Materials Today: Proceedings xxx (xxxx) xxx

Contents lists available at ScienceDirect

Materials Today: Proceedings

journal homepage: www.elsevier.com/locate/matpr

Synthesis, characterization and biological evaluation of some phthalazine derivatives

Mohammed Abed Kadhim [a,*], Abdullah Sh. Abdullah Alani [b], Najeeb Mohammed Hussein [c]

[a] Department of Chemistry, College of Education for Pure Science, University of Anbar, Iraq
[b] The Directorate of Institutional Development and Government Coordination Iraqi Ministry of Education, Iraq
[c] Department of Food Sciences Collage of Agriculture ,University of Anbar, Iraq

ARTICLE INFO

Article history:
Received 3 April 2021
Accepted 11 April 2021
Available online xxxx

Keywords:
Phthalazine
Triazol
Spectroscopic
Antimicrobial activity

ABSTRACT

The aim of this research is to synthesis the derivatives of the compound 1-hydrazineyl-4-(5,6,7,8-tetrahy dronaphthalen-2-yl)-1,2-dihydrophthal-azinone.(4) This compound was prepared in several steps as in Scheme 1,as a reactive starting material with the other compounds containing N, O, and S as they are considered as nucleophiles, and by using different reaction conditions, the derivatives were obtained from (5–10). All reaction were monitored by TLC technique and determination of retention factor (R_f) for some compounds. The structure formula of these compounds were confirmed by using physical and spectral data (FT-IR, ^{1}H NMR, GC–MS). and elemental analyses (C.H.N). The synthesized compounds were screened for their anti-bacterial activity using Amoxicillin as a standard drug.
© 2021 Elsevier Ltd. All rights reserved. Selection and peer-review under responsibility of the scientific committee of the Emerging Trends in Materials Science, Technology and Engineering.

1. Introducation

The heterocyclic compounds can be defined as cyclic compound, containing a minimum of 1 atom besides the carbon and hydrogen and the most common of these elements are oxygen, sulfur and nitrogen. Most of these heterogeneous compounds are extracted from animal and vegetable sources, and they are of great importance in the pharmaceutical industry[1].It has therefore received much attention due to its clinical applications and pharmacological properties, [1–3] phthalazine is one of these heterogeneous compounds consisting of two rings, benzene and pyridazine. where the latter contains two nitrogen atoms, so it has important biological properties, as some phthalazine derivatives have been found that contain a nucleus 2H-Pyridazine-3-one discovered application in the clinical medicine as a result of their pronounced anti-hypertensive properties[4], anti-diabetic[5,6], anticonvulsant [7,8] cardiotonic,[9,10] antithrombotic,[11]anti-microbial,[12,13] vasorelexant,[14] antipyretic, anti-tumor, analgesic, [15–18] and cytotoxic,[19] whereas others showed interesting vasodilator,[20] throughout the past 20 years, there has been a growing interest concerning the syntheses of numerous phthalazine as potential drug candidates for cancer therapy.

2. Experimental

Melting points have been determined on Stuart scientific Melting points SMPLU-K and have been uncorrected. The elemental analyses have been carried out with the use of a Heroes C.H.N fast analyzer at Microanalytically unit, Univ. of Cairo. Reactions have been followed up and the products purification has been conducted on the pre-coated plates of the TLC (i.e. Silica gel), using toluene: ethyl acetate 2:8 as an eluent. Spots have been detected through the exposure to the vapors of the iodine. The FTIR spectra have been recorded on Unicom SP1200 spectrophotometer with the use of the KBr wafer method. ^{1}H NMR spectra have been in DMSO d_6 on a Varian plus instrument (300 MHz). The mass spectra have been recorded on the Shimadzu GC–MS QP 1000EX instrument that operates at 70 eV in the EI mode.

2.1. hydrazinyl-4-(5,6,7,8-tetrahydronaphthalen-2-yl)-1,2-dihydrophthalazine (4)

A solution of thione 3 (0.01 mol ,2.9 g), and hydrazine hydrate (0.015 mol) in ethanol (30 mL) was heated under reflux for 3 h. The solid that obtained after cooling was filtered off and crystallized from the ethanol to given 4 ,30% yield , m.p. 195–197°C. EIMS (70 eV) *m*/*z* (%): M+, 291 (26), 273 (28), 246 (30). IR (KBr) ν: 3100–3300 cm^{-1}, attributed to NH and NH2. Anal calcd for C18H20N4: C, 73.94; H, 6.89; N, 19.16; found C, 73.48; H, 5.90; N, 18.41.

