Original Article

Lactam-Heterocycles Compounds (Synthesis, Organic Revealing, Bacterial and Fungal Estimation)

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Abstract

Many antimicrobial chemical compounds were prepared and they gave good killing and inhibition results, but lactam compounds were more effective in inhibiting the growth of bacteria and fungi. In addition to their medicinal use, antifungals are also used to control mold growth on damp materials in homes. Sodium bicarbonate, when applied to surfaces, acts as an antifungal. Another compound that also acts as an antifungal is a mixture of hydrogen peroxide with a thin layer of paint that neutralizes mold and coats the surface to prevent vesicles from forming. In this study seven organic compounds from lactam derivatives were prepared and identified by spectroscopic techniques (Infrared Ray, Proton Resonance, Mass)–spectra, also biological revealing (fungi and bacteria) and other laboratory diagnosis.

Keywords: Azo, Imine, Schiff Base, Aldamine, Azomethine.

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INTRODUCTION

In medicine, antifungal drugs are used to treat infections such as tinea pedis, ringworm and candidiasis, by exploiting the differences between mammalian cells and fungal cells. It kills the fungi without seriously affecting the host[1-3]. Unlike bacteria, both humans and fungi are multicellular organisms. So fungal cells and human cells[4,5] are similar at the molecular level, which makes it more difficult to find an antifungal target to attack[6-9]. Accordingly, there are often some side effects of some of these medicines. Some of these side effects can be fatal if the medication is not used properly[10-12]. The spread and resistance of fungi and bacteria to antibiotics made researchers resort to preparing compounds more resistant to the activity of fungi. The researchers counted the death of 5 million people in 2019 due to diseases related to antibiotic[13-17] resistance, as well as the death of 1.2 million people, due to direct antibiotic resistance. In the same year, statistics indicate that AIDS caused the death of 860,000 people in the world[18-22], while the number of victims of the malaria epidemic reached 640,000 people. Most deaths from antibiotic-resistant diseases[23-28] occurred due to respiratory infections, such as pneumonia and bloodstream infections, which may lead to sepsis[29-32].

EXPERIMENTAL PART

It is known that all the organic compounds that are prepared must be carried out under spectroscopic tests and analyzes to prove their chemical structures and structure through frequencies in spectral bands, absorptions in Infrared devices, Proton resonance devices, and Mass spectra that were carried out outside the diameter at the University of Isfahan in Iran, which gave accurate measurements and Specificity of the prepared compounds, as well as measurements of the percentage of microbial growth inhibition of fungi and bacteria selected for study at the University of Tehran.

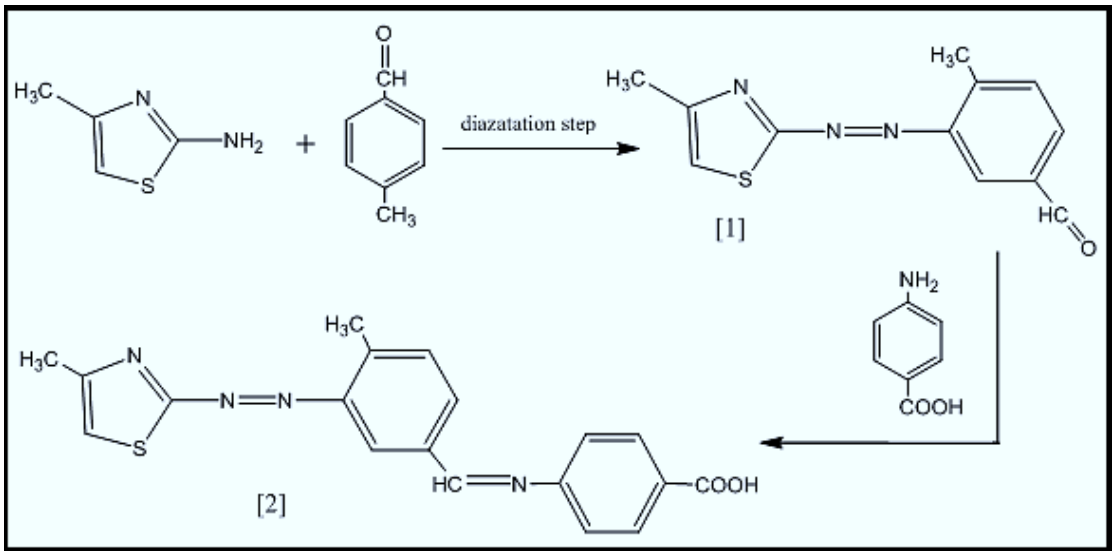
Construction of Thiazole-Azo Compound {1} [6, 7]

2-Amino-4-methyl thiazole (0.01) mole dissolved in concentrated hydrochloric acid with cold solution of sodium nitrite at cooling temperature, then solution of p-methyl benzaldehyde in basic medium was added, after that the precipitation separation, washed by distilled water, dried to give compound {1} appreciative to ways[6, 7]

