Synthesis, and Antimicrobial Evaluation of New hydrazone Derivatives of (2,4-dinitrophenyl) hydrazine

Article *in* Research Journal of Pharmacy and Technology · April 2022

DOI: 10.52711/0974-360X.2022.00292

3 authors:

Halah A. Sahib
University of Baghdad
6 PUBLICATIONS **11** CITATIONS
SEE PROFILE

Mohammed Kamil Hadi
University of Baghdad
19 PUBLICATIONS **35** CITATIONS
SEE PROFILE

Maadh Qusay Abdulkadir
University of Baghdad
12 PUBLICATIONS **18** CITATIONS
SEE PROFILE

ISSN 0974-3618 (Print)
0974-360X (Online)

www.rjptonline.org

RESEARCH ARTICLE

Synthesis, and Antimicrobial Evaluation of New hydrazone Derivatives of (2,4-dinitrophenyl) hydrazine

Halah A. Sahib*, Mohammed K. Hadi, Maadh Qusay Abdulkadir*
Department of Pharmaceutical Chemistry, College of Pharmacy, University of Baghdad, Baghdad, Iraq.
*Corresponding Author E-mail: **hala.abd@copharm.uobaghdad.edu.iq**

ABSTRACT:
In this work, novel compounds of hydrazones derived from (2,4-dinitrophenyl) hydrazine were synthesized. Benzamides derivatives and sulfonamides derivatives were prepared from p-amino benzaldehyde. Then these compounds were condensed with (2,4-dinitrophenyl) hydrazine through Imine bond formation to give hydrazones compounds. The compounds were characterized using FT-IR (IR Affinity-1) spectrometer, and ^{1}HNMR analyses. The majority of the compounds have a moderate antimicrobial activity against "Gram-positive bacteria staphylococcus Aureus, and staphylococcus epidermidis, Gram-negative bacteria Escherichia coli, and Klebsiella pneumoniae, and fungi species Candida albicans" using concentrations of 250 µg\ml.

KEYWORDS: (2,4-dinitrophenyl) hydrazine, Schiff base, Hydrazone, Amide, Sulfonamides, Antibacterial and Antifungal activity.

INTRODUCTION:

In medicinal chemistry, the chief goal is to synthesize promising activity compounds acting as therapeutic agents with lower side effects[1]. Nowadays, the world is depleted from efficacious antibiotics due to the emergence of resistant organisms[2,3]. As a result, this led to an increase in resistant infections, which motivated the scientists to design analogs of compounds as alternative biological active agents to overcome these infections[4].

Hydrazones have been considered an important class in medicinal chemistry[5] and therefore Hydrazones are crucial organic functional groups, possessing an azomethine proton. It is used for designing a new biologically active compound. Hydrazones can be synthesized through the reaction of hydrazides or hydrazines with aldehydes and ketones by displacement of oxygen with =NNHR functional moiety[6]. Hydrazones have numerous activities, like antitubercular, antiviral, antibacterial, antitumoral, and antimalarial properties[7-10].

Elham S Darwish et al. have been evaluated new hydrazones of sulfonamide for gram - ve, gram + ve and antifungal activity[11]. Gregory L. Backes et al. have been generated and synthesized a large library of hydrazone and hydrazide of benzoic acid derivatives. The prepared compounds showed potent antifungal activity with minimum mammalian cell toxicity[12]. However, hydrazones synthesized from 2,4-dinitrophenylhydrazine by Sergio Ortiz et al., and Alberta Ade et al. showed weak antimicrobial properties[13,14].

On the one hand, sulfonamides are a well-known class in medicinal chemistry[15] possessing the general formula A-SO2NHR. They exhibit various biological activities, like "antifungal, antibacterial, carbonic anhydrase inhibition, diuretic, antithyroid, anti-inflammatory, antiglaucoma, antiviral, and antineoplastic, hypoglycemic" etc.[16-18] Muhammad Abdul Qadir et al., Christiana Nonye et al., Rane YS et al., and Bhusari KP et al. have been developed novel sulfonamide derivatives with improved antibacterial[19-22]

On the other hand, amides are an important part present in a large array of medicinal drugs. Amides are undoubtedly one of the popular essential pharmaceutical active cores in organic chemistry since it is found in essential molecules such as "peptides, pharmaceutical

Received on 19.07.2021 Modified on 30.09.2021
Accepted on 13.11.2021
Research J. Pharm.and Tech 2022; 15(4):1743-1748.
DOI: 10.52711/0974-360X.2022.00292

agents, naturally occurring molecules, proteins, and alkaloids". As a result, one of the most promising changes in modern organic synthetic reactions is the building of an amide functional group in the molecule. Well-known examples of amides are benzamide C_6H_5–$CONH_2$, acetamide H_3C–$CONH_2$[23]. Tahere et al. synthesized a group of novel benzamide derivatives having good inhibition against "the gram-negative (Escherichia coli), and gram-positive bacteria (Streptococcus and Enterococcus)" bacteria[24]. A group of acetamide derivatives having noticeable inhibitory activities was designed and synthesized by Hui Lu et al. as well as by Jamkhandi CM et al.[25,26].

