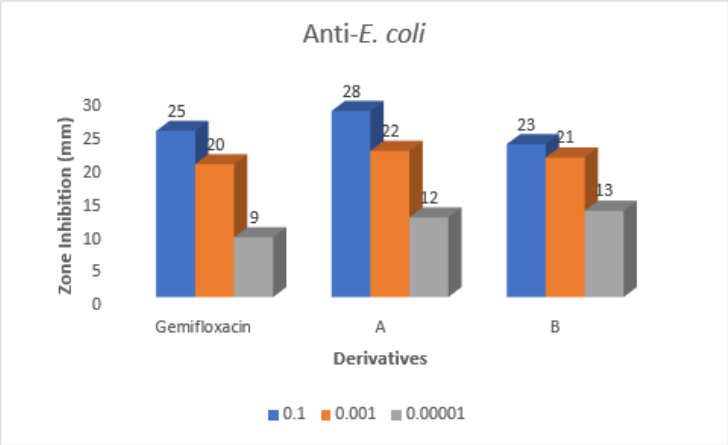

Figure 4: Role of gemifloxacin and azomethine compounds against *E. coli*.

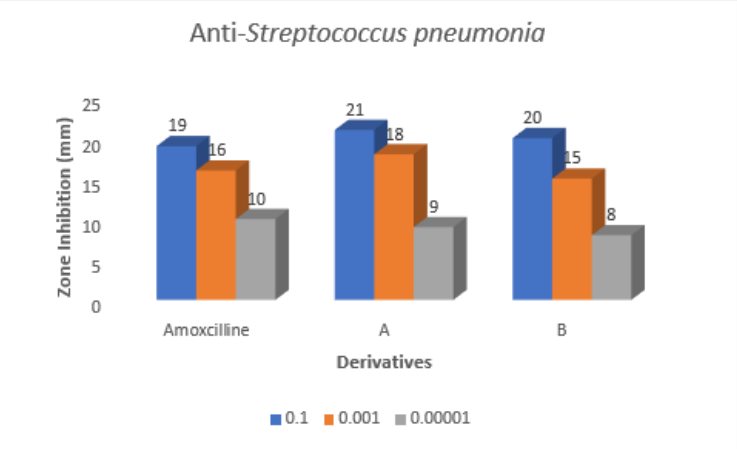

Figure 5: Role of gemifloxacin and azomethine compounds against *Streptococcus pneumonia*.

Gemifloxacin exerts its bactericidal effect by inhibiting the enzymes topoisomerase II (DNA gyrase) and topoisomerase IV, which are essential for bacterial processes such as DNA replication, transcription, repair, and recombination.

Gemifloxacin undergoes little hepatic metabolism. The metabolites generated are of low abundance, comprising less than 10% of the oral dosage provided. The primary metabolites are N-acetyl gemifloxacin, the E-isomer of gemifloxacin, and the carbamyl glucuronide of Gemifloxacin.

Viability Assay MTT

The MTT experiment demonstrated that the derivative (H) exhibited cytotoxicity against the PC3 cell lines. The viability of the cell was assessed at 24 or 48 hours and subjected to different concentrations of each derived chemical, 0 - 320 g/ml. Table 1 displays the cell viability outcomes for derivative (H) (9 – 100) after 24 hours. The results demonstrated a strong correlation between dose with impact on the PC3. This derivative (H) was selected based on its strong inhibitory effects on the urease enzyme, making it the most favorable choice for anti-

cancer drugs. Figure 6 demonstrates the impact of the derivative (H). After 48 hours, the concentration, measured in parts per million, increased, leading to a more significant decrease in the viability of breast cancer cells compared to the 24-hour point. The obtained findings are shown in Table 1.

Table 1: Cell viability levels of compound (H) on PC3 cells increased.

Concentration by (PPM) unit	After 24 hours		After 48 hours	
	Mean	SD	Mean	SD
0	100	2.87528	100	2.85395
20	79.3643	2.10081	44.0072	2.08974
40	59.09712	1.19638	33.7607	2.34177
80	42.1497	1.41220	15.6378	1.39645
160	16.8540	2.77091	9.6631	1.87989
320	8.87754	2.31634	2.9068	1.00168

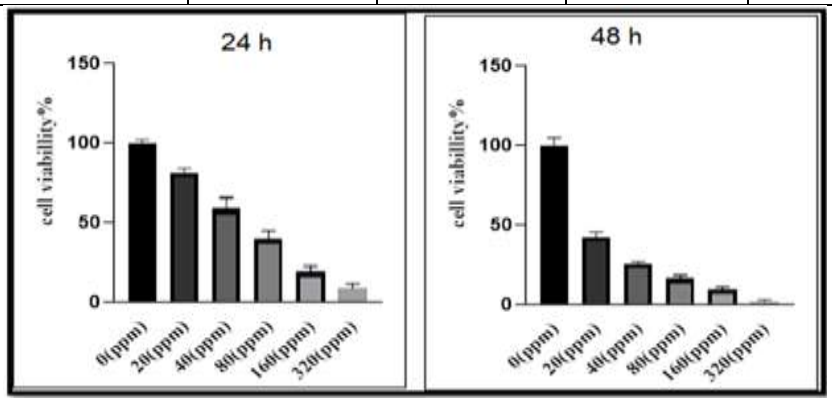

Figure 6: The effect of azomethine compound (A) on the functioning of PC3 cells.

4. CONCLUSION

Azomethine derivatives (G and H) were produced, and their properties were analyzed using FTIR spectroscopy. Chemical interactions between the gemifloxacin medication and aldehyde derivatives initiated the synthesis. In vitro, the antibacterial activity of azomethine derivatives, such as gemifloxacin, was investigated against Bacillus subtilis, Staphylococcus epidermidis, and Escherichia coli. The results showed that certain derivatives had stronger antibacterial characteristics. In the future, we will create novel derivatives via synthesis and subject them to in vitro testing. These derivatives will be examined for their antimicrobial activities and their effects on the survival of PC3 cell lines, which are associated with prostate cancer.

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