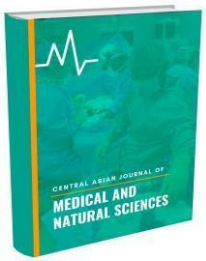

CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
*Volume: 06 Issue: 02 | April 2025 ISSN: 2660-4159*

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*Article*

# Research on Biological Behavior and The Synthesis of Various Heterocyclic Compounds

**Rana Salah Noori Al-Saeagh[1], Maha Hameed Ismael[2], Ahmed Khudhair Al-Hamairy[3], Massar Aamer Merza[4] , Rana Aqeel Ibrahim[5], Rusul Ahmed Mohammed[6]**

1. College of Science for Women, University of Babylon, Iraq.
2. Al-Furat Al-Awsat Technical University, Babylon Technical Institute, Babylon, Iraq.
3. Anesthesia Techniques Department, College of Health and Medical Techniques, Al-Mustaqbal University, 51001, Babylon, Iraq.
4. Hammurabi college of Medicine, Department of Microbiology, University of Babylon, Iraq.
5. Hammurabi College of Medicine, University of Babylon, Iraq.
6. Department of pharmacology & Toxicology, College of Pharmacy, Al Mustaqbal University, Babylon, Iraq

**Abstract:** Heterocyclic compounds are found in almost 90% of new medications. Heterocyclic moiety is also present in several natural products, such as antibiotics like cephalosporins and penicillins, and alkaloids like morphine, vinblastine, and reserpine.Thioxanthone has been the source of three chemical compounds that have been produced as derivatives [S1, S2, and S3]. Every formatted chemical was tracked using melting point and FTIR spectra. This technique is suitable for industrial production and has a high target product productivity, gentle reaction conditions, straightforward purification methods, and high product purity. to further down the cost of production. The agar well diffusion method revealed that all three of the produced compounds had good antibacterial activity against the Gram-positive and Gram-negative bacteria under study, but S3 had the highest activity. To determine if the produced chemicals cause allergic reactions, a skin test for delayed hypersensitivity was conducted, and a test for animal mortality was conducted using killing mice. In test animals, the substances elicit a strong cellular immunological response.

**Keywords:** Thioxanthone, Thiadiazole, Schiff Base, Hypersensitivity, Antibacterial Activity, Heterocyclic Rings, B-Lactams

**Citation:** Al-Saeagh R. S. N., Ismael M. H., Al-Hamairy A. K., Merza M. A., Ibrahim R. A., Mohammed R. A. Research on Biological Behavior and The Synthesis of Various Heterocyclic Compounds. Central Asian Journal of Medical and Natural Science 2025, 6(2), 685-691.

Received: 20th Feb 2025
Revised: 24th Feb 2025
Accepted: 28th Feb 2025
Published: 8th Mar 2025



## 1. Introduction

Cyclic organic molecules with at least one heteroatom are known as heterocyclic compounds. The most prevalent heteroatoms are nitrogen, oxygen, and sulfur, but heterocyclic rings with additional heteroatoms are also well-known [1]. The activity of heterocyclic compounds in many diseases makes them one of the essential families of organic chemicals employed in numerous biological domains. The primary skeleton of many biological components, including DNA and RNA, hemoglobin, chlorophyll, vitamins, and many more, comprises a heterocyclic ring [2]. Some of the most often used organic compounds are Schiff bases, which have been employed as antimicrobial herbicides, urinary antiseptics, and anti-inflammatory drugs [3]. They also have use in a variety of common disorders. Numerous biological activities, such as antifungal, antibacterial, antimalarial, antiproliferative, and anti-inflammatory properties, have also been demonstrated to be present in them [4]. Four-membered cyclic amide ring system of

β-lactam antibiotics, antiviral, antipyretic, analgesic-anti-inflammatory, anticonvulsant, antitubercular, anticancer, antioxidant, anthelmintic, antiglycation, and antidepressant activities [5], as well as a useful building block in organic synthesis. Using the β-lactam structure as a crucial scaffold or a crucial building block for the synthesis of various bioactive heterocyclic compounds might result in a wide range of varied pharmacological applications. Five-membered ring heterocyclic compounds have significant properties of a range of pharmacological agents in addition to antibiotics [6]. It exhibits a number of pharmacological properties, including antiviral, anti-inflammatory and analgesic, antidepressant, antifungal and antibacterial, anti-cancer, and anti-tubercular properties [7].