Hence, we aimed to make a hybrid molecule possessing both amide/ sulfonamide and hydrazone moiety. in an attempt to get improved antimicrobial derivatives of hydrazones. As shown in in figure 1:

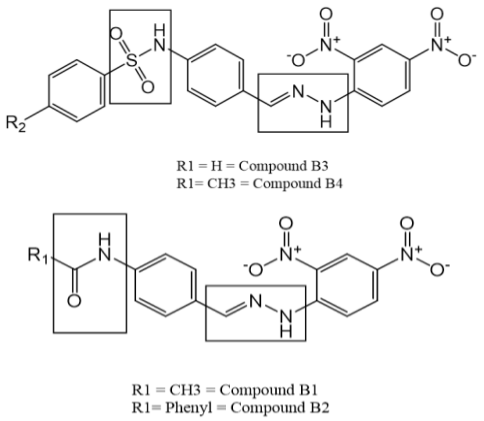


Figure 1: Designed work of new (2,4-dinitrophenyl) hydrazine derivatives (B 1-4)

MATERIAL AND METHODS:

Chemicals were supplied by hyper-chem (China), Fluka-sigma Aldrich is for p-toluene sulfonyl chloride, and Merck-Schuchardt is for benzene sulfonyl chloride. Melting points were uncorrected and detected by using "Stuart SMP3 melting point apparatus. All synthesized derivatives were characterized by spectroscopic analyses (Fourier-transform Infrared (FTIR) spectra were made using FT-IR (IR Affinity-1) spectrometer, Shimadzu, and (Proton nuclear magnetic resonance (^{1}HNMR) using 500 MHz instruments and *DMSO-d6*" as a solvent.

PROCEDURES FOR SYNTHESIS OF THE TARGET COMPOUNDS:

Synthesis of compound 1:

Compound 1 was synthesized by dissolving (0.5gm, 4.13mmole) of p-amino benzaldehyde in dry chloroform (30ml) using a 250ml one neck flat bottom flask. Then, (0.57ml, 4.13mmole) of triethylamine was added dropwise with continuous stirring and simultaneous drop by drop addition of 0.6ml of acetyl chloride on an ice bath. The stirring was continued overnight. The solution's color turned from bright yellow to beige suspension. The resulting mixture was filtered after evaporating some of the solvent volume, then rinsed with distilled water (D.W) and dried with anhydrous $MgSO_4$[27].

N-(4-formylphenyl) acetamide: Beige solid in yield 72%; melting point= 160°C;

R (cm^{-1}): 3236 (N-H of amide, stretching), 3086 (C-H aromatic, stretching), 2993, 2831 (C-H methyl, stretch.), 2731 (C-H aldehyde), 1701 (C=O aldehyde carbonyl stretch.), 1654 (C=O amide carbonyl stretch.), 1593 - 1459 (C=C-C aromatic, stretch.), 1014, 759 (C-H aromatic in plane& out of plane).

^{1}HNMR (*DMSO*) (δ, ppm): 10.74 (s, 1H, NH), 9.91 (1H, s, HCO), 7.81-7.90 (4H, m, Ar-H), 2.32 (s, 3H, CH3).

Synthesis of compound 2:

In a flat dry round flask at 0°C, triethylamine (0.23 ml, 1.65 mmoles) and benzoyl chloride (0.2 ml, 1.8 mmoles) in chloroform (15ml) were added slowly to the p- amino benzaldehyde (0.2gm, 1.65mmoles) solution. The resultant mixture was stirred all night. The precipitate was dried in an oven at 60°C after it was filtered, washed with D.W[28].

N-(4-formylphenyl) benzamide: Faint yellow solid in yield 40%; melting point = 240-244°C;

FTIR (cm^{-1}): 3294 (N-H of amide, stretching), 3055 (C-H aromatic, stretch.), 2738 (C-H aldehyde stretch.), 1693 (C=O aldehyde carbonyl stretch.), 1651 (C=O amide carbonyl, stretch.), 1593 -1473 (C=C-C aromatic, stretch.), 1033, 806 (C-H aromatic in the plane and out of plane bending).

