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SYNTHESIS AND PHARMACEUTICAL ACTIVITY OF TRIAZOLE SCHIFF BASES WITH THEORETICAL CHARACTERIZATION

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Abstract: *In the presence of ethanol solvent and glacial acetic acids, triazole reacted with different aromatic aldehydes such as 4-methoxybenzaldehyde, 4-hydroxybenzaldehyde, and benzaldehyde to form the imines group known as Schiff bases. Triazole Schiff bases are triazole hydrazone and their derivatives, VA, VB, and VC. The structures of these synthetic triazole hydrazone derivatives were characterized by means of FT-IR and mass spectrometry. The purities and quality of the compounds were evaluated using TLC. It was established, that the active ingredient in the synthesised triazole hydrazone was more effective against the infections than cefuroxime.*

Key words: *triazole, hydrazones, biological activities, synthesis, characterization.*
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1. Introduction

Triazoles are heterocyclic organic compounds with three nitrogen atoms arranged in a five-member ring molecular structure. Two kinds of triazoles exist: 1, 2, 4-triazole and 1, 2, 3-triazole. Triazole derivative chemistry has drawn attention because of its practical uses in business, agriculture, and medicine. Furthermore, it is acknowledged that some triazoles are employed in the manufacture of polymers, as well as dyes, photographic chemicals, and analytical reagents 13, 14, and 15. Several five-membered aromatic systems with three heteroatoms arranged symmetrically have been investigated due to their intriguing physiological characteristics. Additionally, it is well known that a variety of 1,2,4-triazole and 1,3,4-thiadiazole derivatives show a wide range of pharmacological characteristics, including antifungal and antibacterial activity. Some examples of currently accessible therapeutically relevant medications that include one of these heterocyclic nuclear are ribavirin, cefazoline, fluconazole, terconazole, and itraconazole [1].

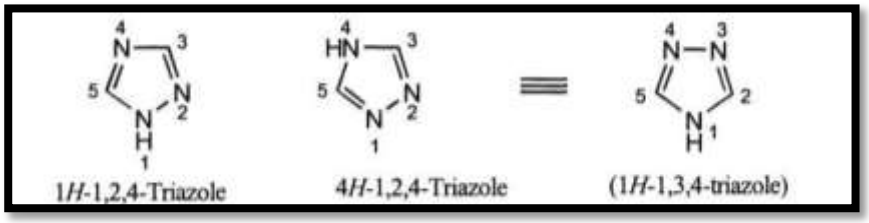


Fig. 1. Isomer structure of Triazoles [2]

1,2,4-Triazoles five-membered heterocycles that include more than two heteroatoms are thought to be formed from pyrrole by the substitution of nitrogen (-N=) atoms of the pyridine type from various places for methine groups (-CH=). The cyclic hydrazidines known as 1,2,4-triazoles have hydrogen atoms (or substituents) on either amide nitrogen six or hydrazide nitrogen 5. 1,3,4-triazole (4H-form) and parent 1,2,4-triazole (lH-form) are in tautomeric equilibrium [2] (Figure 1).

Many of the 1,2,4-triazole system's compounds have been studied as potentially useful therapeutic options due to their dual roles as anti-acetyl cholinesterase and selective COX-2 inhibitors. Triazole Schiff bases' potential as effective DNA probes, antioxidants, antivirals, anti-inflammatories, and analgesics is due to additional heterocyclic groups in them. These substances also show notables cytotoxic qualities. The development of novel 1,2,4-triazole-derived Schiff base compounds based on metals with biological properties including antioxidant, antifungal, and antibacterial properties as chemotherapeutic agents. After metal-ion chelation, their physical activity rises [3].

Functional groupss made up of an imine or azomethine (-C=N-) bond between a carbonyl group and an amine or ammoniac derivative distinguishes Schiff bases from other classes of organic compounds. Hugo Schiff [4], a German chemist who created them for the first time in 1864, is honored by their name. Applications for Schiff bases are many in pharmaceutical chemistry, chemical synthesis, and materials research [5]. They are often used as intermediates in the synthesis of several chemical compounds as well as ligands in coordination chemistry. Schiff bases have been investigated for their potential as anti-inflammatory, antibacterial, and anticancer medicines since they also show biological action [6]**.**

2. Experimental part

Triazole Schiff bases and their new derivatives were investigated using the MS Model: 5973 Agilent Technology (HP) of mass spectral and the melting points equipment (UK). Elemental analysis was done on a flashing thermo analyser C, H, and N. FT-IR spectra were examined in the 200–4000 cm^{-1} range on an infrared spectrophotometer (Shimadzu).