Construction of Thiazole-Azo-Schiff Compound {2} [6, 7]

Thiazole-Azo compound {1} (0.01 mole) mixed with p-anthranilic acid vi condensation reaction in acidic medium (Glac. Acetic) for (3 hrs) from refluxing step, then parting,

drying, manifestation to give Compound {2} appreciative to practices [6, 7]



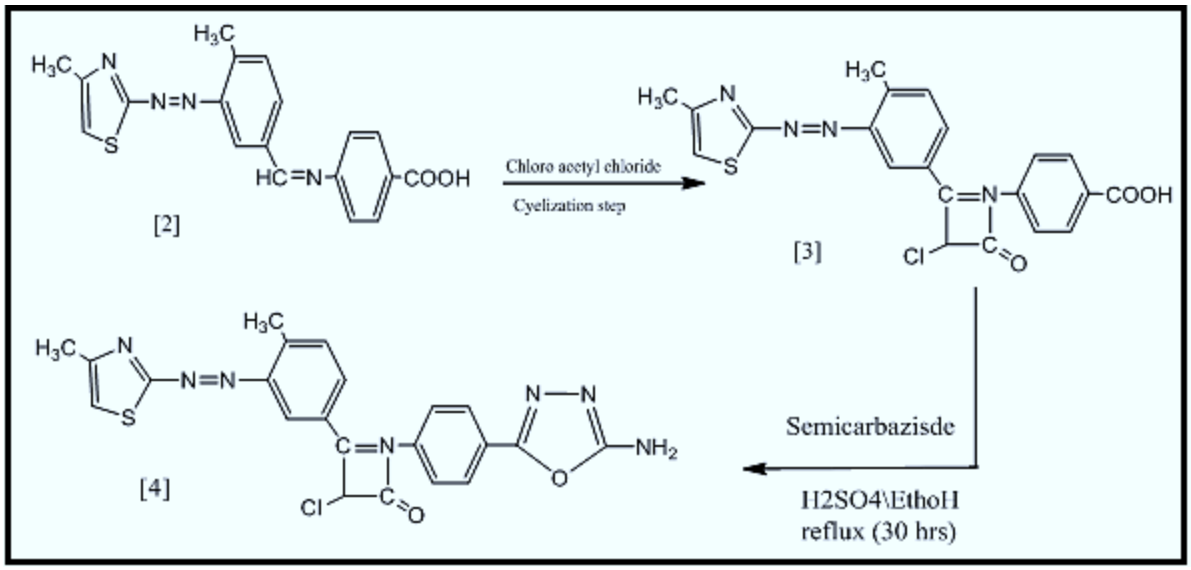
Form.1: Construction of Azo-Schiff Compounds{1, 2}

Construction of Thiazole - Azitidine Compound {3} [6, 7]

Thiazole-Azo-Schiff Compound {2} (0.01 mole) countered with chloroacetyl chloride (0.01 mole) in fusing step by two reactions, then separation, drying, manifestation to Thiazole- Azitidine compound {3} appreciative to practices[6, 7].

Construction of Thiazole - Oxadiazole Compound {4} [6, 7]

Thiazole-Azitidine derivative {3} (0.01 mole) countered with semicarbazide (0.01 mole) in presence of concentrated sulfuric acid by refluxing for (28 hrs), then separation, drying, manifestation to Thiazole-Oxadiazole compound {4} appreciative to practices[6, 7].



Form 2: Construction of Azitidine Compounds{3, 4}

Construction of Thiazole-Malimide Compound {5} [6, 7]

Azitidine-Oxadiazole derivative {4} (0.01 mole) condensed with maleic anhydride (0.01 mole) for (3 hrs) in presence of acetone as a solvent in fusing reaction at (180) C, then separation, drying, manifestation to Azitidine-malimide compound {5} appreciative to practices[6, 7].