^{1}HNMR (*DMSO*) (δ, ppm): 11.06 (s, 1H, NH), 10.88 (1H, s, HCO), 7.92-9.36 (9H, m, Ar-H).

Synthesis of compounds 3 and 4.

In flat dry round flask benzene at 0°C, sulfonyl chloride (0.3ml,1.65 mmoles) for compound (3) and p- toluene sulfonyl chloride (0.3gm,1.65mmoles) for compound (4) were gradually added to the solution of p-amino benzaldehyde (0.2gm, 1.65 mmoles) in pyridine (1mL) respectively. At room temperature, the mixture was stirred for 12 hours. The suspension was then filtered, and the precipitate was mixed with 10% HCl before being filtered. In a desiccated jar, the precipitate was kept dry[29,30].

N-(4-formyl phenyl) benzene sulfonamide:

Bright orange solid in yield 48%; melting point =124-128°C; **FTIR (cm^{-1}):** 3236 (N-H of amide, stretch.), 3062 (C-H aromatic, stretch.), 2916, 2877 (C-H methyl, stretch.), 2765 (C-H aldehyde stretch.), 1685 (C=O aldehyde carbonyl), 1597 -1477 (C=C-C aromatic, stretch.), 1342 (S=O asymmetric stretch.),1157 (S=O, symmetric stretch.), 1087, 721 (C-H aromatic in plane& out of plane).

^{1}HNMR (*DMSO*) (δ, ppm): 10.07 (s, 1H, NH), 9.82 (1H, s, HCO), 7.27- 7.86 (9H, m, Ar-H).

N-(4-formylphenyl) 4-methylbenzene sulfonamide:

Brown solid in yield 63%; melting point = >300°C decomposed; **FTIR (cm^{-1}):** 3309 (N-H of amide, stretch.), 3140 (C-H aromatic, stretch.), 2742 (C-H aldehyde stretch.), 1685 (C=O aldehyde carbonyl), 1593 -1473 (C=C-C aromatic, stretch.), 1334 (S=O asymmetric stretch.),1153 (S=O, symmetric stretch.), 1013, 709 (C-H aromatic in plane& out of plane). **^{1}HNMR (*DMSO*) (δ, ppm**): 9.57 (s, 1H, NH), 9.34 (1H, s, HCO), 6.61- 7.56 (8H, m, Ar-H), 2.29 (s, 3H, CH3).

Synthesis of compound B1:

(2,4-dinitrophenyl) hydrazine (0.12 gm, 0.61 mmoles) was mixed with the ethanolic solution of compound 1 (0.1 gm, 0.61 mmoles) with 2 drops of glacial acetic acid, the mixture was then refluxed for an hour and cooled in ice bath, filtration was used to obtain the precipitate, which was then rinsed with ethanol and air-dried [30].

N-(4-((2-(2,4-dinitrophenyl) hydrazinylidene) methyl) phenyl) acetamide:

orange solid in yield 79%; melting point 260-263 ◦C ; **FTIR (cm^{-1})**: 3236 ??(N-H of amide, stretch.), 3200 (NH, hydrazone stretch.) 3093 (C-H aromatic, stretch.), 2943, 2877(C-H methyl, stretch.), 1670 (C=O amide carbonyl stretch.), 1621 (N-H, imine stretching),1589 -1411 (C=C-C aromatic, stretch.), 1053, 702 (C-H aromatic in plane& out of plane).

^{1}HNMR (*DMSO*) (δ, ppm): 11.64 (s, 1H, NH-N), 10.55 (1H, s, NH-C=O), 7.64 - 8.89 (7H, m, Ar-H), 8.66 (s, 1H, CH=N), 2.31 (s, 3H, CH3).

Synthesis of compound B2:

In 5 ml of methanol, Equimolar of compound (2), (0.1 gm, 0.44 mmole) and (2,4-dinitrophenyl) hydrazine (0.087 gm, 0.44 mmole) were dissolved, and to the resulting mixture, 3-4 drops of piperidine were added. The resultant mixture was refluxed for an hour. When the reaction is completed, it was left to stand for overnight, then the precipitated product was obtained by filtration, rinsed with ethanol, then dried at 60°C [31].