General procedure for synthesis of triazole Schiff bases hydrazones (VA-VC)

2.1. Synthesis of potassium 2-(2-hydroxybenzoyl)hydrazine-1-carbodithioate (II)

In 25 milliliters of ethanol, substituted 2-hydroxybenzohydrazide (0.02 mol) and KOH (0.06 mol) were dissolved. The mixture was then stirred and 0.2 mol CS_2 was added dropwise at room temperature and left there for 12 hours. The yellow of potassium 2-(2-hydroxybenzoyl)hydrazine-1-carbodithioate was produced, filtered, and thoroughly cleaned three times using 100% ethanol [7].

2.2. Synthesis of 2-(4-amino-5-sulfanyl-4*H*-1,2,4-triazol-3-yl)phenol (III)

After dissolving the intermediate potassium dithiocarbazinates in 25 mL of hot water, 0.2 mol of hydrazine hydrate was added. After heating and refluxing for three hours, this combination was put into cold water and acidified using strong hydrochloric acid. 2-(4-amino-5-sulfanyl-4H-1,2,4-triazol-3-yl)phenol [8] was produced as a pink precipitate after the precipitates were filtered, rinsed with water, and recrystallized from ethanol. The chemical was evaluated for purity using the TLC technique, yielding an RF Value of 0.75 and an eluent ratio of 7:3 (ethanol: hexane). Spot pigment may be clearly seen in an iodine chamber [8].

2.3. Synthesis of 2-(4-amino-5-hydrazinyl-4*H*-1,2,4-triazol-3-yl)phenoll (IV)

A combination of 2-(4-amino-5-sulfanyl-4H-1,2,4-triazol-3-yl)phenol (0.05mol) and hydrazine hydrate (0.05mol) in ethanol (100 mL) was boiled for 72 hours, cooled and condensed. After filtering and washing with cold water, the crude product was recrystallized from ethanol to generate 3-hydrazinyl-5-phenyl-4H-1,2,4-triazol-4-amine (III) as a brown crystal

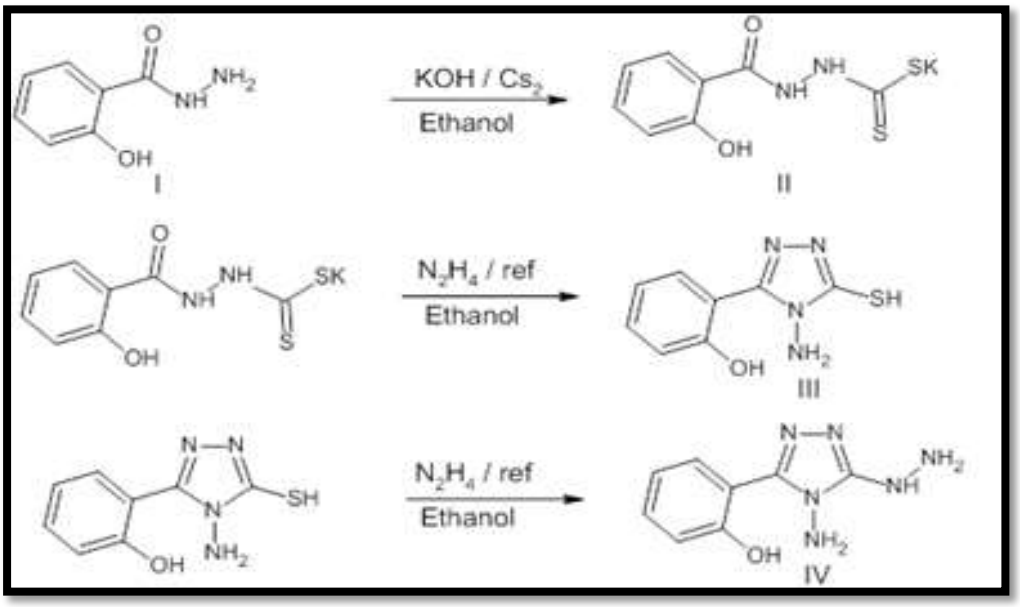
with an 82% yield and a melting point of 210–220°C [9].