## 2. Materials and Methods

### 2.1 Chemical study:

{S1}: Made from 0.03 moles of 2-chlorobenzaldehyde, which was dissolved in 25 milliliters of pure ethanol. We then added 1-2 drops of Glacial Acetic Acid (G.A.A.) while shaking continuously for 20 to 25 minutes on a magnetic stirrer. We then gradually treated it with 0.03 mole of the {S1} chemical to finish the procedure in 8 hours at (65–70) ȣC. For the purpose of recrystallization from 100% ethanol Orange, m.p. C0 (272-274), the mixture was evaporated and the solution dried.

{S2}: Created by dissolving (0.03) mol from {S1} in 25 ml of triethylamine and chloroacetyl chloride, and using Dioxin as a solvent for nine hours at 10 °C. In order to recrystallize the mixture from 100% ethanol, Yellowish Green, m.p. C0 (193–195), the mixture was evaporated and dried.

{S3}: Produced by dissolving 0.03 mol of {S1} in 25 ml of THF as a solvent and shaking continuously to finish the solution. We then added 0.03 mol of glysin gradually to finish the process at 50 °C in 15 hours, yielding an imiadazoldine derivative. The solution was dry for recrystallization by absolute ethanol, Brown, m.p. C0 (122-124).

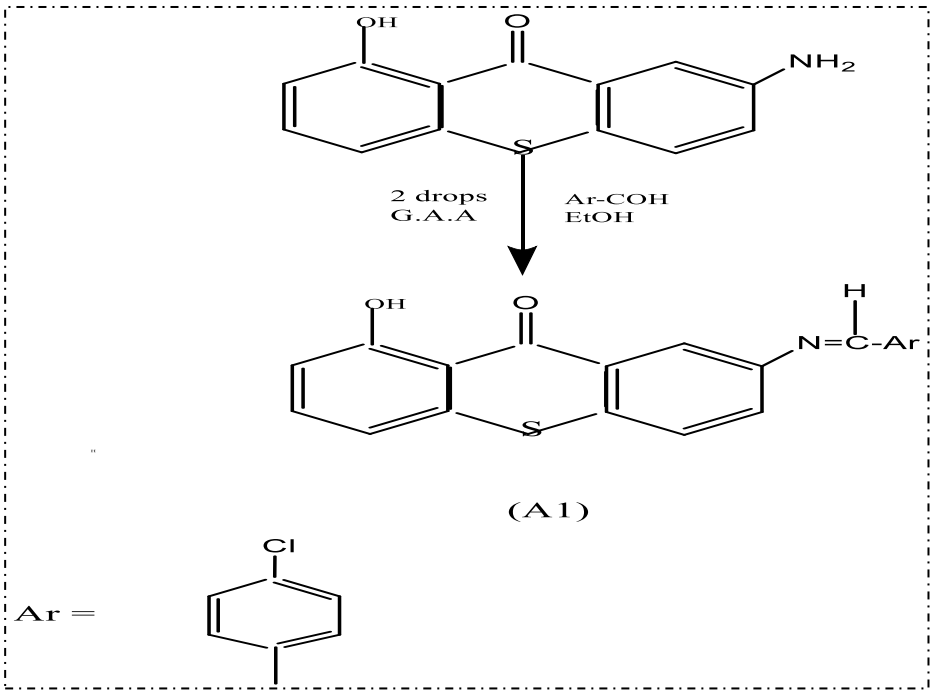


**Figure 1.** Preparation of (A1).

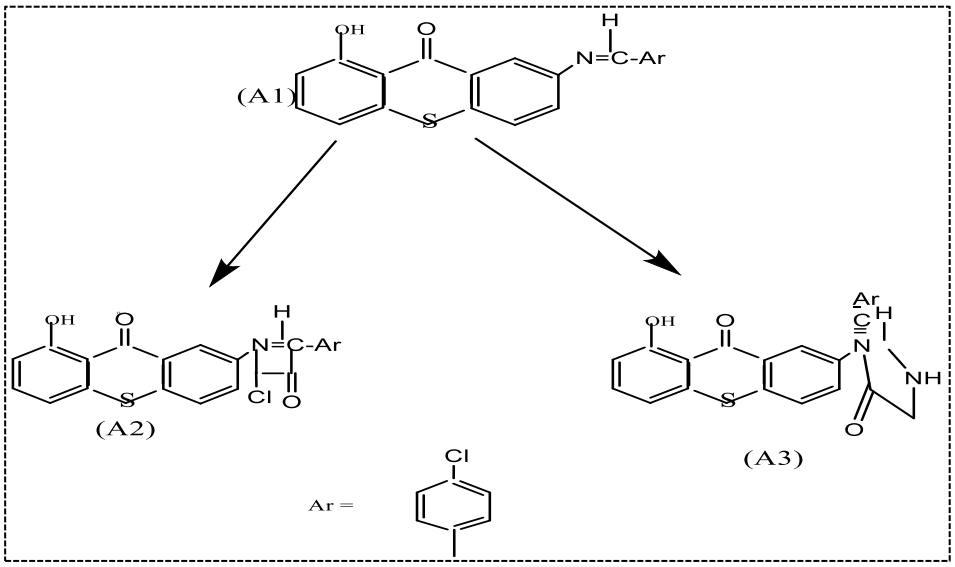


**Figure 2.** Preparation of (A2,A3).

**An examination of biology**

**Test for antibacterial activity:**

Each chemical compound was used in five concentrations: 5, 10, 20, 30, 40, and 50 μg mL-1. The Agar-well diffusion method was used to evaluate the antibacterial activity of the chemical compounds created in the current study using four bacterial species: Shigella flexeneri and Proteus mirabilis (Gram negative), Staphylococcus aureus, and Enterococcus faecalis (Gram positive). A Muller-Hinton agar was streaked with an inoculum bacterial suspension using DMSO as a solvent. On the inoculated streaking media, a sterile cork borer (No. 6) was used to punch a 9 mm hole. In each hole, 200 μL of a chemical substance at each concentration was added. The plates were incubated for 18 hours at 37 °C following an hour of pre-diffusion time. mL was used to measure the inhibitory zone's diameter.

