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Examining The Chemical And Biological Properties of Different Heterocyclic Rings

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Abstract: *Melting point, FTIR, chromatography analysis, and physical properties were used to determine the structures of new heterocyclic compounds that contained 4-aminoantipyrine, which was thought to be a crucial step for the synthesis of some new derivativesGram-positive and gram-negative bacteria (Staphylococcus aureus and Streptococcus mutans) and Shigella flexeneri and Pseudomonas aeruginosa) are evaluated for their antibacterial activity using these substances. Academics and medical applications have shown a great deal of interest in the antipyrine derivatives, which are a popular structural motif among heterocyclic compounds with three nitrogen heteroatoms. Although they are not found in nature, they are used extensively in drug development, organic synthesis, chemical biology, polymer chemistry, and supramolecular chemistry. As a result, developing a straightforward and easy method for the production of antipyrine derivatives is crucial. In contrast to conventional antibiotics, The findings demonstrated the strong antibacterial qualities of each of these substances. Additionally, we discovered that they can induce pro-inflammatory cytokines like IFN-γ, which are released by CD4+ T helper 1 (Th1) cells, to have an immunological effect in vivo in an animal model.. Therefore, this study aims to synthesize some novel derivatives and evaluate their antibacterial activity by examining their capacity to induce the cellular immune response and the histopathological changes in the experimental rabbits' splenic sections.*

Keywords: *Heterocyclic Rings, Antipyrine Derivatives, Biological Activity, Chromatography*

Introduction

The chemistry of antipyrines and their derivatives has attracted a lot of attention lately since they are used as analgesics, antipyretics, and anti-inflammatory medications. The anti-inflammatory, analgesic, immunological, anthelmintic, and insecticidal qualities of its derivatives also attracted a lot of attention (Al Mousawi et al, 2022). The quick development of numerous chromatographic techniques was aided by chromatography and their efforts (Al Mousawi et al, 2022) (Bancroft et al, 1982). The stationary bed in the column chromatography process is contained within a tube. It is possible for the solid stationary phase or support coated with a liquid stationary phase to fill the entire inside volume of the tube (packed column) or to concentrate on or along the inside tube wall, leaving the middle section of the tube open and unhindered for the mobile phase (open tubular column).

Variations in the rates of movement through the medium are computed to determine the sample's varying retention times (Luna, 1978) (Shnawa et al, 2001)