2.4. Synthesis of triazole Schiff bases hydrazones derivatives V

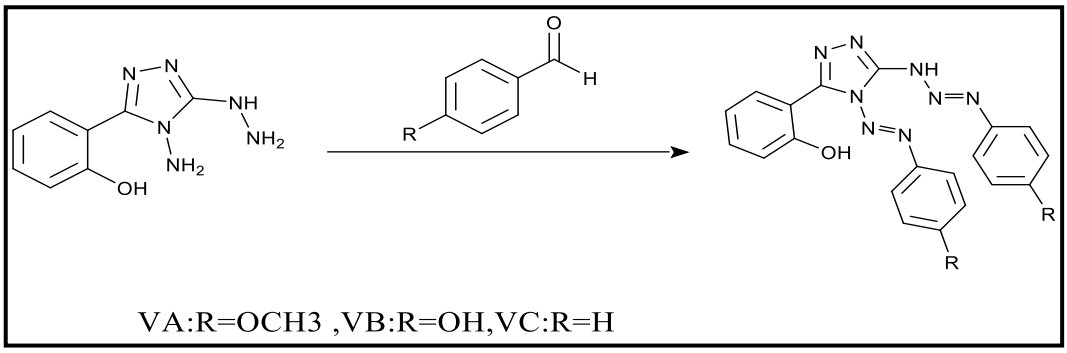
Hot solutions of aromatic aldehyde (1.52 g, 10 mmol) and 2-(4-amino-5-hydrazinyl-4H-1,2,4-triazol-3-yl)phenol (1.92 g, 10 mmol) were combined in 50 mL of ethanol with two drops of glacial acetic acid. The mixture was then allowed to reflux for two hours. The resultant solid product was then filtered, refined by crystallizing it from ethanol, cleaned with diethyl ether, and vacuum-dried over anhydrous calcium chloride. The physiochemical data of synthesized derivatives VA, VB, VC are listed in **Table 1**. Spot pigment was visibly identified in an iodine chamber [10].

Table 1. Physiochemical data of synthesized derivatives VA , VB, and VC

Symbol	Molecular formula	M.W(gm/mole)	Colour	Melting points (°C)	Yield (%)
VA	$C_{24}H_{22}N_6O_3$	442	yellow	221-223	71 %
VB	$C_{22}H_{18}N_6O_3$	414	Yellowish brown	220-222	68 %
VC	$C_{22}H_{18}N_6O$	382	Yellowish brown	222-224	63 %