N-(4-((2-(2,4-dinitrophenyl) hydrazinylidene) methyl) phenyl) benzamide:

Dark orange-red solid in yield 81%; melting point= 215-220°C; **FTIR (cm^{-1}):** 3286 (N-H of amide, stretching), 3200 (NH, hydrazone stretch.) 3001 (C-H aromatic, stretch.), 1689 (C=O amide carbonyl stretch.), 1624 (N-H, imine stretch.), 1597 -1415 (C=C-C aromatic, stretch.), 1010, 721 (C-H aromatic in plane& out of plane). **^{1}HNMR (*DMSO*) (δ, ppm):** 11.68 (s, 1H, NH-N), 11.52 (1H, s, NH-C=O), 7.48- 8.88 (12H, m, Ar-H), 8.5 (s, 1H, CH=N).

Synthesis of compound B3:

In a round bottom flask, compound 3(0.12gm, 0.46 mmole) was added to 20ml of methanolic solution of 2,4-dinitrophenyl hydrazine (0.091gm, 0.46mol). And then five ml of 10% HCl was added to above solution. It was then refluxed for an hour and left overnight. Filtration was used to obtain the precipitate, which was then rinsed with ethanol and air-dried [32].

N-(4-((2-(2,4-dinitrophenyl) hydrazinylidene) methyl) phenyl) benzene sulfonamide:

Orange solid in yield 70%; melting point =239- 242◦C; **FTIR (cm^{-1}):** 3290(N-H of amide, stretch.), 3290 (NH, hydrazone stretch.) 3105 (C-H, aromatic stretch.), 1612 (N-H, imine stretch.), 1558 -1423 (C=C-C aromatic, stretch.), 1018, 717 (C-H aromatic in plane& out of plane). ^{1}HNMR (DMSO) (δ, ppm): 11.53 (s, 1H, NH-N), 10.67 (1H, s, NH-S=O), 6.82- 8.84 (12H, m, Ar-H), 8.73 (s, 1H, CH=N), 2.29 (s, 3H, CH3).

Synthesis of compound B4:

The compound was prepared following the reported reference with modification. In 20ml beaker, (2,4-dinitrophenyl) hydrazine (0.1gm,0.5 mmoles) was added with continuous stirring to 1.5mL of water and 5mL of 95% ethanol and 0.5ml H2SO4, the mixture was filtered and added to compound 4 (0.125gm, 0.45mmole) in a round bottom flask. And then it was refluxed for one hour and left to stand overnight. The residue was filtered and rinsed with ethanol, and then dried in the oven at 60°C [33].

N-(4-((2-(2,4-dinitrophenyl) hydrazinylidene) methyl) phenyl)-4 methylbenzene sulfonamide:

Orange solid in yield 87%; melting point = > 300°C decomposed; **FTIR (cm^{-1}):** 3375 (N-H of amide, stretch.), 3282 (NH, hydrazone stretch.) 3093 (C-H, aromatic stretch.), 2943, 2850(C-H methyl, stretch.), 1612 (N-H, imine stretch.), 1558 -1419 (C=C-C aromatic, stretch.), 1006, 717 (C-H aromatic in plane and out of plane). **^{1}HNMR (*DMSO*) (δ, ppm):** 11.68 (s, 1H, NH-N), 9.57 (1H, s, NH-S=O), 6.62- 8.88 (11H, m, Ar-H), 8.7 (s, 1H, CH=N), 2.29 (s, 3H, CH3).