* Corresponding author.
E-mail address: makm5772@uoanbar.edu.iq (M.A. Kadhim).

https://doi.org/10.1016/j.matpr.2021.04.156
2214-7853/© 2021 Elsevier Ltd. All rights reserved. Selection and peer-review under responsibility of the scientific committee of the Emerging Trends in Materials Science, Technology and Engineering.

Please cite this article as: Mohammed Abed Kadhim, A. Sh. Abdullah Alani and Najeeb Mohammed Hussein, Synthesis, characterization and biological evaluation of some phthalazine derivatives, Materials Today: Proceedings, https://doi.org/10.1016/j.matpr.2021.04.156

Table 1
. The effect of different concentrations of 7-(5,6,7,8-tetrahydronaphthalen-2-yl)–2H-[1,2,4]triazineo[3,4a]phthalazin-3 (4H)-one on inhibiting the growth of Bacillus Subtilis, Salmonella typhimurium , Rhodococcus Equi and Escherichia coli.

Descriptive Statistics				
Dependent Variable: inhibition zone				
type of bacteria	concentration of component 7	Mean	Std. Deviation	N
Bacillus Subtilis	10%	13.00	0.707	5
	20%	14.60	0.548	5
	30%	16.40	0.894	5
	40%	26.60	3.782	5
	control	29.80	0.837	5
	Total	20.08	7.129	25
Rhodococcus Equi	10%	13.00	0.707	5
	20%	15.60	2.408	5
	30%	18.60	0.548	5
	40%	28.40	0.894	5
	control	30.60	1.140	5
	Total	21.24	7.253	25
Salmonella typhimurium	10%	14.80	1.304	5
	20%	15.60	1.140	5
	30%	18.60	0.548	5
	40%	28.00	1.000	5
	control	29.60	1.817	5
	Total	21.32	6.485	25
Escherichia coli	10%	14.00	1.414	5
	20%	15.20	0.837	5
	30%	15.20	1.304	5
	40%	29.60	1.517	5
	control	30.40	2.408	5
	Total	20.88	7.753	25
Total	10%	13.70	1.261	20
	20%	15.25	1.372	20
	30%	17.20	1.704	20
	40%	28.15	2.254	20
	control	30.10	1.586	20
	Total	20.88	7.077	100

2.2. *methyl-7-(5,6,7,8-tetra-hydronaphthalen-2yl)-4H-[1,2,4] triazino[3,4a]phthalazin-4one (5)*

Compound 4 (0.01 mol, 2.9 g) was added to a pyruvic acid (0.01 mol, 0.88 g) in absolute ethanol (50 mL) and The mixture has been heated at 170°C for 1 h. in an oil bath. After the cooling, the solid has been Separated by filtration, then recrystallized from acetic acid To give **5**: pale yellow crystals; m.p 210–212°C; yield 52%, (R_f = 0.46); 1H NMR (DMSO-d 6) δ: 1.3–1.6 (m,4H, tetralin), 2.81–2.87 (m,4H, tetralin moiety), 7.50–7.80 (m, 7H, Ar-H), 2.46 (s, 3H, CH3); IR (KBr) v: 1660 cm^{-1}(C = O),1605 cm^{-1}(C = N), 2920 cm^{-1} (C-Haliphatic), 3150 cm^{-1} (C-Haromatic); MS (70 eV) *m/z* (%): 342.18(M^+, 17). Anal. calcd. for $C_{21}H_{18}N_4O$: C, 73.67; H, 5.30; N, 16.36; O, 4.67; found C, 73.60; N, 16.32; O, 4.57; H, 5.26.