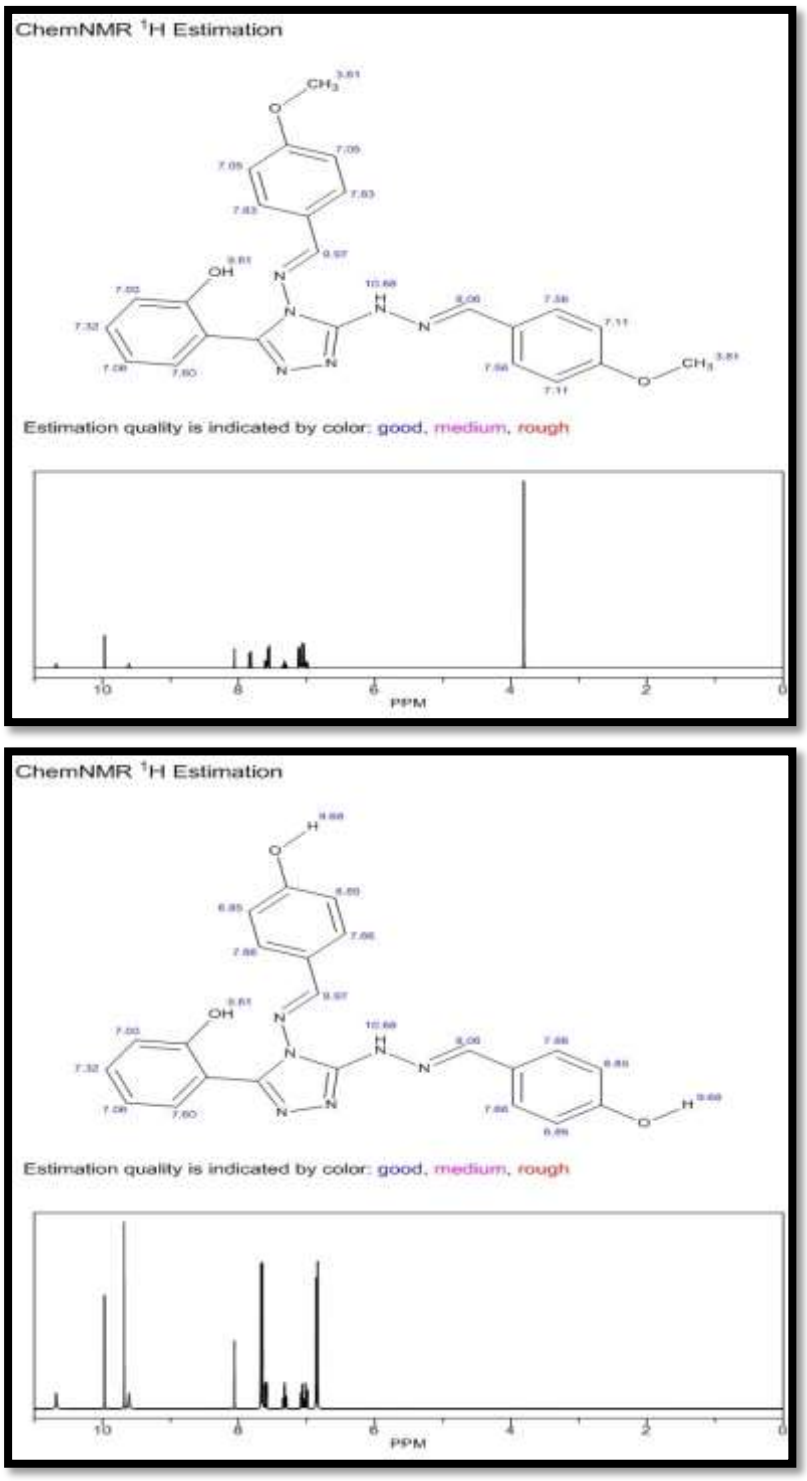


Scheme 1. 2-(4-amino-5-hydrazinyl-4*H*-1,2,4-triazol-3-yl)phenol derivatives



Scheme 2. Triazoloof hydrazones derivatives VA,VB,VC

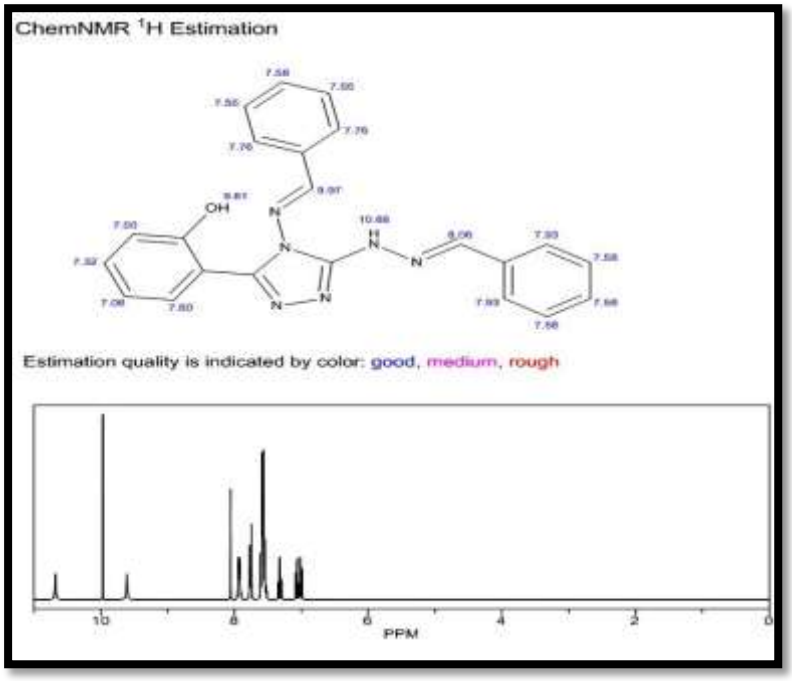
Theoretically H-NMR characterization of synthesized compound:



Scheme 3. Theoretical H-NMR characterization of VA,VB

3. Results and discussion

The physicochemical properties of the synthesized triazole hydrazone derivative shown in **Table 1** display the molecular weight, yield percentage, colour, and melting temperatures of the synthesized compounds. All data represented in **Table 1** and (**Fig. 2, 3, 4**) of the triazole hydrazine derivative VA FTIR, H-NMR, and Mass spectra showed good evidence to identify the structure of synthesized triazole hydrazone derivative.



Scheme 4. Theoretical H-NMR characterization of VC

FTIR (KBr, cm^{-1}) of VA revealed 3404 (O-H), 3188 (N-H), 3091 (C-H) aromatic, 2910 (C-H)Ali, and 1623 (C=N) correspondingly. Hydrazone derivative VB FTIR (KBr, cm-1) revealed the following peaks: 3408 (O-H), 3193 (N-H), 3085 (C-H) aromatic, 2905 (C-H)Ali, and 1625 (C=N). Hydrazone derivative VC FTIR (KBr, cm^{-1}) revealed, in that order, 3407 (O-H), 3194 (N-H), 3095 (C-H) aromatic, 2905 (C-H)Ali, and 1630 (C=N) [11].

The target compounds of triazole hydrazone VA that were synthesised showed molecular ion peaks in their mass spectra at 442, 289, 191, 148, 118, 91, 77, 65, and 53. These peaks correspond to the molecular ion fragments $C_{24}H_{22}N_6O_3$, $C_{24}H_{21}N_6O_2^+$, $C_{10}H_8N_6O_2^+$, $C_8H_9N_5O$, $C_8H_6N_3O^+$, $C_7H_7N_3O$, $C_7H_6N_2O$, C_7H_8, $C_9H_5NO_3$, $C_6H_5^+$, $C_5H_5^+$, and C_4H_3, as shown in (**Fig. 3**) [12].