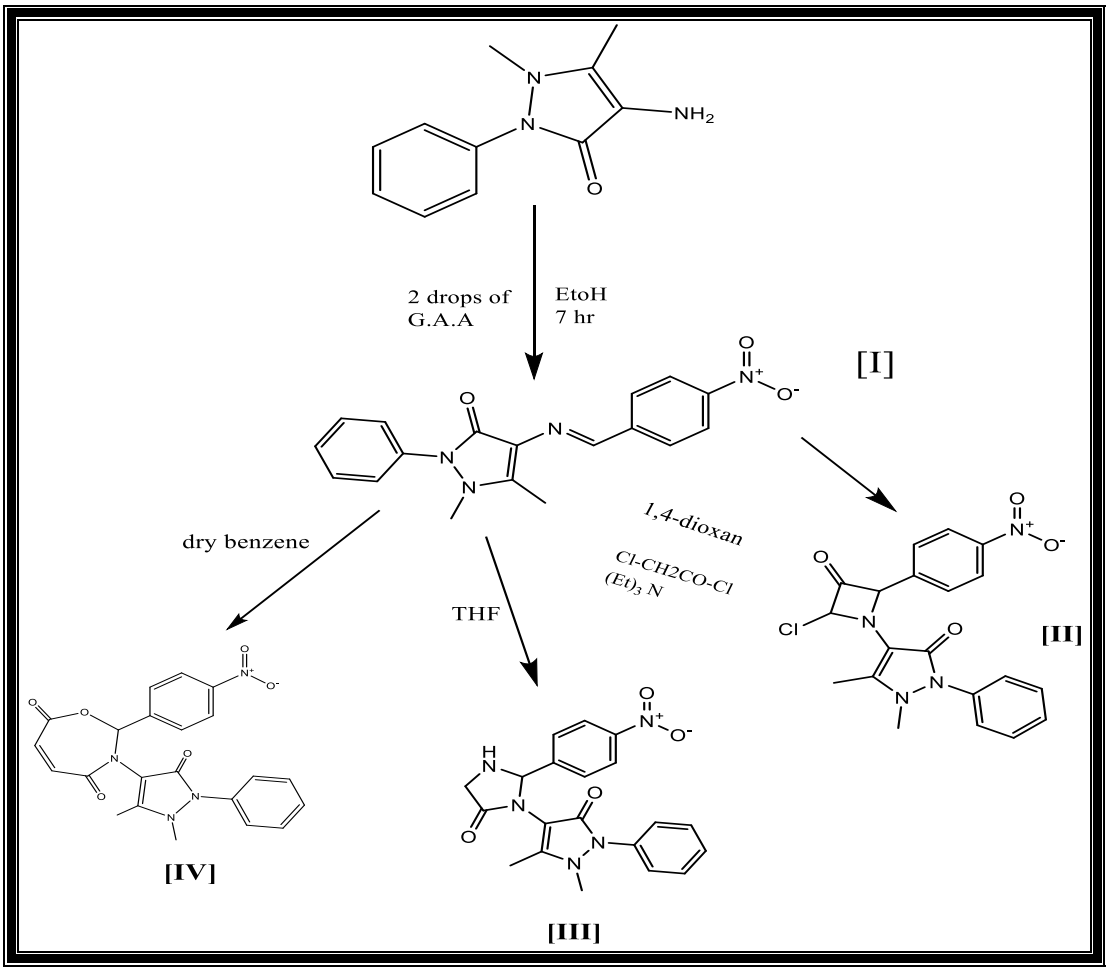
For their use in histological sections and biological evaluation as antioxidant agents, important derivatives include oxazepine chemicals, imidazolidin, and β-Lactam. Additionally, they are considered a crucial instrument for the synthesis of metal complexes and Schiff bases that are physiologically active. (Kabir, S. 2011) besides being used as copper corrosion inhibitors in acidic environments and as precursors for the production of macrocyclic compounds. To produce the Schiff base, 4-amionantipyrine was used, which is also used as an intermediate to create polyfunctionally substituted heterocyclic rings with immunological and antibacterial activities (Kareem et al, 2024). The antibacterial activity of several newly created pharmacological compounds is assessed in this work by contrasting them with the experimental rabbits' ability to trigger a cellular immune response.

Methodology

Every substance was ingested without additional purification from several businesses. The KBr disk-Shemazdo 8300s was used to record the FT-IR spectra·

1. Study of chemicals

Scheme 1. shows the chemical production routes [I–IV].



Result and Dicscussion

1. Chemical study

By using FTIR spectroscopy and its melting point, the Schiff base compound (I) was found. FTIR absorption spectra revealed the demise of absorption bands caused by the starting methyl's NH2 and C=O groups as well as the emergence of a new absorption band in the region (1649) cm-1, which is caused by the azomethine group (C=N stretching). The payrazole ring's C=C caused a peak at 1595 cm-1, and the C=O caused a stretching band at 1718 cm-1. Lastly, a broad, stretching band at around 3392 cm-1 is attributed to the ʊ O-H band's intermolecular hydrogen pairing.

The stretching vibration of the C=O group of the azetidine ring caused the characteristic absorption band to appear in the range (1651-1660) cm-1 in the compound (II)'s FT-IR spectra.

Asymmetric and symmetric bands of the NH group were identified in the region (3226-3294) cm-1 in the compound (III)'s FTIR spectrum. For the produced chemical (III), they also displayed the appearance of an absorption band attributable to the ʊ O-H group tautomeric, and a large band at 1710 cm-1 that might be attributed to the stretching vibration of the imidazolinone ring's carbonyl.

Because of the cyclic amid group (CO-N) in lactam, new bands emerged at 1641 cm-1, which led to the synthesis of oxazepine (IV) through the addition reaction of azomethine C=N with maleic anhydrides in dry benzene. At 1755 cm-1, a lactone caused a band (Ramos, 2022).