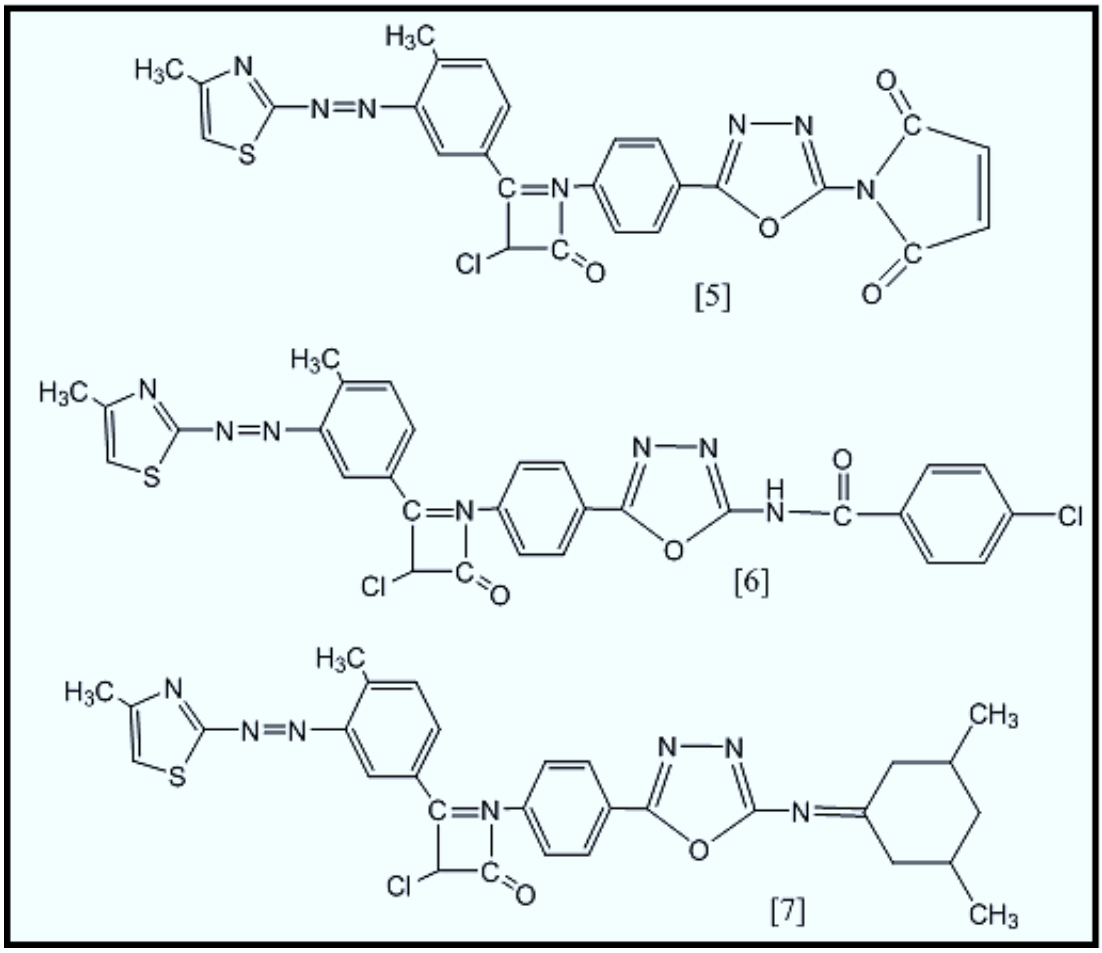
Construction of Azitidine - Amide Compound {6} [6, 7]

Azitidine-Oxadiazole derivative {4} (0.01 mole) condensed with p-chloro ethylbenzoate (0.01 mole) for (2 hrs), then

separation, drying, manifestation to Azitidine- Amide compound {6} appreciative to practices[6, 7].

Construction of Azitidine - Amide Compound {7} [6, 7]

Azitidine-Oxadiazole derivative {4} (0.01 mole) condensed with 3,5-dimethyl-cyclohexanone (0.01 mole) for (4 hrs) in acidic medium (Glac. Acetic), then separation, drying, manifestation to Azitidine - Anil compound {7} appreciative to practices[6, 7]



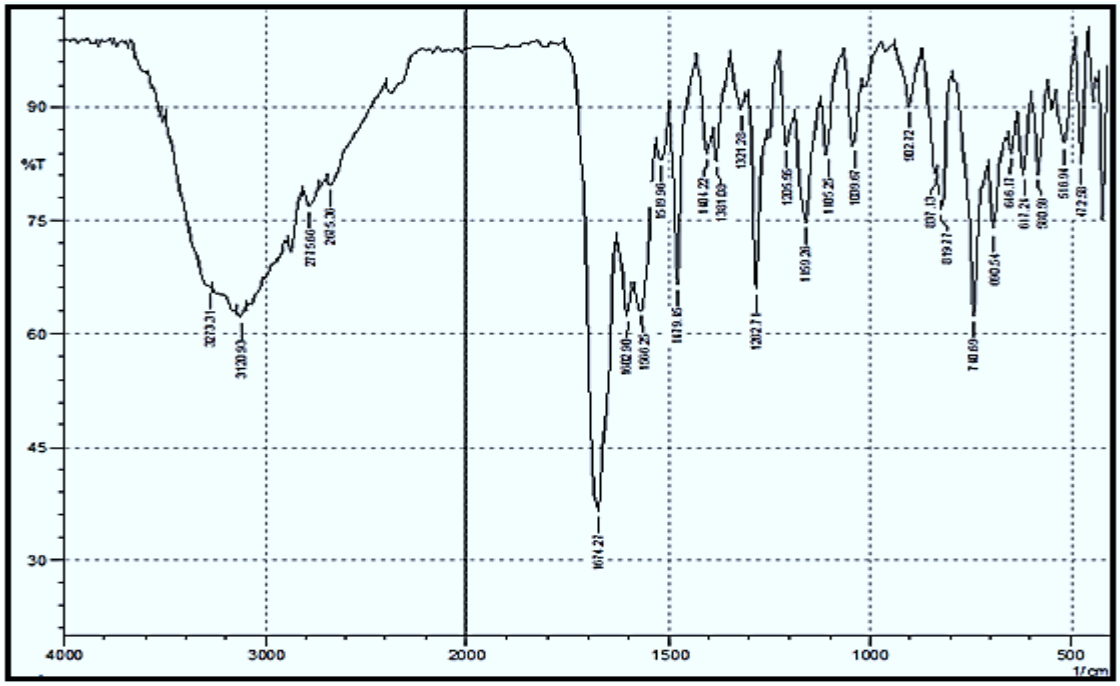
Form 3: Construction of AZitidine-Oxadiazole Compounds{5,6, 7}