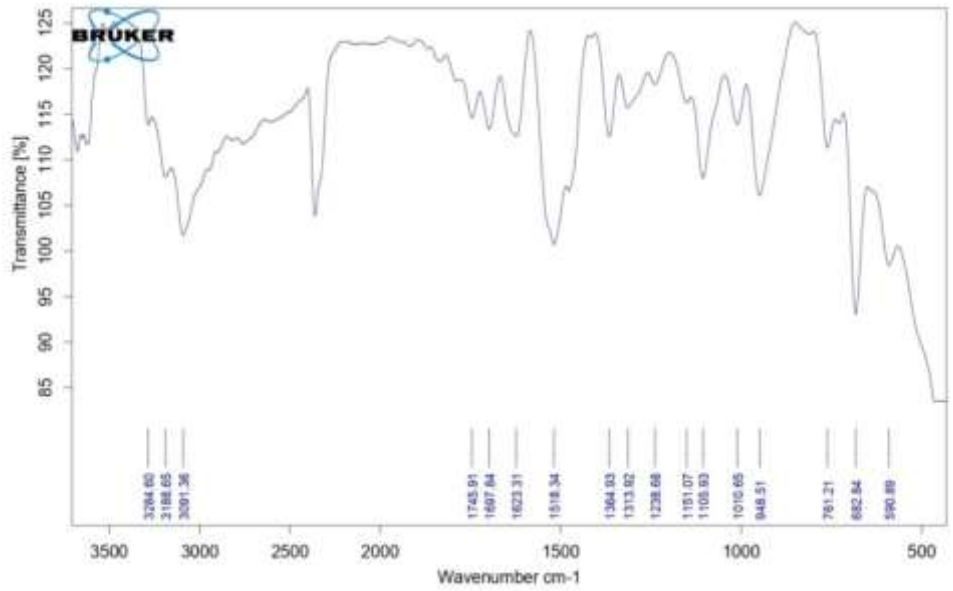


Fig. 2. FT-IR spectrum of triazole hydrazones VA

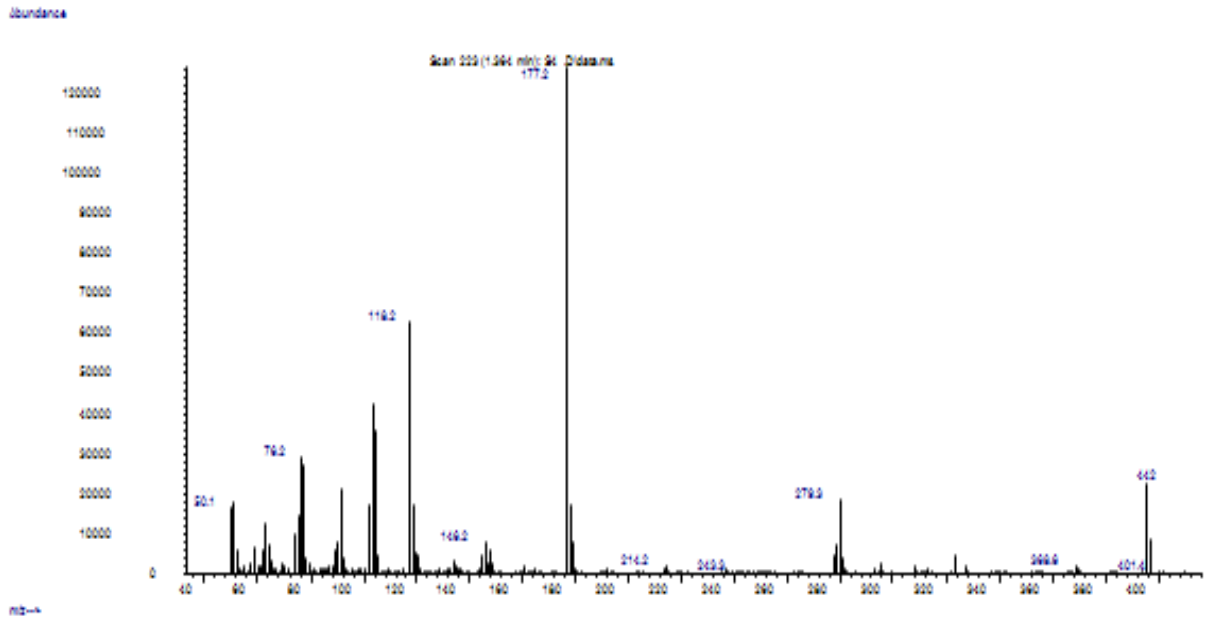


Fig. 3. Mass spectra of triazole hydrazones VA

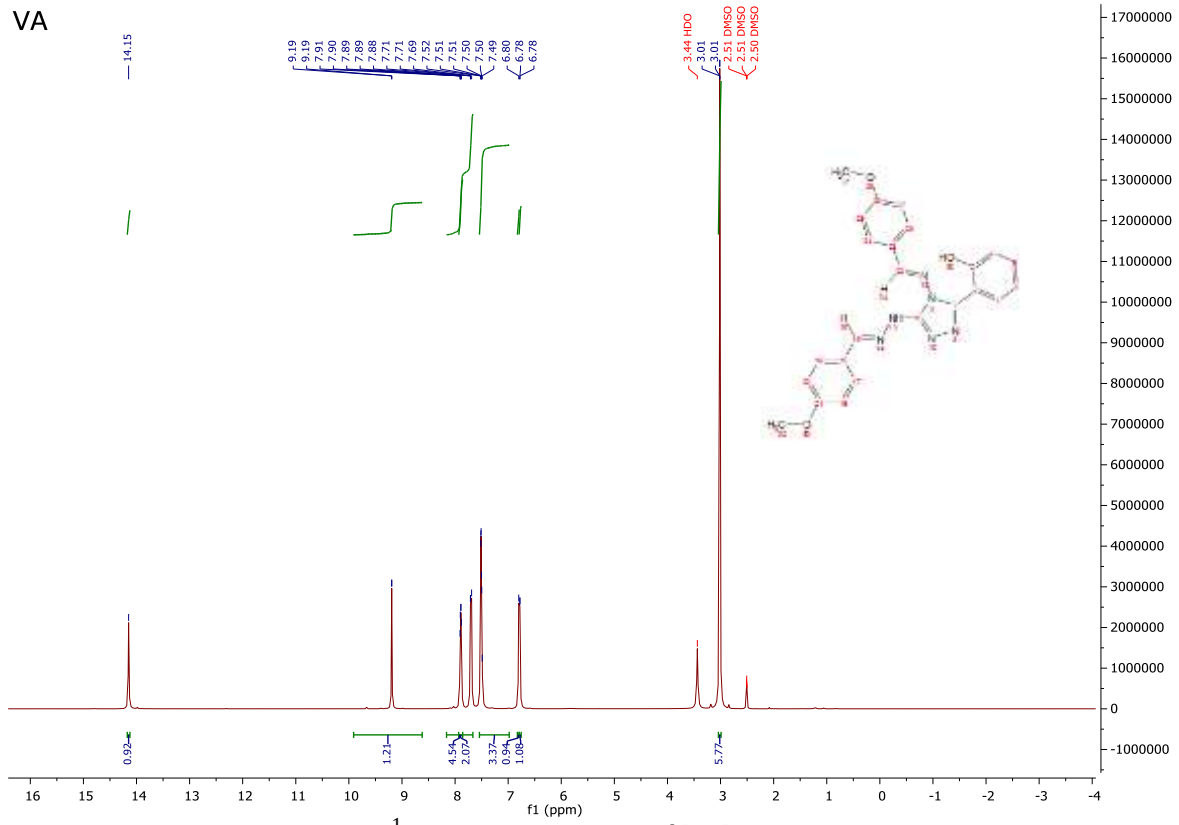


Fig. 4. ^{1}H–NMR spectrum of hydrazones VA

H-NMR Images **Fig. 4** [15] show the ^{1}H-NMR spectrum data of the synthesized compound of triazole hydrazine VA. Regarding the aromaticc portion of the spectrum, many signals that show up in the range of 6.07 to 8.12 ppm are thought to be related to the aromatic ring. On the other hand, the second signal is a singlett that has reverted to the Azomethine group CH=N– chemical shift value that was seen in 9.1 ppm [16]. Additionally, we observed that singlet signals at (14.04 ppm) in the ^{1}H-NMR spectrum were assigned to NH of triazolo

ring, respectively, while OH interference with aromatic ring. Additionally, we observed that two singlet signals at (3.1) ppm in the ^{1}H-NMR spectrum were assigned to six proton of OCH_3 [17], [18].

