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Microwave Assisted Synthesis, Spectroscopy Characterization of Amoxicillin Linked Azomethine as Medical Applications

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Abstract: In this study, a new amoxicillin linked azomethine synthesis (A1-A3) by reacting amoxicillin with different aldehydes such as 2-hydroxy5-hexylBenzaldehyde, 4-Hexoxybenzaldehyde, and 2-methoxybenzaldehyde. FT-IR characterized the derivatives (A1-A3). All the derivatives (A1-A3) were evaluated against microorganisms such as *Streptococcus pneumonia* and *E. coli* by zone inhibition method. The findings demonstrated that certain derivatives exhibit superior antibacterial properties in comparison to the efficacy of the original drug. The produced azomethine derivative A1 has the most promising antimicrobial properties against *Staphylococcus aureus* by zone inhibition 23 mm at higher dosages. However, derivative A2 reduced efficacy at lower dosages requires more investigation to improve potency and stability. Evaluation of prostate cancer (PC3) by using MTT assay that gives a positive result at high concentration.

Keywords: Azomethine, Amoxicillin, Prostate Cancer, Bacteria.

Introduction

Enhancing research and development (R&D) productivity is a paramount challenge for drug companies. Recent advancements in proteomics and genomics have resulted in a significant increase in the ability of therapeutic targets [1], prompting manufacturers of medicines to invest heavily in advanced screening techniques and synthetic chemistry in order to discover additional potential medicines for these new objectives [2]. Nevertheless, lead product modification and conventional clinical chemistry continue to be the impediments in the process of developing drugs.

Creating chemical molecules with specific biological characteristics is labor-intensive and costly [3, 4]. As a result, there is heightened interest in developments and concepts that enable expedited manufacture and testing of organic compounds to discover molecules with desirable properties. Microwave-assisted organic synthesis (MAOS) is a notable high-speed technique [5].

Microwave-assisted warming under regulated circumstances is a crucial tool for pharmaceutical chemistry and the creation of drugs since it often significantly decreases responses, generally from days or hours to minutes or even seconds. A multitude of process settings, including temperature, duration, solvent changes, additives, catalysts, and substrate molar ratios, may be assessed within a few hours in order to maximize the intended chemical outcomes [6]. A compound collection may thereafter be created swiftly using an automatic or sequentially (automated) style [7]. Moreover, MAOS methodology often enables the identification of innovative chemical processes since the high

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settings achievable with microwave heating may result in atypical sensitivity that is not consistently replicable using traditional warming methods. This aims to broaden the overall chemical universe, specifically within the domain of biologically pertinent pharmaceutical chemistry [8].

Schiff bases are important for generating useful compounds via substitution reactions and are used in industry and biology [9]. They also have a variety of biochemical advantages, including anti-inflammatory, chemical inhibition, electron collecting, pain alleviation, and antioxidant properties [10].

In this study, new imine derivatives (A1-A3) were synthesized, and FTIR and biological medicine were characterized as anti-bacterial agents.

Material and Methods

Materials

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

Methods

Synthesis of Amoxicillin Linked Azomethine by Microwave Assisted

A mixture of amoxicillin (1.0 mmol, 0.419 g) and (1.0 mmol) 2-hydroxy-5-hexylBenzaldehyde, 4-hexoxybenzaldehyde, and 2-methoxy benzaldehyde, respectively, in anhydrous methanol (20 mL), in the presence of three drops of glacial acetic acid, and the reaction mixture was heated inside a microwave oven for 1 min. (at 210 W, such as 30% microwave power). The reaction's progress was assessed using thin-layer chromatography (TLC). Upon the end of the process and subsequent the cooling process, the result was acquired and recrystallized using the appropriate solvent (Chloroform and Methanol; 80:20) [11].