Results and Discussion

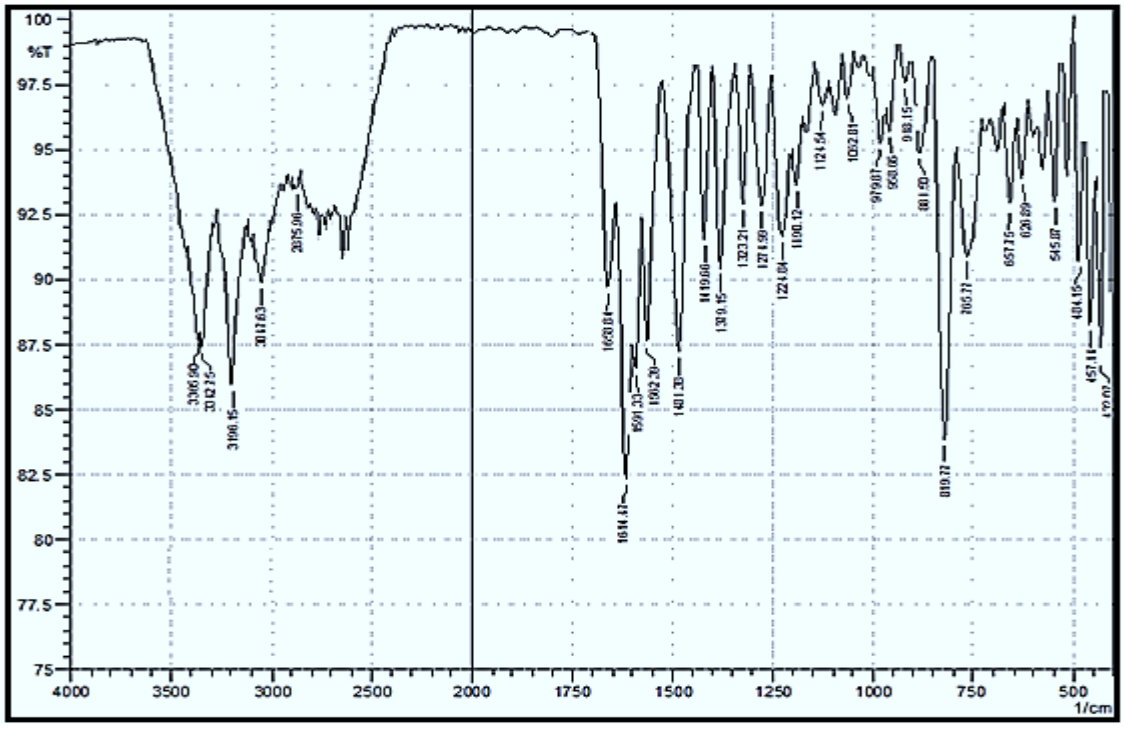
The main objective of this study is to prepare compounds that reduce the growth of fungi and bacteria and equal the strength and efficiency of some antivirals, as the bacteria are considered resistant to antibiotics, and may cause inflammatory infections in humans and animals that are more difficult to treat than those caused by their non-antibiotic resistant counterparts. Antibiotic resistance increases medical costs, extends hospitalization, and increases mortality.

FT.IR - Diagnosis

This chemical diagnosis gave sturdy values of assemblies of synthesized Thiazole-Azitidine-derivatives [1-7] by presence vibrant groups of frequencies at {(1452,1496) to (1462, 1500)} cm^{-1} consequently in all prepared compounds for Azo group (-N=N-), while appearance frequency at (1702) cm^{-1} for (C=O) carbonyl group of aldehyde in Thiazole- Azo compound {1},appearance frequency at (1713) cm^{-1} for carbonyl group of carboxyl (CO-OH) and band at (1626) cm^{-1} for imine group (CH=N) that disappearance while other frequency appeared at (1678) cm^{-1} for carbonyl of amide group (-CO-N) in Azitidine compound {3}, frequencies at (3196, 3242) for amine group (NH_2) in oxadiazole compound [4], all spectral revealing appreciative to literatures[15].