The mass spectral analysis of the ion fragmentss confirmed the composition of the synthesised triazole schiff bases VB. The molecularr ion peaks at 414, 282, 191, 160, 149, 134, 108, 93, 65, and 53 are part of the molecular ion fragments $C_{22}H_{18}N_6O_3$, $C_{10}H_8N_6O_2^+$, $C_8H_9N_5O$, $C_8H_6N_3O^+$, $C_7H_7N_3O$, C_7H_8, $C_9H_5NO_3$, $C_5H_5^+$, and C_4H_3. The target of triazole hydrazone VC that was synthesised has molecular ion peaks in its mass spectrum at 382, 282, 191, 160, 149, 134, 108, 93, 65, 53 [13]. These peaks are part of the molecular ion fragments $C_{22}H_{18}N_6O$, $C_{10}H_8N_6O_2^+$, $C_8H_9N_5O$, $C_8H_6N_3O^+$, $C_7H_7N_3O$, $C_7H_6N_2O$, C_7H_8, $C_9H_5NO_3$, and $C_5H_5^+$ [14].

4. Biochemical action

VA, VB, and VC, the active ingredientss of synthesised triazole hydrazones, were chemically producedd and evaluated in vitro using the agar cups methodd. The antimicrobiall properties of streptococcus [19], aeromonas [20], aureus [21], pseudomonas [22], klebsiellae [23], acinetobacter [24], and staphylococcus [25] were assessedd. The data in **Table 2** indicates that the activee component in the synthesised triazole schiff bases [26].was more efficientt against the pathogens thann CEFUROXIMEE, which was selectedd to combat Acinetobacter. The results are listed in **Table 2** [27].