2. Chromatographic Study

The majority of the compounds' migration will be with the stream, moving them away from other molecules that the stationary phase will hold onto for a longer period of time. Its concentrations in the moving and stationary regions are equal to the ratio of the times spent in each, which is called the partition coefficient. In situations involving a solid phase, the phrase "adsorption isotherm" is frequently employed. The solute affinity for the stationary phase acts as a resistive force, while the flowing fluids act as the driving force for solute migration.; The analyst manipulates the combination of these forces to create the gap. The chosen compounds separated based on molecular weight and the interaction between the active groups in the compounds in the chromatography technique's separation column, according to the results (Aljamalil, 2020).

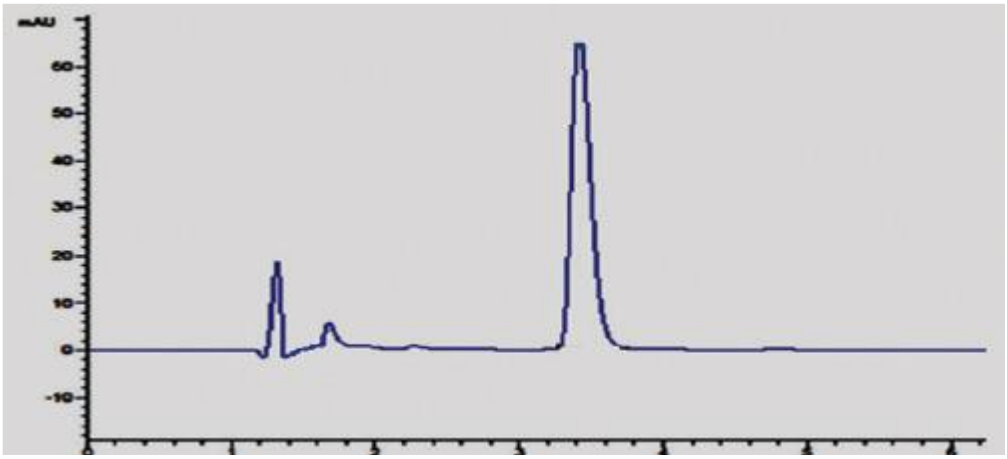
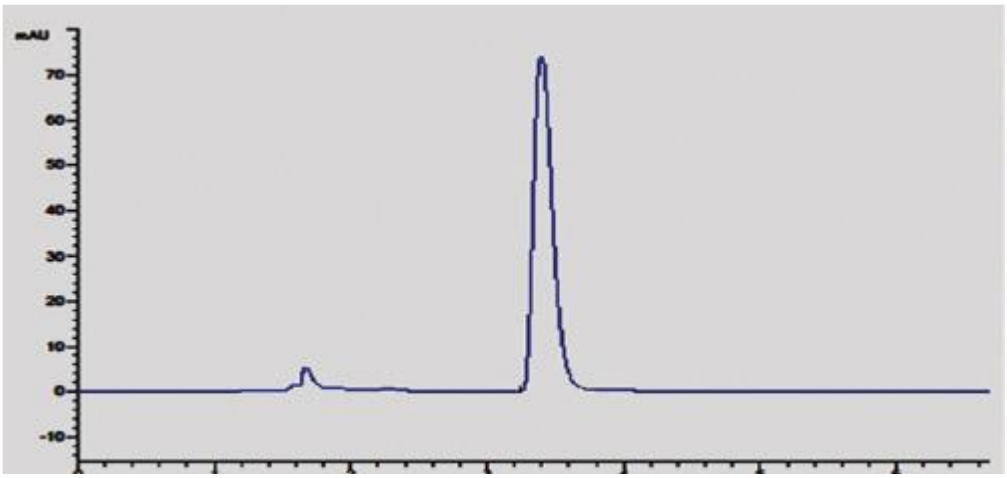
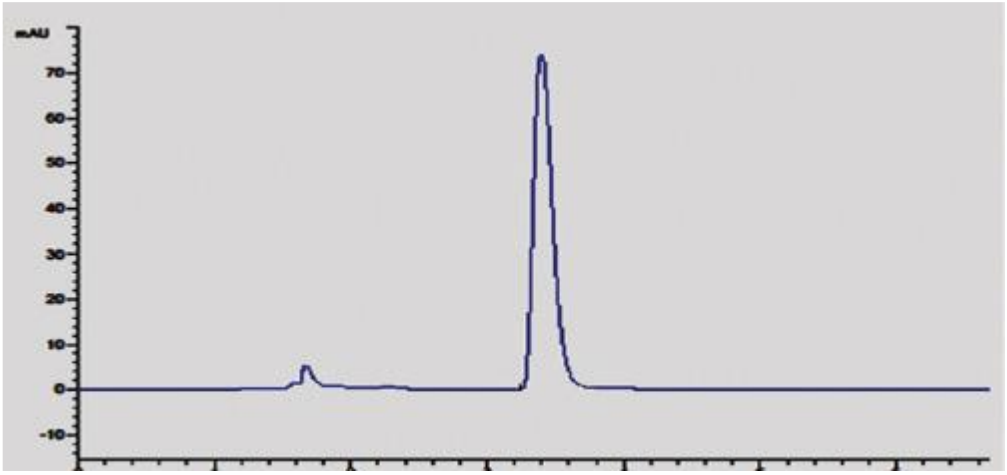