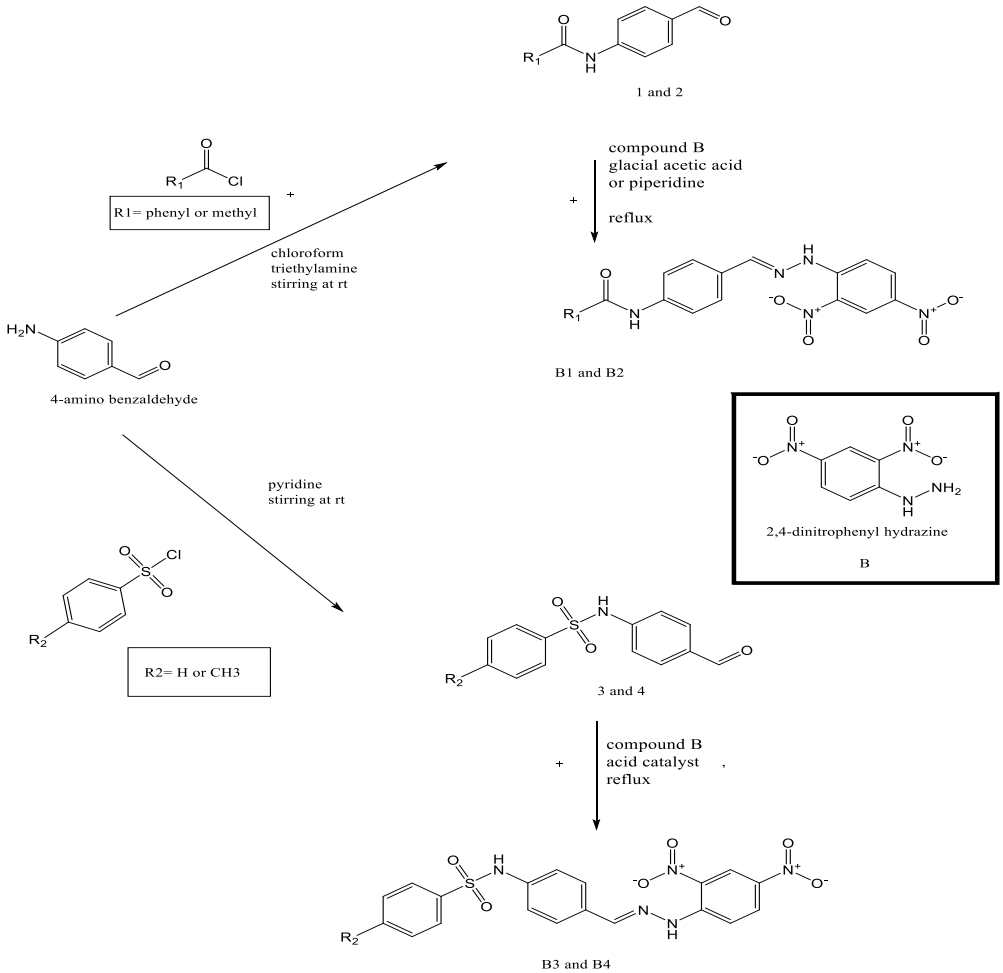
RESULTS AND DISCUSSION:

Chemistry:

As shown, scheme 1 demonstrates the synthesis steps of compounds B1–B4. The synthesis involves amide formation starting from p-amino benzaldehyde reaction with acyl chlorides (benzoyl or acetyl chloride), or reaction with sulfonyl chlorides derivatives (benzene or p-toluene sulfonyl chloride) to afford acetamide derivative (compound 1), benzamide derivative (compound 2), benzene sulfonamide derivative (compound 3) and 4-methylbenzene sulfonamide derivative (compound 4), respectively. Then, new hydrazones hybrids with amide/sulfonamide moieties were prepared by condensation of the lately synthesized

compounds (1,2,3 and 4) with (2,4-dinitrophenyl) hydrazine giving final compounds (B1, B2, B3, and B4), respectively.

The synthesized compounds were characterized, and their structures were verified by "FTIR and ^{1}HNMR" spectral analyses. IR spectra for compounds (1 and 2) show characteristic bands: 3236 and 3294 for (N-H of amide, stretching); 2731 and 2738 for (C-H aldehyde); 1701 and 1693 for (C=O aldehyde carbonyl stretching); 1654 and 1651 for (C=O amide carbonyl stretching), respectively. However, compound 1 shows additional two bands at 2993, 2831 attributed to (C-H methyl, stretching). Whereas compounds (3 and 4) show the following bands: 3236 and 3309 for (N-H of amide, stretching); 2765 and 2742 for (C-H aldehyde stretching); 1685 and 1685 for (C=O aldehyde carbonyl); 1342 and 1334 for (S=O asymmetric stretching), 1157 and 1153 for (S=O, symmetric stretching), respectively. However, compound 4 has additional two bands at 2916, 2877 accounted for (C-H methyl, stretching). For compounds (B1-B4), the disappearance of the characteristic aldehyde band and appearance of bands (1612-1624) cm-1 was a strong clue for Schiff base formation, i.e., the linkage has occurred between the amide/ sulfonamide core and (2,4-dinitrophenyl) hydrazine. ^{1}HNMR spectra of the compounds were agreeable with the assigned structures: Compounds (1 and 2) show singlet signals at δ= 10.74 and 11.06 ppm attributed to the proton of the amide group. While the proton signal due to CHO of the aldehyde appears as a singlet at δ= 9.91 and 10.88 ppm, respectively. A sharp singlet peak integrated for 3H at δ= 2.32 is related to the methyl group in compound 1. While Compounds (3 and 4) show singlet signals at δ= 10.07 and 9.57 ppm attributed to the proton of the amide group. While the proton signal due to C<u>H</u>O of the aldehyde appears as a singlet at δ= 9.82 and 9.34 ppm, respectively. A singlet band of 3H at δ= 2.29 is related to the methyl group in compound 4. For compounds (B1-B4), the disappearance of the characteristic aldehyde signal and the appearance of singlet signal at δ= (8.66, 8.5, 8.73, and 8.7 ppm, respectively) were a sign for Hydrazone formation.



