



Ministry of Higher Education

and Scientific Research

Babylon University College of Pharmacy

Synthesis of (β -lactams) compounds from (Indole-derivative) and Studying their biological activity

Research submitted by:

Julanar Jawad kadhim

Zahraa Jaafar Tuama

Saja abd Salman

Supervised by:

Dr.Aseel fadhil kareem

Dedication

**To my father and mother with all love and
gratitude...**

To everyone supported me..

Abstract

Heterocyclic compounds found key structural in pharmaceutical chemistry ,found in many biomolecules like enzyme ,vitamin and biological active compound such as anti fungal ,anti-inflammatory ,antibacterial ,antioxidant, anticonvulsant, antiallergic, anti HIV,,anti diabetic,anti cancer activity (1).3concentration of chemical compound 5mg,10mg,15mg that we tested against,Psudomonous arogenousa Show ability to inhibition growth of bacteria.

key word: Indole ,heterocyclic compound , Schiff base

‘Biological Activity.

Introduction :

A heterocyclic compound, also known as a heterocycle, is a kind of organic chemical compound in which some or all of the atoms in its molecules are connected in rings that include at least one atom of an element other than carbon (C). The prefix hetero- (from Greek heteros, meaning "other" or "other") refers to the noncarbon atoms, or heteroatoms, in the ring, while the cyclic component (from Greek kyklos, meaning "circle") denotes that at least one ring structure is present in such a combination. Heterocyclic compounds have a general structure that resembles cyclic organic compounds with only carbon atoms in the rings—for example, cyclopropane (with a three-carbon-atom ring) —but the heteroatoms give heterocyclic compounds physical and chemical properties that are often quite different from those of their all-carbon-ring analogs. Many biological materials required for life are heterocyclic molecules. Nucleic acids, for example, are long chains of heterocyclic units bound together by other kinds of molecules., vitamins, and antibiotics, are heterocyclic compounds. Synthetic heterocycles are used as medications, insecticides, colors, and polymers in modern life (2)

Indole is a component of a variety of essential chemicals found in nature and is extensively diffused in the environment. Synthesized indoles and their modified derivatives are well-known in the pharmaceutical business for their therapeutic effects. Indole analogs are used in a variety of items, including vitamin supplements, coloring, over-the-counter medications, taste enhancers, and perfumes. Indole has been demonstrated to regulate a variety of physiological processes, including the host immunological response, as well as influencing bacterial biofilm development and pathogenicity [3].

Through the enzymatic breakdown of tryptophan, around 85 bacterial species, including Gram-positive and Gram-negative bacteria, create indole [4].

Indole may be chemically changed inside the same bacterial cell or picked up and modified by bacteria that do not make indole. 3-methylindole (skatole) is the most prevalent indole analog discovered in nature, [5].

Bacterial indole production is a key phenotypic feature that has long been used to distinguish, identify, and diagnose enteric bacterial infections. the essential component, para-dimethylaminobenzaldehyde, on the other hand, interacts with a broad range of indole-containing molecules [6].

The imine or azomethine ($-C=N-$) functional group is found in Schiff bases. Hugo Schiff was the first to describe them as the condensation products of primary amines with carbonyl compounds. Schiff bases are a kind of organic chemical that has a broad range of uses in a number of domains, including analytical, biological, and inorganic chemistry. Due to a wide range of biological

actions such as anti-inflammatory, analgesic, antibacterial, anticonvulsant, antitubercular, anticancer, antioxidant, anthelmintic. The nitrogen atom of azomethine may interfere with normal cell functions by forming a hydrogen bond with the active centers of cell components [7].