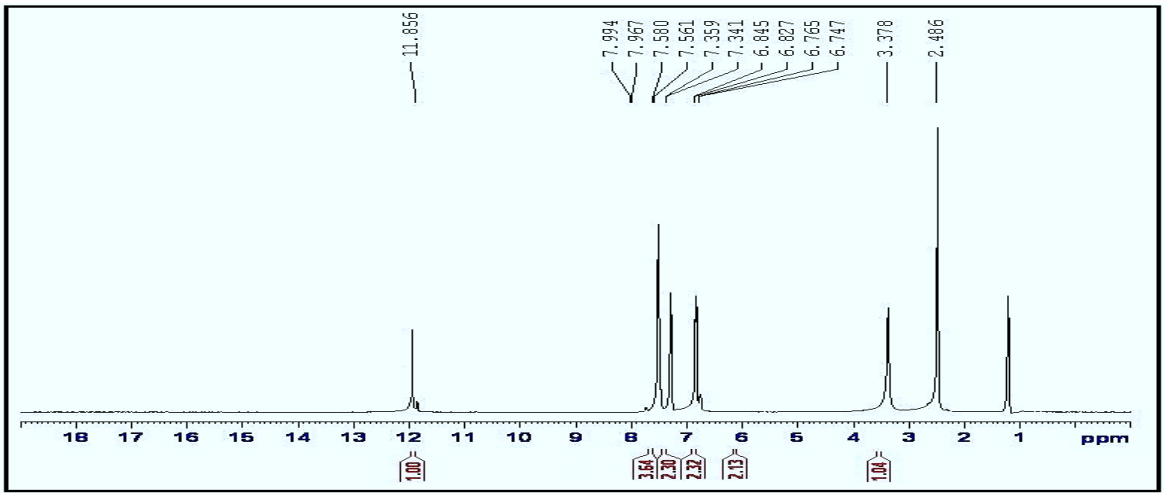
Form (1): I.R of Thiazole-Azitidine Compound{3}



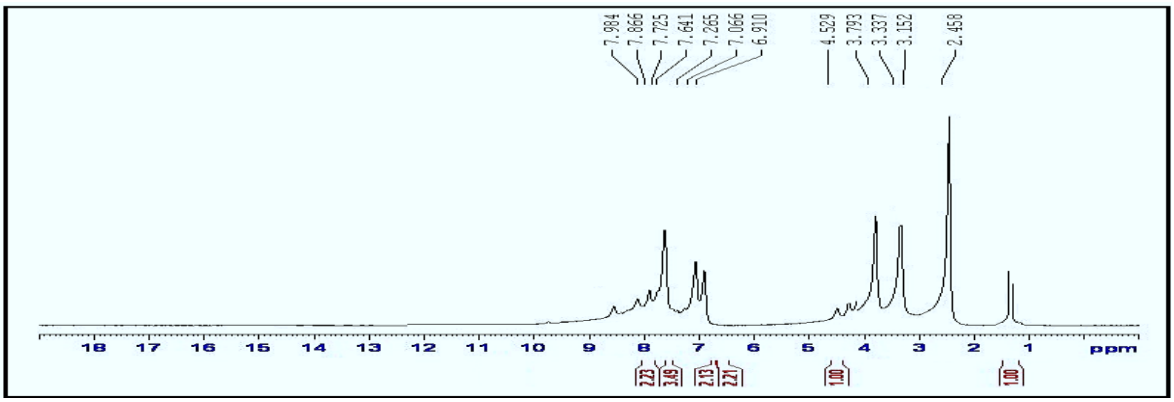
Form (2): I.R of Azitidine-Oxadiazole Compound{4}

^{1}H.NMR - Diagnosis

This chemical diagnosis gave sturdy values of assemblies of synthesized Thiazole-Azitidine-derivatives [1-7] by presence vibrant groups of peak at δ (8.34) for proton of (CH=N) in anile group and peak at δ (12.09) for proton of (CO-OH) in carboxyl group in Thiazole-Imine compound[2],while Oxadiazole-Azitidine compound [4] gave peak at δ (4.89) for protons of (NH_2) in amine group, all spectral revealing appreciative to literatures[15].