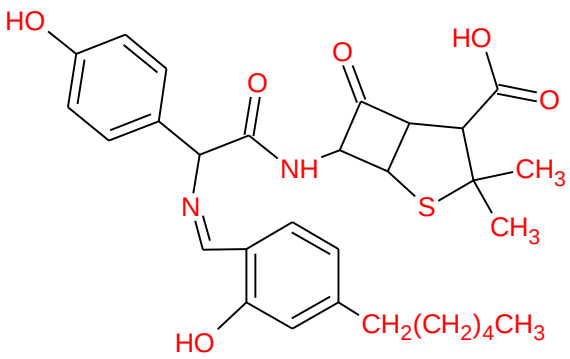
Evaluation of the antibacterial efficacy of amoxicillin and Azomethine compounds (A1-A3)

Multiple bacteria, such as Streptococcus pneumoniae and Escherichia coli, were cultured on Muller-Hinton agar media employing sterile loops and spotting methods, commencing with the fluid growth [12]. A separate well was formed in the agar media. A concentration of 0.1, 0.01, and 0.00001 µl of the appropriate dilution of Azomethine derivatives (A1-A3) was administered to all wells, yielding effective consumption. The container was securely sealed and positioned in an environment maintained at 37 ºC overnight for assessment the next day [13, 14].

Results and Discussion

The spectral study of the amoxicillin-linked azomethine compounds was evident in FTIR, indicating the absence of the amine group from the amoxicillin derivatives (A1-A3).

Imine derivative (A1): Color a yellow, Molecular Formula is $C_{30}H_{36}N_2O_6S$, M.p. 278-282 °C, Yield: 69%. FTIR (cm^{-1}): 3396 (hydroxyl group), 3026 (C-H of aromatic ring) [15], 1612 (imine group), 1593 (C=C of aromatic ring) [14, 16].



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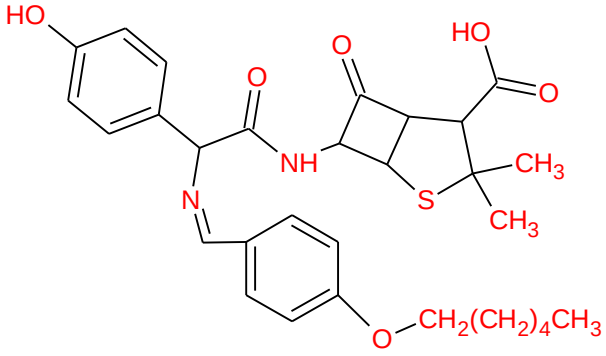
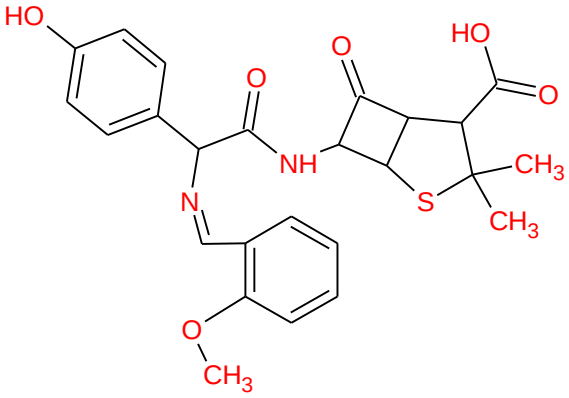
Imine derivative (A2): Color a Brwon yellowish, Molecular Formula is $C_{30}H_{36}N_2O_6S$, M.p. 246-250 °C, Yield: 70%. FTIR (cm^{-1}): 3321 (hydroxyl group), 3026 (C-H of aromatic ring) [17], 1622 (imine group), 1600 (C=C of aromatic ring) [18].



Imine derivative (A3): Color a Light Brown powder, Molecular Formula is $C_{25}H_{26}N_2O_6S_2$, M.p. 232-236 °C, Yield: 72%. FTIR (cm^{-1}): 3284 (hydroxyl group), 3021 (C-H of aromatic ring), 1638 (imine group), 1583 (C=C of aromatic ring) [19].