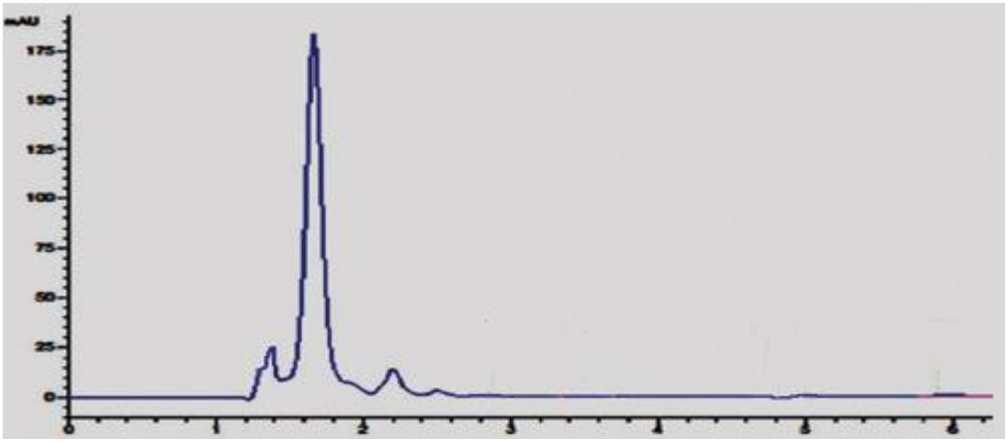
Figure 1. Compounds [I–IV] Chromatogram Conclusion



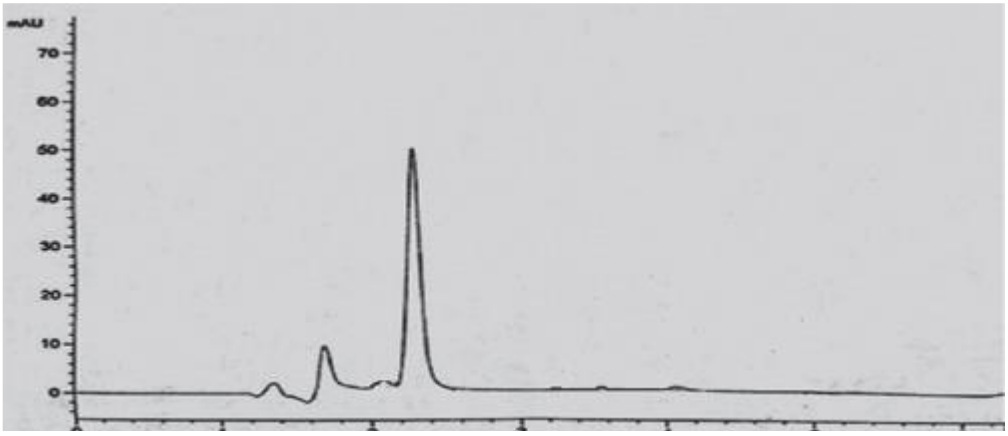
The compound (I)



substance (II)



compound (III)



element (IV)