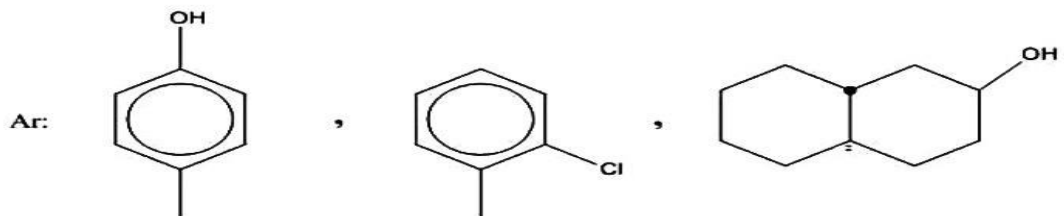
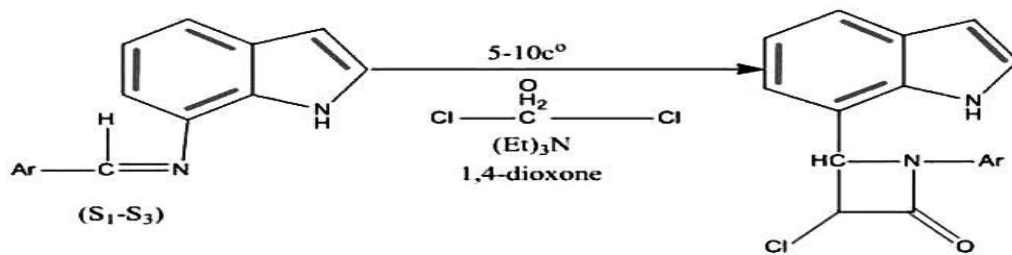
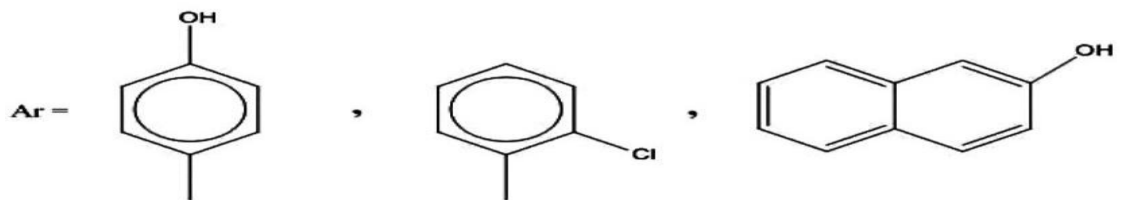
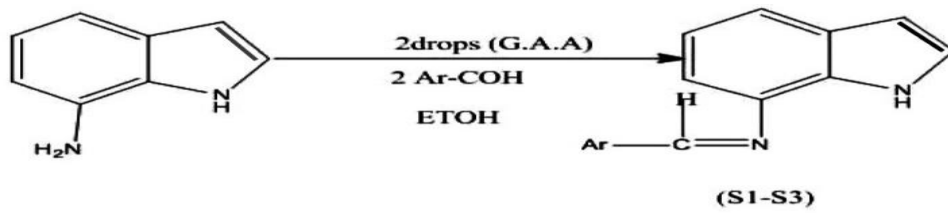
Schiff bases are utilized as catalysts, intermediates in chemical synthesis, dyes, pigments, polymer stabilizers, and corrosion inhibitors, among other things. Through ring closure, cycloaddition, and replacement reactions, Schiff bases have been used as synthons in the creation of a variety of industrial and physiologically active chemicals such as formazans, 4-thiazolidinines, benzoxazines, and so on [8].

Antibiotics known as beta-lactams are used to treat and manage bacterial infections. This activity will focus on the mechanism of action, adverse event profile, and other important factors (e.g., off-label uses, dosing, pharmacodynamics, pharmacokinetics, monitoring). Antibiotics known as beta-lactams are one of the most often prescribed medication groups, having a wide range of therapeutic applications. Their introduction, which began in the 1930s, revolutionized the battle against bacterial infectious illnesses (9).

Chemical Study:

We synthesis beta lactams by dissolving Indole derivatives in 20ml ETOH and 2 drop of glacial acetic acid and boiling the mixture for 4 hours .

Chloroacetyl Chlorid was added to Schiff base which result in formation and boiling for 14 hours .Drying the sedimentation then re-crystalized by added triethylamine give β -lactams(10).as show in scheme:

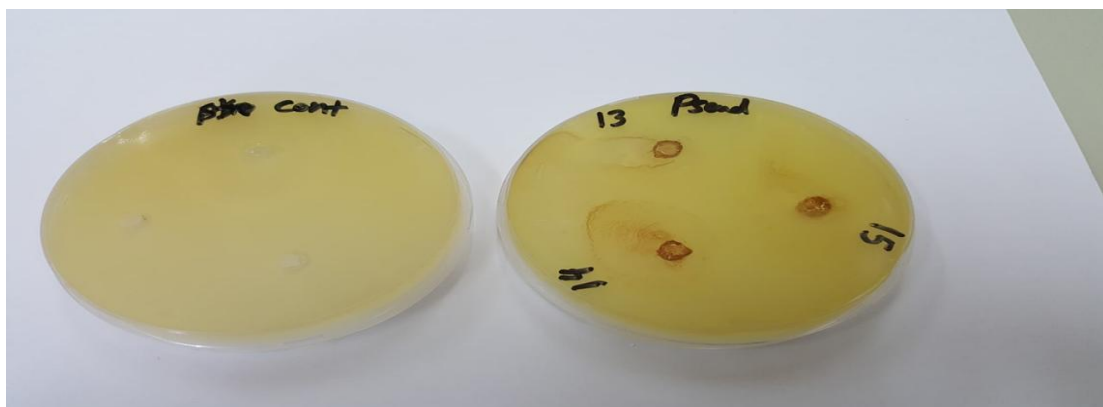


2-Microbiological Study:

The aim of study to determine microbiological activity of heterocyclic compound on bacterial growth (11). The chemical compound were tested for their biological activity in vitro against microorganism ,*Pseudomonas aeruginosa* ,its gram negative bacteria(12)by using three concentration (5mg,10mg,15mg)after dissolved in Dimethyl sulfoxide as solvent .