**For delayed hypersensitivity, perform a skin test.**

To administer intradermal injections of mefenamate derivatives at three different dosages (10, 20, and 30 μg mL-1), thirty male rabbits (Oryctalagus cuniculus) aged two to three months were selected. The compounds were first dissolved in DMSO (dimethyl sulfoxide) as the solvent. The test group consisted of 27 rabbits (three for each of the three concentrations of each chemical) that had had the morphological zone of their hair shaved. The control group consisted of three rabbits that received the same injections of sterile normal saline [8]. This method was exclusive to this investigation. Results using various calibrating techniques were positive. When the rabbit's double fold thickness was measured 24, 48, and 72 hours later, the injection location had necrosis, erythema, and indurations.

**Mice are used in the killing test.**

This test was conducted to look into the fatal consequences of the chemical substances. After being removed, 30 male Swiss mice weighing between 18 and 22 g had their tail veins injected with 0.5 mL of these substances at varying concentrations. After 24 to 72 hours, the positive result was observed. Deaths of the animals indicated that the test had yielded favorable results.

## 3. Results and Discussion

**Identification of (Thioxanthone) derivatives by FT.IR:**

{S1} : Due to (C=N), frequnse at (1658) was owing to (C-S), frequnse at (2931) was owed to (CH) aliphatic, frequnse at (3350, 3375) was owed to (NH2) of amine and (OH),

frequnse at (3041) was owed to (C-H) aromatic, and frequnse at (1677) was owed to (C=O).

{S2} : At (1293), frequnse was owing to (C-N); at (760-820), frequnse was owed to (C-Cl); at (1776), frequnse was owed to (N-C=O); at (785), frequnse was owed to (C-S); at (1672), frequnse was owed to (C=O); at (2839), (C-Hali) as well as at (3074)..

{S3} : (C=O)Amide, (C=C) at (1595), (C=N) Endocyclic at (1541), (N-H) at (3111), (O-H) at (3462), (C-Harom) at (3064), and (C-Hali) at (2944) were responsible for the frequnse at (1608 ).