Table 2. The diameter zone of growth of bacteria inhibition (mm) by plant extracts

Types of Isolates	Antimicrobial Agent			
	CEFUROXIMEE	**VA**	**VB**	**VC**
Staphylococcuss aureus	**I**	**R**	**I**	**S**
E. colii	**R**	**R**	**S**	**I**
Streptococcuss	**R**	**R**	**S**	**R**
Pseudomonass	**I**	**R**	**S**	**I**

S - sensitivity; **I** - intermediate; **R** - resistance

5. Conclusion

In the current study, triazole hydrazones VA, VB, and VC were synthesized and characterized by various physical features, such as melting point and colour, as well as by various spectral techniques, such as IR and mass spectra. Additionally, it was shown, that, the IR spectra showed five significant bands on 3404 3188, 3091, 2910, 1623, and 1699, respectively, of IVA, which corresponded to (O-H), (N-H), (C-H) Aromatic, (C-H)Ali, and (C=N). It provides strong backing for the synthesis of derivativess of triazole Schiff bases. The ion peak of the mass fragment was seen at the target compounds that were synthesised and displayed molecular ion peaks at 442, 425, 282, 191, 160, 149, 134, 108, 93, 65, and 53. These molecular ion peaks are associated with the molecular ion fragment $C_{24}H_{22}N_6O_3$, $C_{24}H_{21}N_6O_2^+$, $C_{10}H_8N_6O_2^+$,$C_8H_9N_5O$, $C_8H_6N_3O^+$, $C_7H_7N_3O$, $C_7H_6N_2O$, C_7H_8, $C_9H_5NO_3$, $C_5H_5^+$, and C_4H_3, which is associated with the molecular ion of the synthesised structure triazole hydrazones VA. The composition of the synthesized triazole hydrazones VA was validated by the ion fragment mass data.

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NƏZƏRİ XARAKTERİSTİKALI TRIAZOL ŞİFF ƏSASLARININ SİNTEZİ VƏ FARMASEVTİK AKTİVLİYİ

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Xülasə: Triazol etanol həlledicisi və buzlu sirkə turşusunun iştirakı ilə 4-metoksibenzaldehid, 4-hidroksibenzaldehid və benzaldehid kimi müxtəlif aromatik aldehidlərlə reaksiyaya girərək Şiff əsasları kimi tanınan iminlər qrupunu əmələ gətirir. Triazol Şhiff əsasları triazol hidrazon və onların törəmələri, VA, VB və VC-dir. Bu sintetik triazol hidrazon törəmələrinin strukturları FT-İR və kütlə spektrometriyası vasitəsilə xarakterizə edilmişdir. Birləşmələrin təmizliyi və keyfiyyəti TLC-dən istifadə edərək qiymətləndirilmişdir. Müəyyən edilmişdir ki, sintez edilmiş triazol hidrazonun tərkibindəki aktiv tərkib sefuroksimə nisbətən infeksiyalara qarşı daha təsirlidir.
Açar sözlər: triazol, hidrazonlar, bioloji aktivlik, sintez, xarakteristika.

СИНТЕЗ И ФАРМАЦЕВТИЧЕСКАЯ АКТИВНОСТЬ ТРИАЗОЛЬНЫХ ОСНОВАНИЙ ШИФФА С ТЕОРЕТИЧЕСКОЙ ХАРАКТЕРИСТИКОЙ

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Аннотация: В присутствии растворителя этанола и ледяной уксусной кислоты триазол взаимодействовал с различными ароматическими альдегидами, такими как 4-метоксибензальдегид, 4-гидроксибензальдегид и бензальдегид, с образованием иминной группы, известной как основания Шиффа. Триазольные основания Шиффа представляют собой триазолгидразон и их производные VA, VB и VC. Структуры этих синтетических производных триазолгидразона были охарактеризованы с помощью ИК-Фурье и масс-спектрометрии. Чистоту и качество соединений оценивали с помощью ТСХ. Установлено, что действующее вещество синтезированного триазолгидразона более эффективно против инфекций, чем цефуроксим.
Ключевые слова: триазолы, гидразоны, биологическая активность, синтез, характеристика.