Scheme1: Synthetic pathway of (2,4-dinitrophenyl) hydrazine derivatives

Table 1: In Vitro Antibacterial Activity and Antifungal Activity

Compound Name	Conc. µg/ml	*S. aureus*	*S. epidermidis*	*E. coli*	*K. pneumoniae*	*C.albicans*
		Zone of inhibition(mm)				
Compound 1	250	15	12	12	11	12
Compound 2	250	-	12	12	12	-
Compound 3	250	12	11	11	10	-
Compound 4	250	15	12	12	10	
Compound B1	250	14	11	12	10	11
Compound B2	250	-	-	11	-	-
Compound B3	250	-	-	11	-	-
Compound B4	250	18	17	13	13	16
Amoxicillin	10	39	17	37	-	33
Streptomycin	300	19	24	20	15	31
Fluconazole	25	18	18	14	10	14
DMSO	-	-	-	-	-	-

(-) = No activity – slightly active (zone of inhibition between 5 – 10 mm),
moderately active (zone of inhibition between 10-20 mm),
highly active (zone of inhibition more than 20 mm)

ANTIMICROBIAL STUDY:

The Antimicrobial activity was performed using well diffusion method. Two types of "Gram-negative bacteria Klebsiella pneumonia and Escherichia Coli and two types of Gram-positive bacteria Staphylococcus aureus and staphylococcus epidermidis were used for testing the in-vitro antibacterial activity, and the fungi species Candida albicans" for testing the in-vitro antifungal activity, using amoxicillin and streptomycin as antibacterial standards and Fluconazole as antifungal standard while DMSO is used as a solvent. The result shown in table 1 indicates the majority of the compounds had a moderate level of activity against the aforementioned compounds using concentrations of 250 µg\ml.

CONCLUSIONS:

To briefly summarize, a group of new hydrazones derivatives, having amide/ sulfonamide functionality, were synthesized by reacting aldehyde-containing amide/sulfonamide moiety with (2,4-dinitrophenyl) hydrazine. The synthesized compounds were evaluated in vitro for their antimicrobial effects against "Gram-positive bacteria Staphylococcus Aureus, and staphylococcus epidermidis, Gram-negative bacteria Escherichia coli, and Klebsiella pneumoniae, and fungi species Candida albicans". According to the antimicrobial activity data, the majority of the compounds are moderately active against the aforementioned pathogens.

REFERENCES:

1. Lombardino JG, Lowe JA. The role of the medicinal chemist in drug discovery—then and now. Nature Reviews Drug Discovery. 2004 Oct;3(10):853-62. Doi.org/10.1038/nrd1523
2. Abbas HA, Kadry AA, Shaker GH, Goda RM. Resistance of Escherichia coli and Klebsiella pneumoniae isolated from different Sources to β-lactam Antibiotics. Research Journal of Pharmacy and Technology. 2017;10(2):589-91. Doi: 10.5958/0974-360X.2017.00116.0
3. Aljanaby AA, Aljanaby IA. Profile of antimicrobial resistance of aerobic pathogenic bacteria isolated from different clinical infections in Al-Kufa central hospital-Iraq during period from 2015 to 2017. Research Journal of Pharmacy and Technology. 2017;10(10):3264-70. Doi: 10.5958/0974-360X.2017.00579.0
4. Adusei E., Adosraku R., Oppong-Kyekyeku j. and Jibir Y. Resistance modulation action, time-kill kinetics assay, and inhibition of biofilm formation effects of plumbagin from Plumbago zeylanica Linn: Journal of Tropical Medicine, 2019. Doi: 10.1155/2019/1250645
5. Radi MF, Husain SS, Zaki AN, Sultan AA, Hamed WM, Khamis WM. Synthesis and Characterization of some new Schiff base Compounds derived from 4-Amino benzoic acid and study their biological activity. Research Journal of Pharmacy and Technology. 2019;12(5):2207-12. Doi: 10.5958/0974-360X.2019.00368.8
6. Abdulhamza HM, Farhan MS. Synthesis, Characterization and Preliminary Anti-inflammatory Evaluation of New Fenoprofen Hydrazone Derivatives. Iraqi Journal of Pharmaceutical Sciences. 2020 Dec 30;29(2):239-44. Doi.org/10.31351/vol29iss2pp239-244
7. De Oliveira Carneiro Brum J, França TC, LaPlante SR, Villar JD. Synthesis and biological activity of hydrazones and derivatives: A review. Mini-reviews in medicinal chemistry. 2020 Mar 1;20(5):342-68. Doi: 10.2174/1389557519666191014142448
8. Ali MR, Marella A, Alam MT, Naz R, Akhter M, Shaquiquzzaman M, Saha R, Tanwar O, Alam MM, Hooda J. Review of biological activities of hydrazones. Indonesian Journal of Pharmacy. 2012 Oct 1;23(4):193-202. Doi.org/10.14499/indonesianjpharm23iss4pp193-202
9. Popiolek L. Hydrazide–hydrazones as potential antimicrobial agents: overview of the literature since 2010. Medicinal Chemistry Research. 2017 Feb;26(2):287-301. Doi: org/10.1007/s00044-016-1756-y
10. Rahmani SE, Lahrech M. Evaluation of the Antioxidant Activity of some Hydrazone Schiff's bases bearing Benzotriazole Moiety. Research Journal of Pharmacy and Technology. 2018;11(9):4104-7. Doi: 10.5958/0974-360X.2018.00754.0
11. Darwish ES, Fattah AM, Attaby FA, Al-Shayea ON. Synthesis and antimicrobial evaluation of some novel thiazole, pyridone, pyrazole, chromene, hydrazone derivatives bearing a biologically active sulfonamide moiety. International Journal of Molecular Sciences. 2014 Jan;15(1):1237-54. Doi: 10.3390/ijms15011237
12. Backes GL, Neumann DM, Jursic BS. Synthesis and antifungal activity of substituted salicylaldehyde hydrazones, hydrazides, and sulfohydrazides. Bioorganic & medicinal chemistry. 2014 Sep 1;22(17):4629-36. Doi.org/10.1016/j.bmc.2014.07.022.
13. Ade A, Amengor CD, Brobbey A, Ayensu I, Harley BK, Boakye YD. Synthesis and Antimicrobial Resistant Modulatory Activity of 2, 4-Dinitrophenylhydrazone Derivatives as Agents against Some ESKAPE Human Pathogens. Journal of Chemistry. 2020 Oct 7;2020. Doi.org/10.1155/2020/2720697.
14. Ortiz S, Nelson R, Kesternich V, Pérez-Fehrmann M, Christen P,