Bioactivity: The research investigates the antibacterial efficacy of manufactured penicillin derivatives (A1, A2, A3) and regular Penicillin G against *Staphylococcus aureus*. A 0.1 mg/ml of azomethine derivative A2 has the most potent antibacterial action, producing a 26 mm zone of inhibition, surpassing azomethine derivative A1 (23 mm) and Penicillin G (18 mm). The azomethine derivative A3 has modest activity (19 mm), akin to Penicillin G. The efficacy diminishes at lower concentrations (0.001 and 0.00001 mg/ml), a trend seen consistently across all evaluated substances. A 0.001 mg/ml concentration of A2 exhibits the highest efficacy (19 mm), followed by azomethine derivative A1 (17 mm) and azomethine derivative A3 (14 mm). At a concentration of 0.00001 mg/ml, activity is negligible for all drugs, with azomethine derivative A2 exhibiting the greatest inhibition at 10 mm.

The elevated activity of azomethine derivative A2 at all doses indicates enhanced antibacterial efficiency against Staphylococcus aureus compared to other produced derivatives and Penicillin G. The comparatively diminished efficacy of Penicillin G underscores the promise of these synthetic compounds, particularly azomethine derivative A2, as enhanced antibacterial medicines.

Table 1: Study investigates the antibacterial properties of synthesized penicillin and azomethine (A1-A3).

Synthesized Derivative	Concentration g / ml	Zone inhibition (mm)	
		Streptococcus pneumonia	*E. coli*
Penicillin	0.1	18	28
A1	0.1	23	22

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	0.001	17	17
	0.00001	8	11
A2	0.1	26	18
	0.001	19	16
	0.00001	10	13
A3	0.1	19	19
	0.001	14	17
	0.00001	7	12

β-Lactams function by disrupting peptidoglycan formation, an essential element of the cellular membranes of bacterial cells. The final transpeptidation, which is the stage in the synthesis of the layer of peptidoglycan, is mediated by the transpeptidases, enzymes that interact with the antibiotic [20]. The enduring attachment of the β-lactam core to penicillin-binding proteins over time disrupts the cell wall architecture, obstructing the final transpeptidation process step that links the straight peptide g chain Polymers. Thus, while coupled, it expands the spectrum of AMX's effectiveness by involving isolates of bacteria that demonstrate sensitivity to AMX and produce β-lactamase. The emergence of β-lactamase production has gained prominence in respiratory conditions, including H. influenzae and M. catarrhalis [21].

AMX is easily absorbed in the digestive tract after being taken orally as a liquid or capsule. Variations in the metabolism of AMX have been noted throughout distinct parts of the gastrointestinal tract, with significant intake occurring in the top part of the small intestine and limited absorption in the small intestine. AMX has a bioavailability in the oral cavity ranging from 70% to 90%, with peak concentrations in the circulation occurring between 60 minutes post-ingestion [22].

Cell toxicity of the manufactured compound A2 was assessed as a tumor suppressor employing the MTT stability assay

The test assesses cell toxicity after a 24-hour injection with derivative A2 at various doses (0–320 µg/ml). The correlation between derivative A2 dosage and its impact on the health of cells was measured. At the 24-hour interval, the minimum strength of cell life (22.3%) was recorded at the maximum concentration (320 µg/ml), while cells treated with nothing exhibited 100% vitality. Table 1 presents the mean values and standard deviations for cell viability across various concentrations, affirming the reliability of the data, as shown in Figure 6. The observations indicate that the derivative A2 functions as a tumor regulator with notable lethal effects on PC3 cells, particularly at elevated doses.

Table 1: Cell viability rates of derivative A2 induced PC3 cell.

Concentration (PPM)	After 24 h	
	Mean	SD
0	100	2.806964
20	75.98541	2.438943
40	62.12188	1.122134
80	53.43301	1.057290
160	31.78508	2.386957
320	22.29731	2.467347

Conclusion

Difference amoxicillin-linked azomethine derivatives (A1-A3) were synthesized and analyzed using FTIR. The synthesis started with chemical interactions between amoxicillin and aldehyde derivatives.

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The in vitro antibacterial efficacy of azomethine derivatives, such as amoxicillin, was evaluated against *Staphylococcus epidermidis* and Escherichia coli. The synthesized azomethine derivative A2 has the most promising antibacterial efficacy against *Staphylococcus aureus*, especially at elevated doses. The azomethine derivative A2 is positioned as a viable option for further development in antimicrobial treatment. Nonetheless, its diminished efficiency at lower doses necessitates more research to enhance potency and stability. The derivative 2 gives a good result as a PC3 cell line.