**An examination of biology**

**Testing for antibacterial activity:**

Every chemical component that was tested showed inhibitory effect against the bacteria under study, as shown in Table 1 (Fig. 3). The kind of chemical molecule and its concentration affected the antibacterial activity. Compared to the other two compounds, the antibacterial activity of the S3 was higher.. The sizes of the inhibition zones demonstrated that the increased compound concentration resulted in increased antibacterial activity, which is why the S1 and S2 showed minimal impacts.. According to numerous investigations, active groups and their antibacterial properties increase with higher concentrations [9]. This result is consistent with those findings. The ability of these compounds to damage bacterial cell walls and membranes and change their permeability, or to exhibit an impact on a cell's metabolic pathway and disrupt cell proteins, followed by a decrease in their activity that could potentially inhibit growth and cell death, may be the basis for their antibacterial activity. The molecules' physical and chemical properties determine how effective these compounds are against germs.

**Table 1.** The widths of the inhibition zones (mm) of thioxanthone derivatives against bacteria at varying concentrations.

| Type of Compound | Concentrations of Thioxanthone erivatives ( μg/ml) | Inhibition zone (mm) | | | |
|---|---|---|---|---|---|
| | | Gram-positive Bacteria | | Gram Negative Bacteria | |
| | | *S. aureus* | *E. faecalis* | *Sh. Flexeneri* | *P. mirabilis* |
| S1 | 5 | 8 | 0 | 7 | 0 |
| | 10 | 10 | 8 | 9 | 7 |
| | 20 | 15 | 10 | 14 | 10 |
| | 30 | 25 | 21 | 20 | 15 |
| | 40 | 38 | 35 | 34 | 31 |
| | 50 | 40 | 39 | 36 | 34 |
| S2 | 5 | 10 | 10 | 10 | 10 |
| | 10 | 14 | 12 | 11 | 8 |
| | 20 | 18 | 15 | 14 | 12 |
| | 30 | 25 | 20 | 18 | 11 |
| | 40 | 28 | 23 | 20 | 18 |
| | 50 | 31 | 26 | 23 | 22 |
| S3 | 5 | 10 | 8 | 10 | 7 |
| | 10 | 15 | 12 | 11 | 9 |
| | 20 | 25 | 20 | 14 | 14 |
| | 30 | 32 | 30 | 19 | 14 |
| | 40 | 39 | 37 | 34 | 31 |
| | 50 | 45 | 42 | 38 | 36 |