Marcourt L. Synthesis and antifungal activity of diaryl hydrazones from 2, 4-dinitrophenylhydrazine. Journal of the Chilean Chemical Society. 2016 Sep;61(3):3081-4. Doi.org/10.4067/S0717-97072016000300015.
15. Mohsein HF, Majeed NS, Al-Ameerhelal TA. Synthesis and Characterization of some new Heterocyclic compounds containing a Sulfonamide Moiety. Research Journal of Pharmacy and Technology. 2019;12(7):3282-8. Doi: 10.5958/0974-360X.2019.00555.9
16. Bagul SD, Rajput JD, Tadavi SK, Bendre RS. Design, synthesis, and biological activities of novel 5-isopropyl-2-methylphenolhydrazide-based sulfonamide derivatives. Research on Chemical Intermediates. 2017 Apr;43(4):2241-52. Doi.org/10.1007/s11164-016-2759-5
17. Olfat A. Nief, Zainab Z. Mahamad, Nahida A. Jinzeel, Firyal W. Askar. Synthesis and Antimicrobial Activity of Some Sulfonamide Derivatives containing various Heterocyclic Moieties. Research J. Pharm. and Tech. 2019; 12(6):2943-2948. Doi: 10.5958/0974-360X.2019.00495.5
18. Patel KD, Patel CN, Patel GM. Synthesis and Antidiabetic Activity of Novel 4-((2, 4-Dioxothiazolidin-5-ylidene) methyl) Substituted Benzene Sulphonamide. Asian Journal of Research in Pharmaceutical Science. 2015;5(1):1-7. Doi: 10.5958/2231-5659.2015.00001.6
19. Abdul Qadir M, Ahmed M, Iqbal M. Synthesis, characterization, and antibacterial activities of novel sulfonamides derived through condensation of amino group-containing drugs, amino acids, and their analogs. BioMed research international. 2015 Feb 24;2015. Doi.org/10.1155/2015/938486
20. Igwe CN, Okoro UC. Synthesis, characterization, and evaluation for antibacterial and antifungal activities of n-heteroaryl substituted benzene sulphonamides. Organic Chemistry International. 2014 Nov 27;2014. Doi.org/10.1155/2014/419518
21. Rane YS, Varma RR, Patil LS, Athlekar SV, Chowdhary AS, Bobade AS. Synthesis and antimicrobial activity of 5-substituted-2-(1-H-benzimidazole) sulfonamides. Asian Journal of Research in Chemistry. 2010 Jun 28;3(2):335-8.
22. Bhusari KP, Amnerkar ND, Khedekar PB, Kale MK, Bhole RP. Synthesis and in vitro antimicrobial activity of some new 4-amino-N-(1, 3-benzothiazol-2-yl) benzenesulphonamide derivatives. Asian Journal of Research in Chemistry. 2008; 1(2):53-7.
23. Ojeda-Porras A, Gamba-Sánchez D. Recent developments in amide synthesis using nonactivated starting materials. The Journal of organic chemistry. 2016 Dec 2; 81(23):11548-55. Doi.org/10.1021/acs.joc.6b02358
24. Hosseyni Largani T, Imanzadeh G, Zahri S, Noroozi Pesyan N, Şahin E. A facile synthesis and antibacterial activity of novel pyrrolo [3, 4-b] quinoline-2 (3H)-yl) benzamides. Green Chemistry Letters and Reviews. 2017 Oct 2; 10(4):387-92. Doi.org/10.1080/17518253.2017.1380233
25. Lu H, Zhou X, Wang L, Jin L. Synthesis and Antibacterial Evaluation of N-phenylacetamide Derivatives Containing 4-Arylthiazole Moieties. Molecules. 2020 Jan;25(8):1772. Doi.org/10.3390/molecules25081772
26. Jamkhandi CM, Disouza JI. Synthesis and Antimicrobial Evaluation of 2-(1H-1, 2, 3-Benzotriazol-1-yl) N-Phenylacetamide Derivatives. Research Journal of Pharmacy and Technology. 2012; 5(8):1072-5. Doi: 10.5958/0974-360X
27. ALi H, Mohammed MH, Ismeal SH. Synthesis, Characterization, and Alpha Glucosidase Inhibition Activity of New Phthalimide Derivatives. Iraqi Journal of Pharmaceutical Sciences (P-ISSN: 1683-3597, E-ISSN: 2521-3512). 2018 Jun 5; 27(1):100-8. Doi.org/10.31351/vol27iss1pp100-108
28. Bousfield TW, Pearce KP, Nyamini SB, Angelis-Dimakis A, Camp JE. Synthesis of amides from acid chlorides and amines in the bio-based solvent Cyrene™. Green Chemistry. 2019; 21(13):3675-81. Doi.org/10.1039/C9GC01180C
29. Saour KY, Al-Bayati RI, Hadi MK. Synthesis of New Coumarin and 2-quinolone Derivatives with Expected Biological Activities. Iraqi Journal of Pharmaceutical Sciences. 2012; 21(2):42-50. Doi.org/10.31351/vol21iss2pp42-50
30. Sahib HA, Dakhel ZA, Hadi MK. Synthesis and Preliminary Antimicrobial Activity Evaluation of New Amide Derivatives of 2-aminobenzothiazole.IJDDT, 2021; 11(4): 1259-1261. DOI: 10.25258/ijddt.11.4.23
31. Sahib HA, Mohammed MH. Synthesis and Preliminary Biological Activity Evaluation of New N-Substituted Phthalimide Derivatives. Iraqi Journal of Pharmaceutical Sciences. 2020 Jun 25; 29(1):247-52. Doi.org/10.31351/vol29iss1pp247-252
32. Muften RA, Saour KY, Mahmood AA. Synthesis and Antimicrobial Evaluation of New 6 and7 Substituted Derivatives of Coumarin. Iraqi Journal of Pharmaceutical Sciences (P-ISSN: 1683-3597, E-ISSN: 2521-3512). 2014; 23(1):35-41. Doi.org/10.31351/vol23iss1pp35-41
33. Badal MM, Hossain MZ, Maniruzzaman M, Yousuf MA. Synthesis, identification, and computational studies of novel Schiff bases N-(2, 6-dibenzylidenecyclohexylidene)-N′-(2, 4-dinitrophenyl) hydrazine derivatives. SN Applied Sciences. 2020 Nov; 2(11):1-9. Doi.org/10.1007/s42452-020-03745-4
34. Frey J, Schneider F, Schink B, Huhn T. Synthesis of short-chain hydroxy aldehydes and their 2, 4-dinitrophenylhydrazone derivatives, and separation of their isomers by high-performance liquid chromatography. Journal of chromatography A. 2018 Jan 5; 1531:143-50. Doi.org/10.1016/j.chroma.2017.11.046