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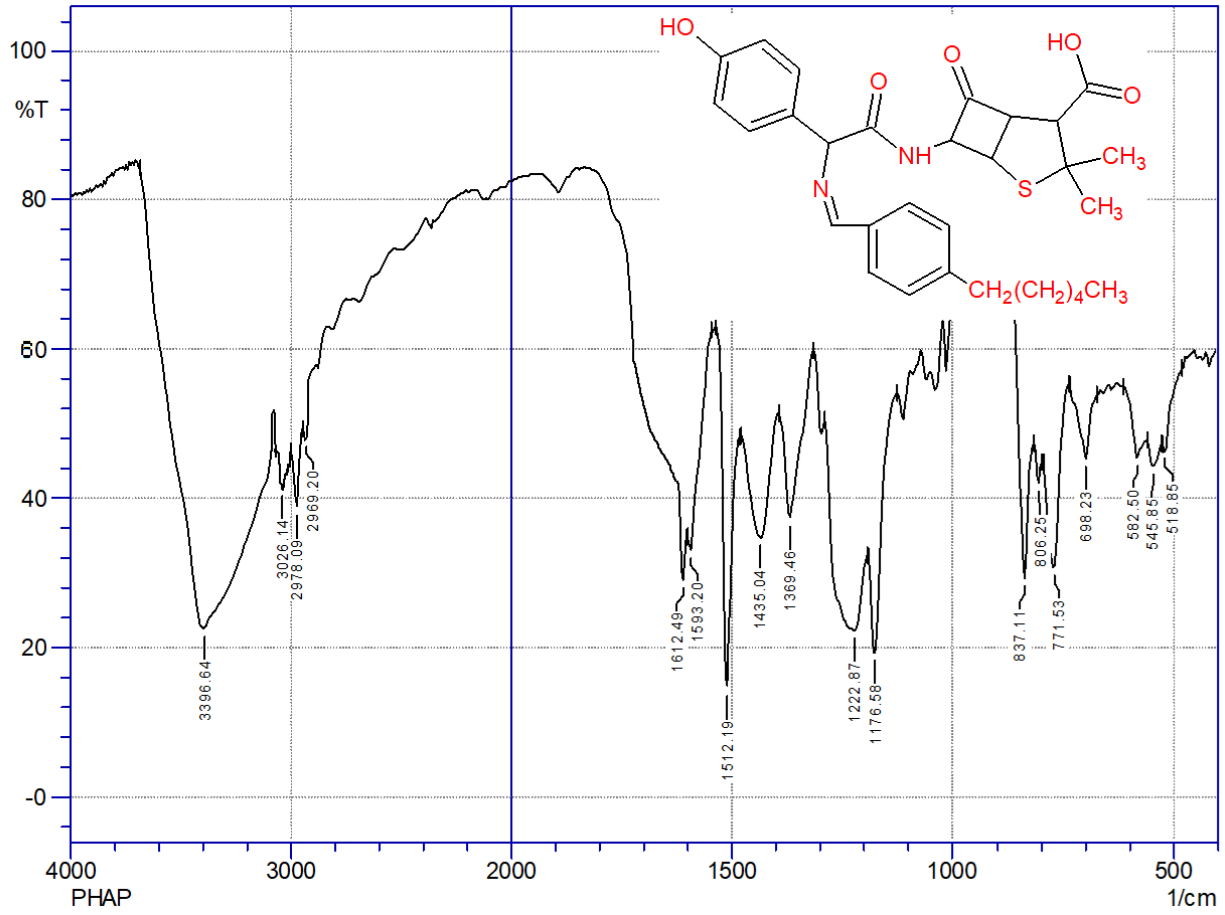

Figure 1: FTIR of derivative A1.