3. Investigation of Bacteria

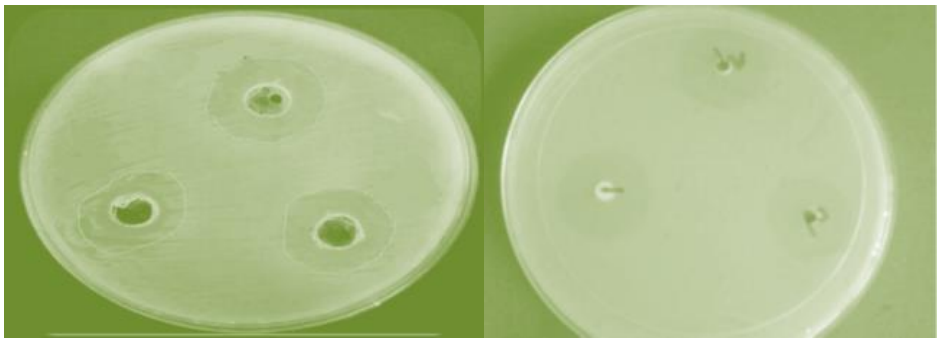
Shigella flexeneri, Streptococcus mutans, Pseudomonas aeruginosa, and Staphylococcus aureus are among the microorganisms that have been researched for their antibacterial properties. Table 1 shows The type of bacterial isolates, their kind, and the amounts of chemical substances were the factors that affected this activity, as shown in Figure 2 (Abuelhassan, 2023).

Table 1. Chemical compound concentration-dependent inhibition zone widths (mm) against bacterial growth

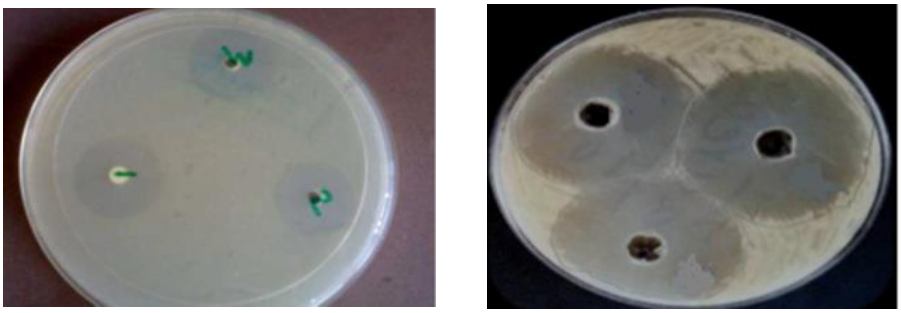
Chemical compounds	Concentrations (μg mL^{-1})	Mean of inhibition zone (mm)			
		Bacteria of the Gram-positive type		Bacteria that are Gram-negative	
		Staphylococcus aureus	*Streptococcus mutans*	*Shigella flexeneri*	*Pseudomonas aeruginosa*
I	10	8	12	9	8
	20	15	12	11	14
	30	20	18	19	22
II	10	9	12	10	11
	20	13	15	17	20
	30	21	24	25	28
	10	9	13	10	11

III	20	16	16	15	18
	30	23	24	28	30
IV	10	11	12	12	14
	20	15	18	25	23
	30	25	28	30	33

According to the above table, every chemical compound exhibited antibacterial activity against both kinds of bacteria, with compounds III and IV showing the strongest effects against every bacterial species examined in this search. These findings were in line with (Nashaan, 2023). due to their impact on the permeability of the bacterial cell wall, which denaturates proteins, alters the metabolic pathway, and may cause the bacterial cell to die (Zhang, 2024).