Form (3): H.NMR-revealing of Azitidine Compound{3}



Form (4): H.NMR-revealing of Compound{5}

Mass – Dignosis

The revealing of the tetrazole derivatives of thiazole-azitidine gave additional identification of structured compounds {1-7} that appeared fractions of functional groups in equivalent molecular weight., every spectral revealing appreciative to literatures[15], some figures (5, 6):

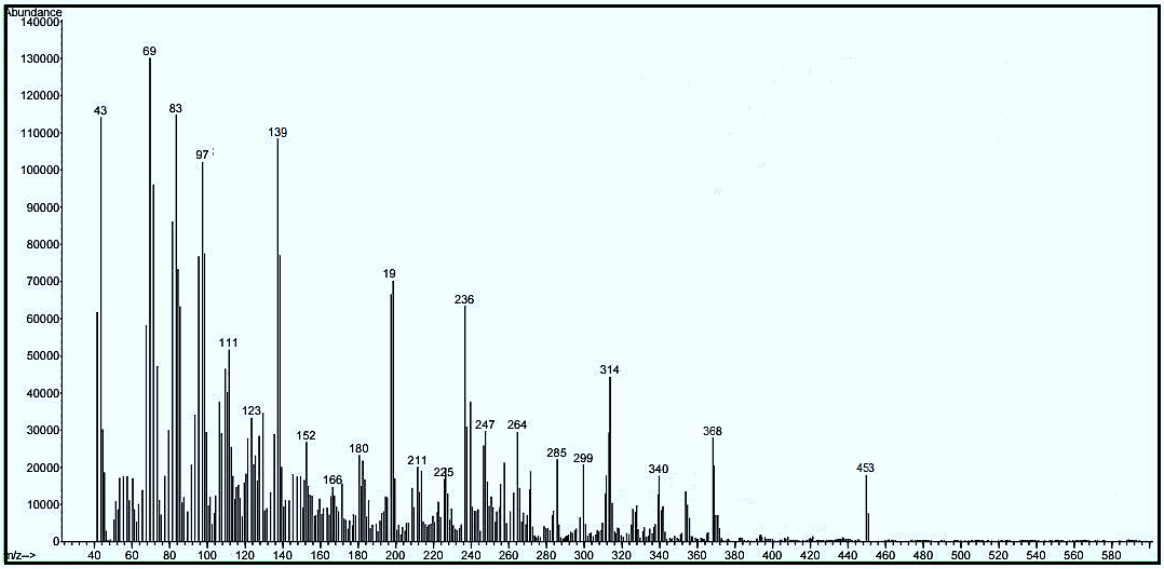


Fig. (5): Mass Diagnosis of Azitidine-Malimide Compound {5}

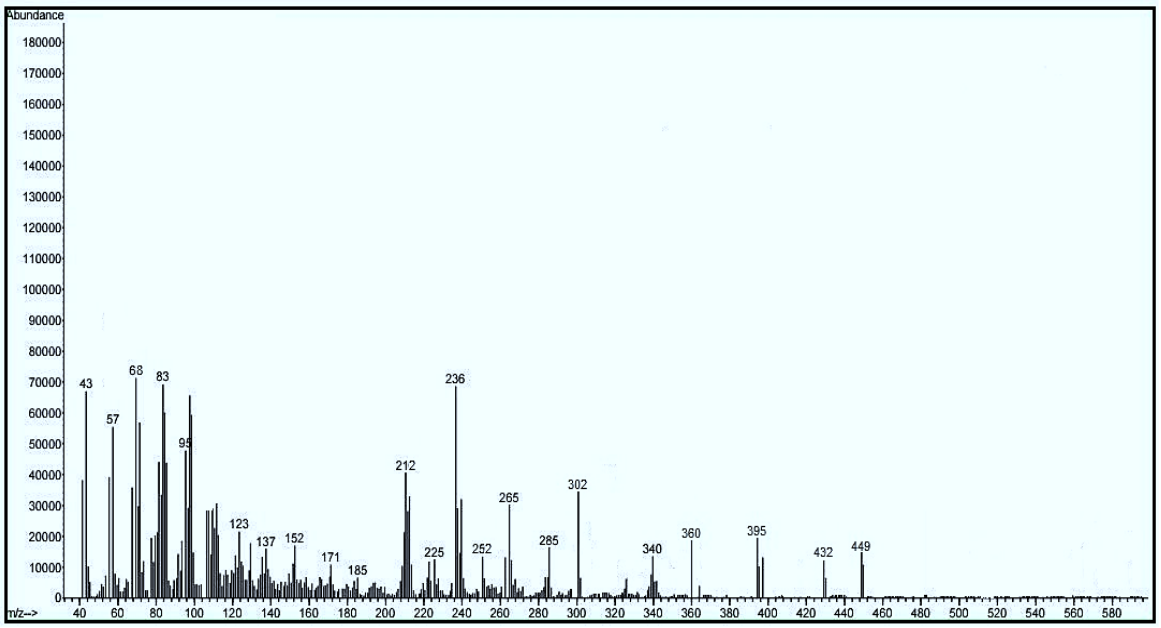


Fig. (6): Mass Diagnosis of Azitidine-Oxadiazole Compound {7}

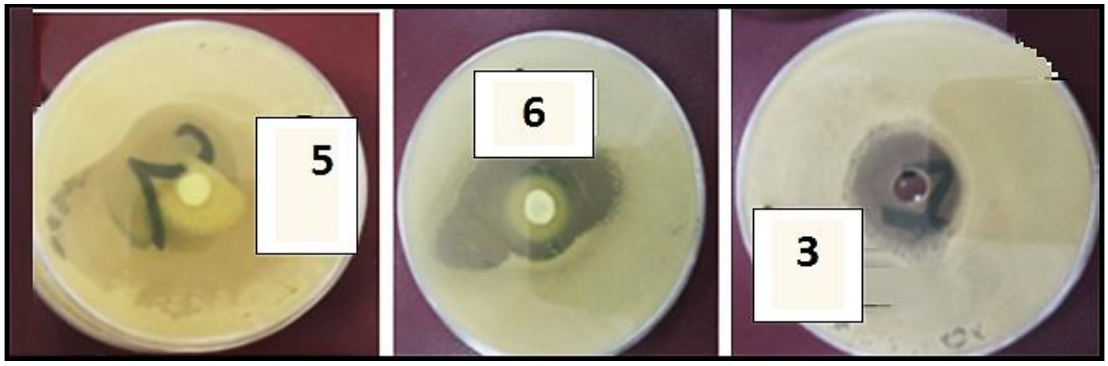
Assessment of the effectiveness of Thizole-Azitidine compounds against Bacteria [6]

Although some new antibiotics are being developed, none of them is expected to be effective in combating the most dangerous forms of antibiotic-resistant bacteria. Given the mobility and frequency of people nowadays, antibiotic resistance is a global problem that requires efforts from all countries and many sectors to solve it. More expensive medicines should be used in cases where first-line antibiotics are no longer able to treat an infection. Longer hospital stays for ailments often increase health care costs and place economic burdens on families and communities. The advances of modern medicine are being jeopardized by antibiotic resistance, and organ transplants, chemotherapy and surgeries, such as caesarean sections, are becoming more and more dangerous without effective antibiotics to prevent and treat infections.,In recent paper, we used categories of bacteria that are among the sources of numerous human infections, some of bacteria is Gram positive, symbolized through *(Staphylococcus aureus, Streptococcus pneumonia*), and the second category is Gram negative, symbolized by *(E.Coli)* at (three concentrations :10, 30, 60 micro gram) with blank[6] (DMSO).

Table.1: Assessment of the effectiveness of Thizole-Azitidine compounds against Bacteria in Conc. (30 micro gram)

Compounds	*Staphylococcus aureus*	*Streptococcus pneumonia*	*Escherichia.Coli*
Compound {1}	+	+	+
Compound {2}	+	++	++
Compound {3}	++	++	++
Compound {4}	++	++	+++
Compound {5}	+++	+++	+++
Compound {6}	+++	+++	+++
Compound {7}	+++	+++	++

(+) : inhibition (4-7) mm
(++) : inhibition (8-12) mm
(+++) : inhibition (13-16) mm