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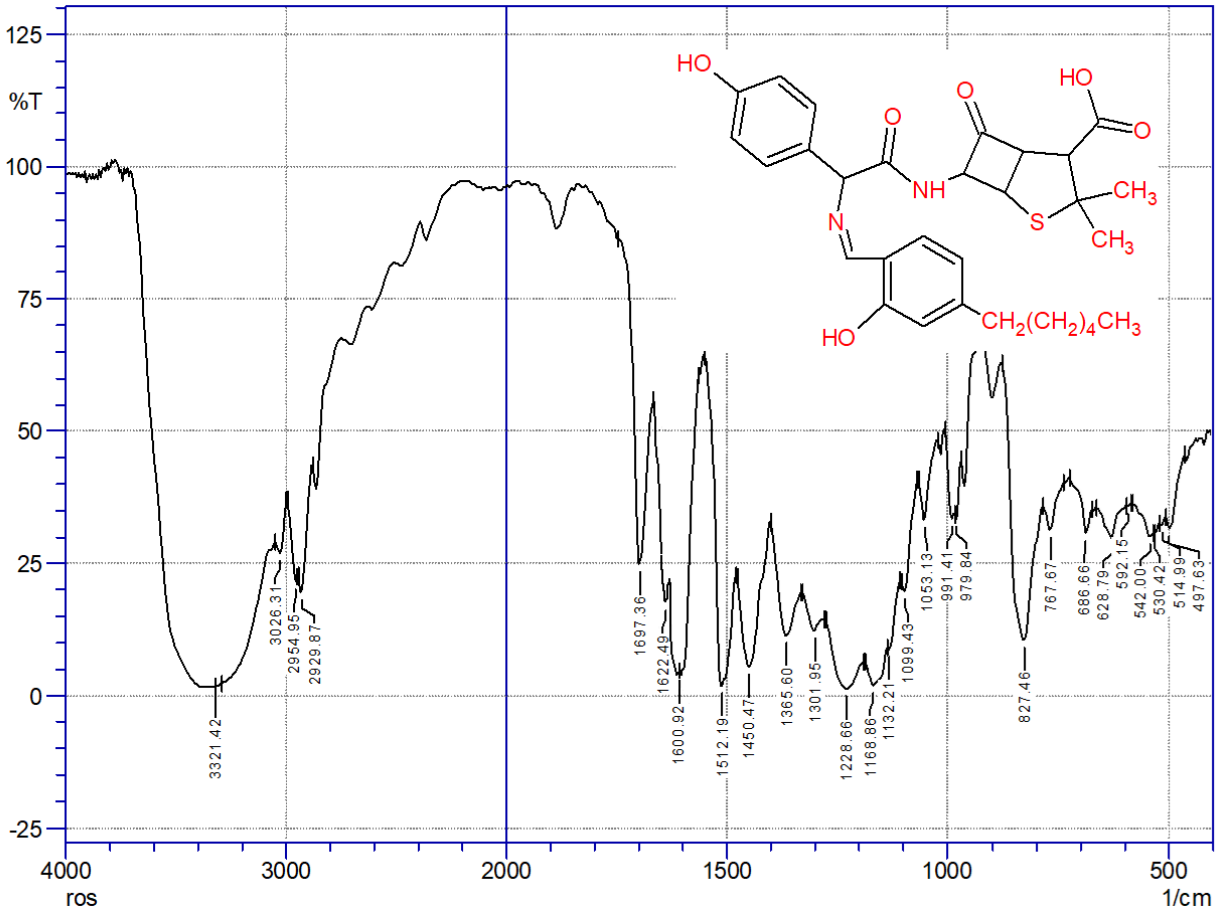

Figure 2: FTIR of derivative A2.