Staphylococcus aureus **Streptococcus mutants**



Shigella flexeneri **Pseudomonas aeruginosa**

Figure 2. Investigation of chemical compounds' antibacterial activity [II, III, IV] against various bacterial isolate samples

4. Investigation of Immunity

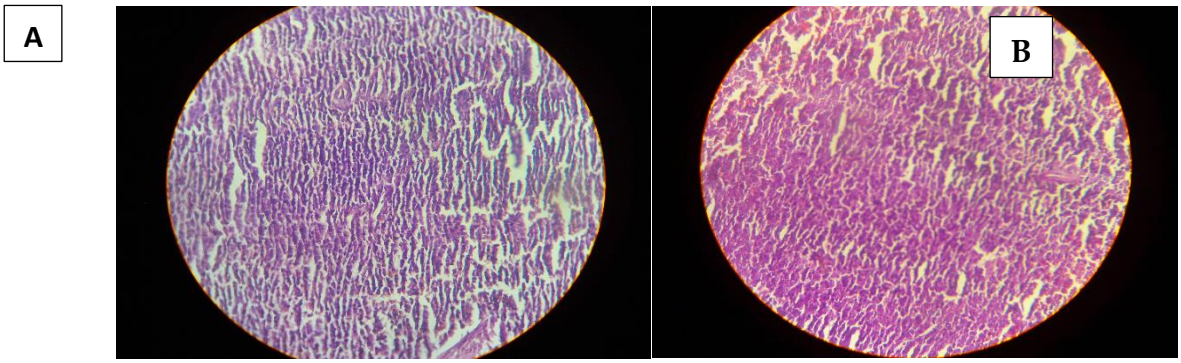
The systemic concentrations of INF-γ in immunized rabbits with chemical compounds at varying concentrations can be used to estimate the induction of the cellular immune response. Table 2 shows a significant increase ($p \leq 0.05$) in the concentrations of this cytokine due to Th1 activation, which occurs when these compounds survive in various immune cells and induces cell-mediated immunity (Kareem, 2023).

Table 2. shows the levels of INF-γ in rabbits that received chemical compound vaccinations.

Chemical compounds	Concentrations of INF-γ (Iu\ml) M±S.D.		
	Tested groups	Control group	*P – value
I	5.84±0.00	5.73±0.04	0.000[a]
	6.51±0.10		0.000[a]
	9.14±0.01		0.000[b]
II	6.65±0.00		0.000[a]
	9.04±0.01		0.000[b]
	9.65±0.03		0.000[b]
III	6.05±0.00		0.000[a]
	9.64±0.21		0.000[b]
	12.65±0.05		0.000[b]
IV	7.65±0.00		0.000[a]
	13.84±0.01		0.000[b]
	17.43±0.15		0.000[c]

***p ≤ 0.05**

When immunized with (III & IV) at high concentration (30 μg mL-1), as shown in Fig., the histopathological sections of dissected rabbit spleens immunized with chemical compounds showed an increase in the number of stimulated lymphocytes and the infiltration of inflammatory cells was very low compared with control groups. All other groups showed no effect against the four chemical compounds. This is regarded as one of the tissue's defense systems against the causal agent, which can happen even when there isn't a sickness (Sharma, 2022).



The spleen of rabbits that were immunized with chemical compounds III and IV is shown in Fig. 3" Both the control group (A) and the tested groups (B) exhibit inflammatory cell infiltration.

Conclusion

In conclusion, this study successfully synthesized and characterized several novel heterocyclic derivatives of antipyrine using techniques such as FTIR spectroscopy, chromatography, and melting point analysis. The results revealed that these derivatives exhibited significant antibacterial activity against both Gram-positive and Gram-negative bacteria, with compounds III and IV demonstrating the highest potency (Kaur, 2021). Furthermore, immunological studies showed that these compounds effectively induced cellular immune responses, with notable increases in IFN-γ levels and lymphocyte stimulation. Histopathological analysis confirmed minimal inflammatory infiltration, indicating low toxicity. Overall, these findings highlight the potential of these heterocyclic derivatives in pharmaceutical applications, particularly as promising antibacterial agents with immunomodulatory properties. Future research should focus on further optimizing these derivatives and exploring their clinical efficacy (Hu, 2022).

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