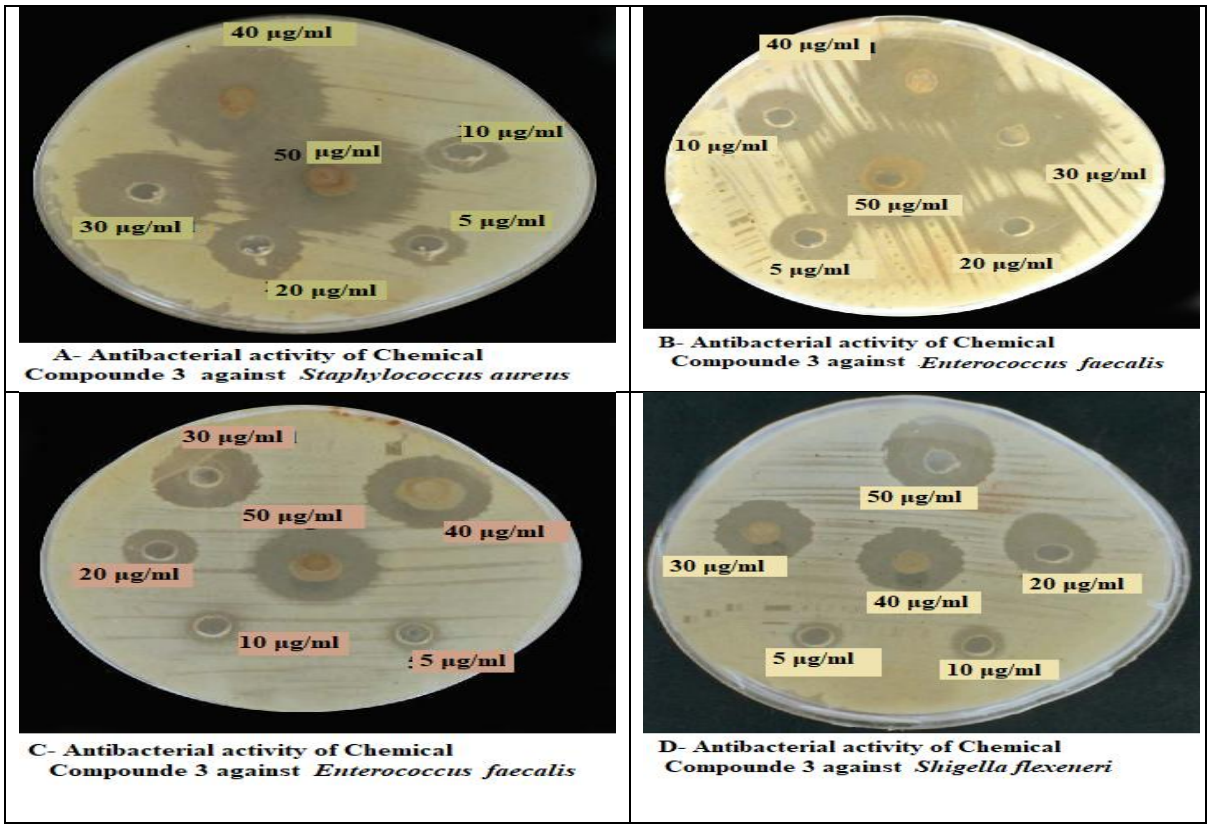


**Figure 3.** The chemical compound developed in this study has antibacterial activity against various bacterial species.

**Design of Experiments**

**Test for delayed hypersensitivity on the skin**

The effects of thio-imidazole compounds on the experimental rabbit's skin were assessed using a delayed type hypersensitivity test (Table 2). Signs of cellular sensitivity that cause hypersensitivity, such as redness, thickness, and necrosis, appeared 24 hours after these chemicals were injected, indicating the immune response.. Because these compounds are easy to use, reasonably priced, and yield vivid colors, they are frequently used to dye cotton, silk, and wool. because they function as antigens that activate "Th1 and Th2" and may be [T] dependent kinds. In animals, these compounds stimulated the cell-mediated immune response in vivo [10]. During the skin test, T-cells generate TNF, which acts on endothelial cells in dermal blood arteries to trigger the successive expression of adhesion molecules. Erythema and indurations develop and peak 24–72 hours after these molecules infiltrate the leukocytes, mostly lymphocytes and macrophages, at the reaction site after 4 hours. The test animals may experience difficult hypersensitivity reactions since the applied heteropigments do not pierce their skin very deeply. By using diverse substances, intradermal testing might be more exact and sensitive.

**Mice are used in the killing test.**

In our mice killing test, the S3 chemical at a dosage of 30 mg mL-1 only killed one mouse, which might have been caused by the physiological conditions of the animals or the surrounding conditions. The hetero rings are readily absorbed by the body through skin contact, inhalation, and dust intake since they are water soluble. Some of them may be used as food coloring without causing sensitivity. Due to human sensitivity to some sensitizing stimuli being higher than that of animals, the results of experimental sensitization of animals may not necessarily match what might be expected in people.

**Table 2.** Testing for chemical compound sensitivity in vaccinated rabbits using skin delayed type.

| Type of Compound | Concentrations of Mefenamate derivatives (μg/ml) | Skin test \ Hours | | |
|---|---|---|---|---|
| | | 24 | 48 | 72 |
| S1 | 10 | - | - | - |
| | 20 | E (4mm) | - | - |
| | 30 | E (9mm) | - | - |
| S2 | 10 | E (8mm) | EI (8mm) | - |
| | 20 | E (10mm) | EI (10mm) | - |
| | 30 | EI (11mm) | EI (11mm) | EIN (11 mm) |
| S3 | 10 | - | - | - |
| | 20 | E (7mm) | EI (7mm) | EIN (7 mm) |
| | 30 | EI (12mm) | EIN* (12mm) | EIN (12 mm) |

E- Erythema, I- Induration, N- Necrosis *Reaction area (mm) With negative result for all control groups.

## 4. Conclusion

Since the applied hetero-pigments did not penetrate very deeply into the skin of the examined animals, it was found that the prepared Schiff base derivatives from Thioxanthone were stable, showed similar activity to the thio drug's reduction of inflammation in vitro, and some had greasy or sticky strength. Activating Th1 and Th2 cells may make it difficult to cause hypersensitive reactions from chemicals that strongly elicit a cellular immune response. According to the kind and concentration of the chemical compound, all evaluated chemical compounds showed varying inhibitory effect against the examined bacteria, indicating that they could eventually be utilized to treat a wide range of illnesses.

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