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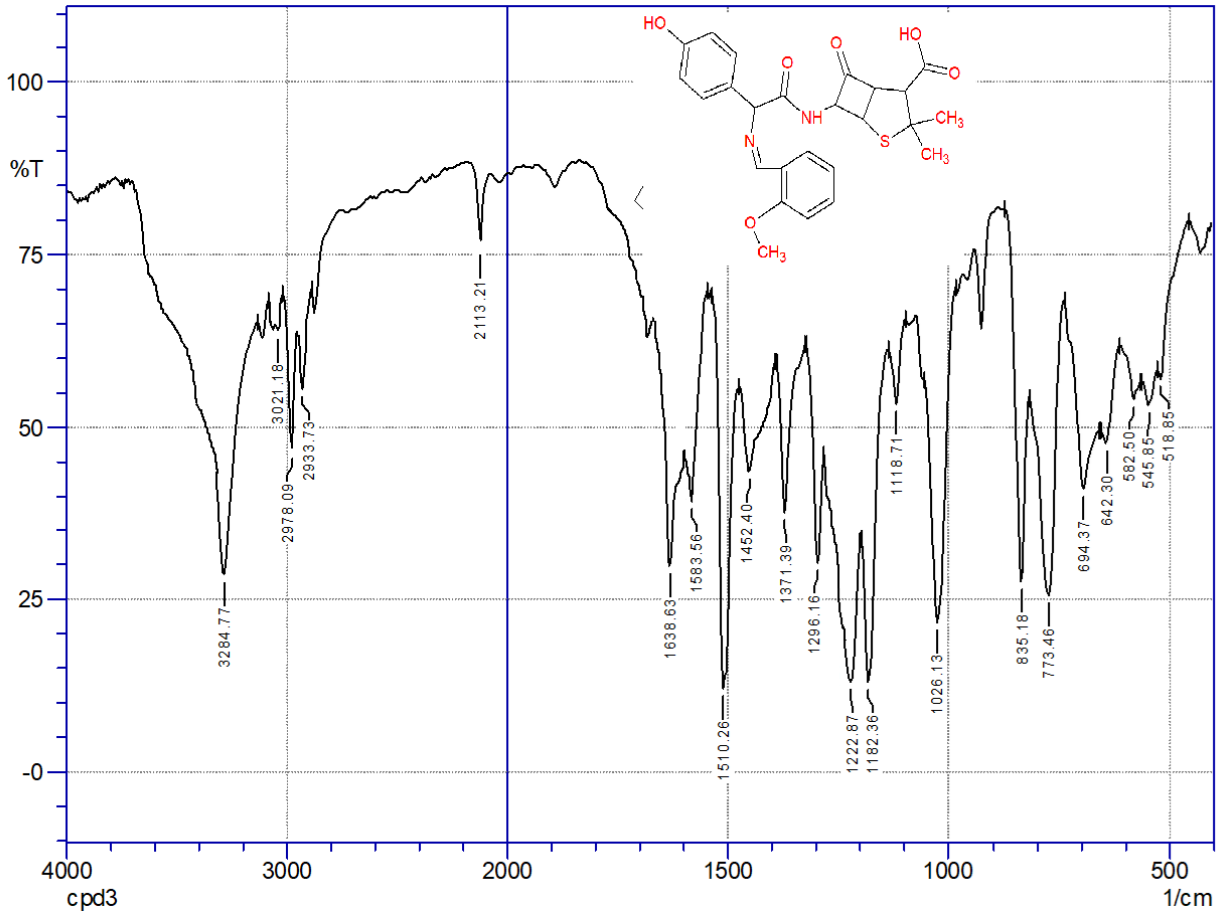

Figure 3: FTIR of derivative A3.