Isolation of bacteria:

Isolation obtained from microbiology department collage of medicine at Babylon University, recultured on specific culture media,then incubate at 37°C for 24 hours for isolation.



Results and Discussion:

In this study researchers focus on heterocyclic have been found key structural in pharmaceutical chemistry ,found in many biomolecules like enzyme ,vitamin and biological active compound such as anti fungal ,anti-inflammatory ,antibacterial ,antioxidant, anticonvulsant, antiallergic, anti HIV,,anti diabetic,anti cancer activity (13).

The chemical compound that we tested biological activity at three concentration

(5mg,10mg,15mg)against *Pseudomonas aeruginosa* show inhibition bacterial growth with mean inhibition zone(13mm,14mm,15mm).

conclusions:

Heterocyclic compound that we tested Show ability to inhibit the growth of micro organism with different inhibition zones .

Acknowledgements

We are gratitude to Dr. Aseel for supervising this research ,also we are gratefully acknowledge to microbiology department collage of medicine at Babylon University for their facilities .

References :

1- DEN (USA): PCHHAX ,Der Pharma Chemica, 2017, 9(13):141-147 Biological Importance of Heterocyclic Compounds, Abbas Al-Mulla, Department of Chemistry, Faculty of Sciences, Kufa University, Iraq

2-Thomas L. Gilchrist "Heterocyclic Chemistry" 3rd ed. Addison Wesley: Essex, England, 1997. 414 pp

- 3-Domka J, Lee J, Wood TK. 2006. YliH (BssR) and YceP (BssS) regulate *Escherichia coli* K-12 biofilm formation by influencing cell signaling. *Appl Environ Microbiol* 72:2449–2459.
- 4- Lee JH, Lee J. 2010. Indole as an intercellular signal in microbial communities. *FEMS Microbiol Rev* 34:426–444.
- 5-Wikoff WR, Anfora AT, Liu J, Schultz PG, Lesley SA, Peters EC, Siuzdak G. 2009. Metabolomics analysis reveals large effects of gut microflora on mammalian blood metabolites. *Proc Natl Acad Sci U S A* 106:3698 – 3703.
7. Reller LB, Mirrett S. 2005. Motility-indole-lysine medium for presumptive identification of enteric pathogens of Enterobacteriaceae. *J Clin Microbiol* 2:247–252.
6. Scott JE, Qian R, Henkel W, Glanville RW. 2011. An Ehrlich chromogen in collagen cross-links. *Biochem J* 209:263–264.
9. Hijarrubia MJ, Aparicio JF, Casqueiro J, Martin JF. 2001. Characterization of the lys2 gene of *Acremonium chrysogenum* encoding a functional alpha-amino adipate activating and reducing enzyme. *Mol Gen Genet* 264:755–762.
7. A. Bhattacharya, V. C. Purohit, and F. Rinaldi, “Environmentally friendly solvent-free processes: novel dual catalyst system in Henry reaction,” *Organic Process Research and Development*, vol. 7, no. 3, pp. 254–258, 2003.
- 8 A. Bhattacharya, V. C. Purohit, and F. Rinaldi, “Environmentally friendly solvent-free processes: novel dual catalyst system in Henry reaction,” *Organic Process Research and Development*, vol. 7, no. 3, pp. 254–258, 2003.
- 9 .Thakuria B, Lahon K. The Beta Lactam Antibiotics as an Empirical Therapy in a
 13. Developing Country: An Update on Their Current Status and Recommendations to Counter the Resistance against Them. *J Clin Diagn Res.* 2013 Jun;7(6):1207-14.
- 10 - Ajay K Bose, Maghar S Manhas, James M van der Veen, Shamsher SBari, Dilip R Wagle *Tetrahedron* 48 (23), 4831-4844, 1992
- Stereoregulated synthesis of β -lactams from schiff bases derived from threonine esters
11. L.Barth Reller, Melvin Weinstein, James H. Jorgensen Mary Jane Ferraro , *Antimicrobial Susceptibility Testing: A Review of General Principles and Contemporary Practices*, Published: 01 December 2009
12. Pachori P., Gothwal R., Gandhi P. Emergence of antibiotic resistance

Pseudomonas aeruginosa in intensive care unit; a critical review. *Gene Funct. Dis.* 2019;6:109 – 119. doi: 10.1016/j.gendis.2019.04.001

13- DEN (USA): PCHHAX Der Pharma Chemica, 2017, 9(13):141-147
Biological Importance of Heterocyclic Compounds ‘ Abbas Al-Mulla ‘

Department of Chemistry, Faculty of Sciences, Kufa University, Iraq