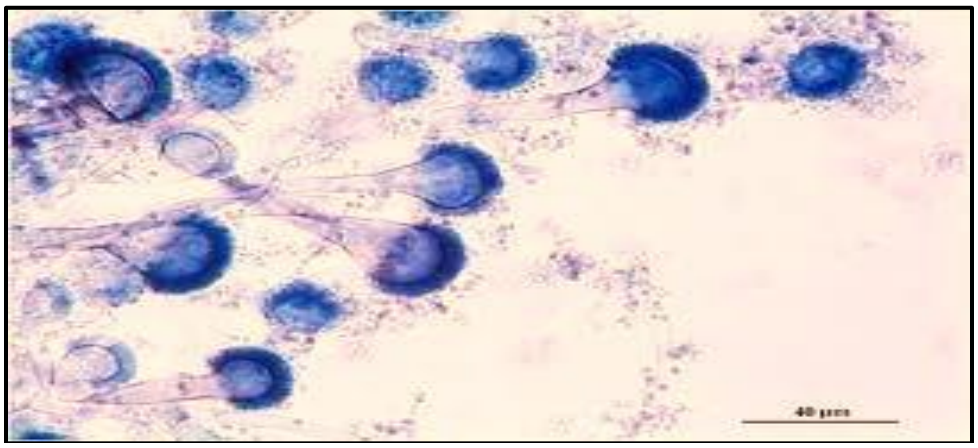


Form. 7: Inhipition of Azitidine Derivatives on Streptococcus pneumonia

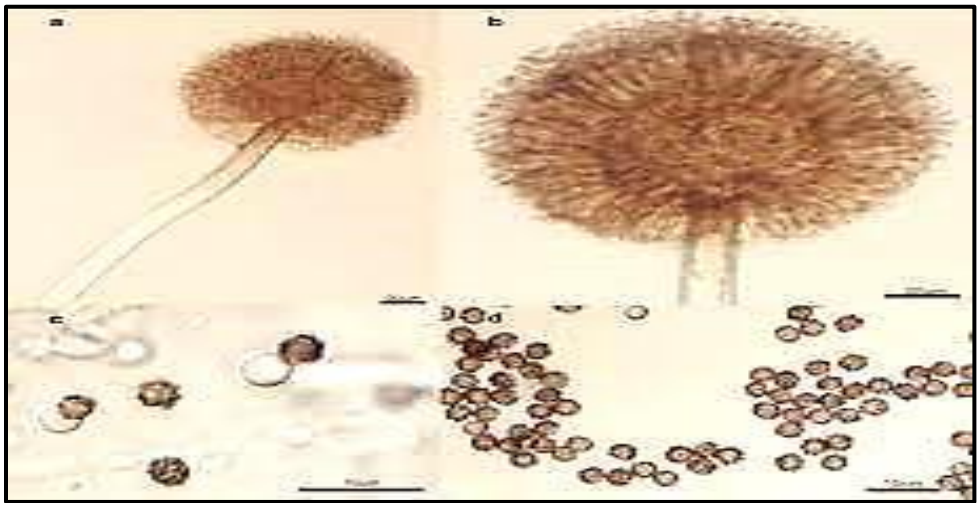
Assessment of the effectiveness of Thizole-Azitidine compounds against Fungi [6]

Today, many scientific studies are trying to spread awareness to reduce the use of antibiotics. Excessive use of them has caused the development of fungal strains that are immune to various types of antibiotics and diseases caused by these fungi are difficult to treat, and may become a major cause of death and disability.

The most dangerous of all of this is that there is a high possibility of the emergence of new strains of fungi that the current antibiotics may not be able to treat, so remember before you use antibiotics to use them correctly, and this means: the right dose, the right timing, and for an appropriate period that does not exceed it.



Form. 8: A. flevus



Form. 9: A. neger

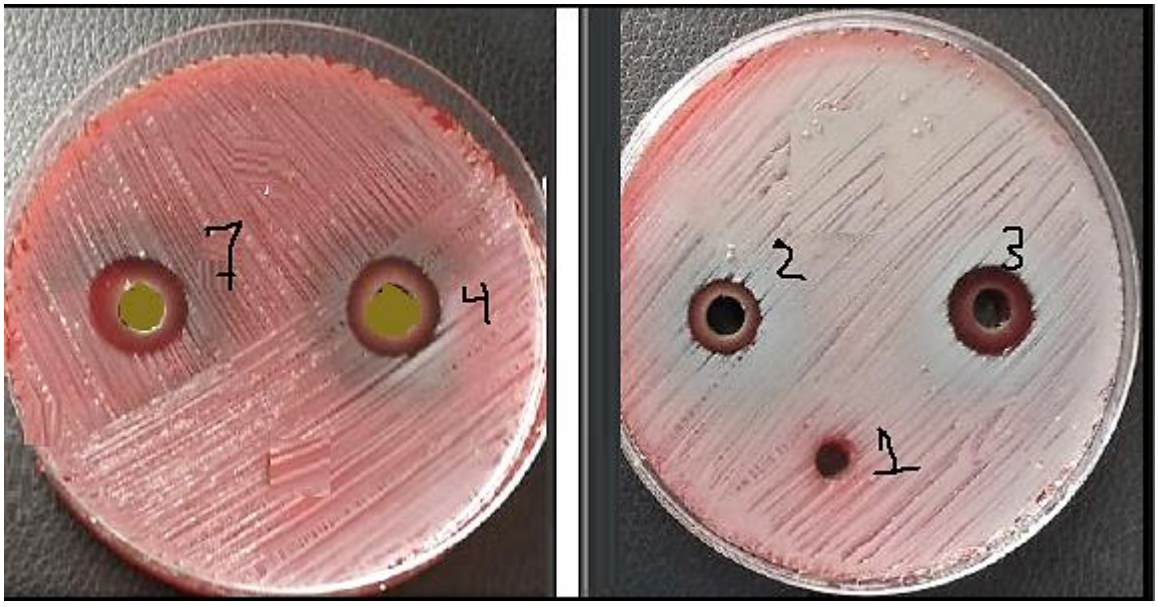
Table.2: Assessment of the effectiveness of Thizole-Azitidine compounds against Fungi in Conc. (40 micro gram)

Compounds	*Fungi : A.flevus*	*Fungi : A. neger*
Compound {1}	+	+
Compound {2}	+	+
Compound {3}	++	++
Compound {4}	++	++
Compound {5}	+++	+++
Compound {6}	+++	+++
Compound {7}	++	++

(+) : inhibition (4-6) mm

(++) : inhibition (7-12) mm

(+++) : inhibition (13-16) mm



Form. 8: Inhipition of Azitidine Derivatives on A. flevus

CONCLUSIONS

The World Health Organization organized the new data and revealed the degree of antimicrobial resistance globally, and issued a clear alert that urgent action is needed "if we are to stay ahead in the race against antimicrobial resistance" to antibiotics. Other experts argue that it is necessary to improve monitoring of resistance levels in different countries and regions. This study and its results confirmed a good inhibitory ratio for the growth of fungi as well as bacteria for all the prepared compounds

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