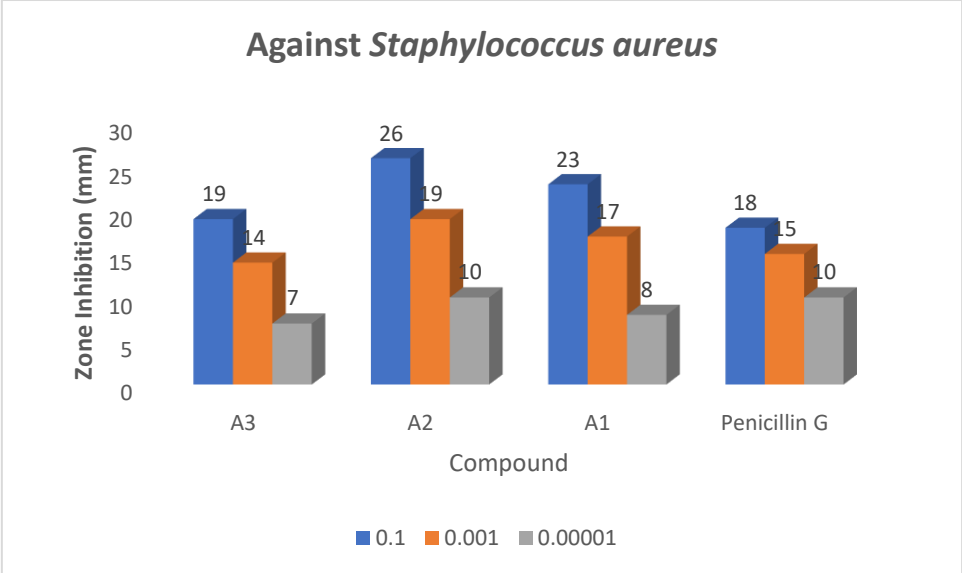

Figure 4: Biological activity of synthesized derivatives against *staphylococcus aureus*.

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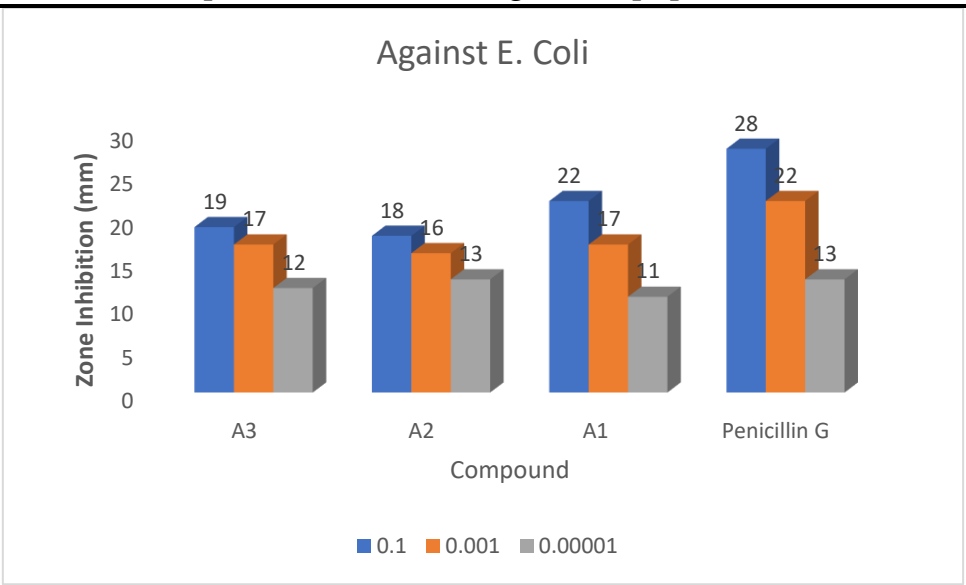

Figure 5: Biological activity of synthesized derivatives against *E. Coli*.

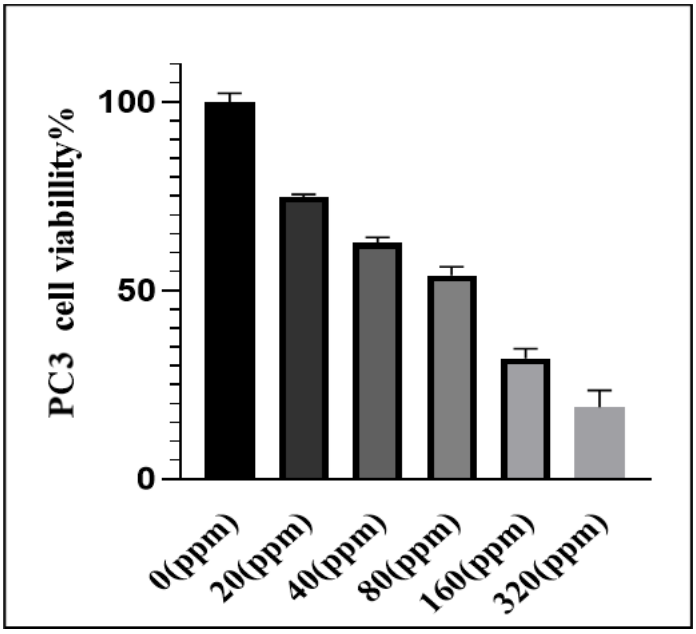

Figure 6. Effect derivative A on PC3 cell viability %.