2.2.1. *7-(5,6,7,8-tetrahydronaphthalen-2-yl)–2H-[1,2,4]triazineo [3,4a]phthalazine-3,4dione (6)*

A compound 4 (0.01 mol ,2.9 g) and diethyl oxalate (0.01 mol, 1.46 g) in absolute ethanol (30 mL) refluxed for 8 h. After cooling at room temperature, the solid has been re-crystallized from absolute ethanol for giving **6**: yellow crystals; yield 55%; m.p 230–234°C (R_f = 0.50); ^{1}H NMR (DMSO d_6) δ:07.05–08.20(m,6H, ArH & NH of triazine); I.R. (KBr)v:3320 cm^{-1}(NH), 1689–1676 cm^{-1} (C = O), 1610 cm^{-1} (C = N); MS (70 eV) *m/z* (%): 345.12 (M +,1.50). Anal. calcd. for: $C_{20}H_{16}N_4O_2$ C, 69.76; N, 16.27; H, 4.68; found C, 69.73; N, 16.25; H, 4.66.

2.2.2. *7-(5,6,7,8-tetrahydronaphthalen-2-yl)–2H-[1,2,4]triazineo [3,4a]phthalazin-3 (4H)-one (7)*

A compound 4 (0.01 mol, 2.9 g) and ethyl bromoacetate (0.03 mol, 5.01 g) in the absolute ethanol (30 mL) It has been heated for 15 h. under the reflux. After cooling in room temperature the solid has been separated, filtered, and recrystallized from absolute ethanol gave **7**: yellow crystals; yield 60%; m.p 240-242○C (R_f = 0.38);1H NMR (DMSO – d_6) δ:01.7–02.1(m,4H, tetralin), 02.79–02.85 (m,4H, tetralin moiety) 4.30 (s, 2H, CH2 of triazine), 06.86–08.30 (m,7H, Ar-H and NH of triazine); I.R. (KBr) v:3280 cm − 1(NH), 1650 cm − 1(C = O), 1620 cm − 1(C = N), 2910 cm − 1C-Haliphatic; MS (70 eV) *m/z* (%): 331.15 Anal. calcd. for $C_{20}H_{18}N_4O$:

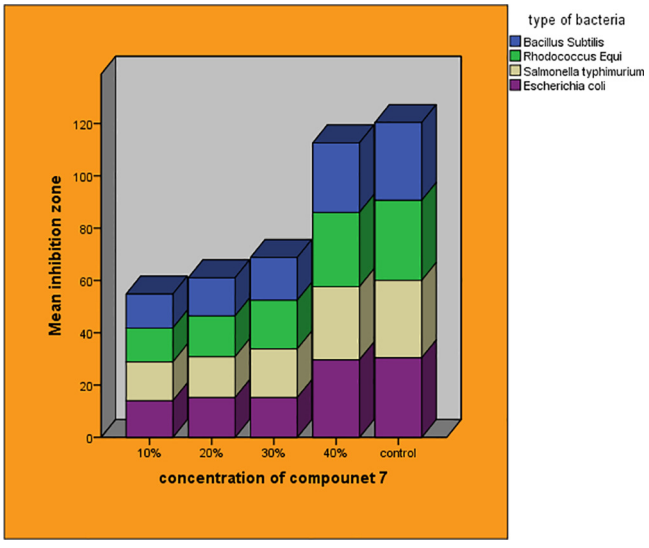

Fig. 1. effect of different concentrations of 7-(5,6,7,8-tetrahydronaphthalen-2-yl)–2H-[1,2,4]triazineo[3,4a]phthalazin-3 (4H)-one on inhibiting the growth of Bacillus Subtilis, Salmonella typhimurium, Rhodococcus Equi and Escherichia coli.

Table 2
. The effect of different concentrations of 3-methyl-7-(5,6,7,8-tetra-hydronaphthalen-2yl)-4H-[1,2,4]triazino[3,4a]phthalazin-4one on inhibiting the growth of Bacillus Subtilis and Salmonella typhimurium.

Descriptive Statistics				
Dependent Variable: inhibition zone				
type of bacteria	concentration of component 5	Mean	Std. Deviation	N
Bacillus Subtilis	10%	12.80	0.837	5
	20%	15.60	1.140	5
	30%	17.80	0.837	5
	40%	26.60	1.140	5
	control	29.20	1.304	5
	Total	20.40	6.583	25
Salmonella typhimurium	10%	14.00	1.581	5
	20%	15.60	1.140	5
	30%	18.60	1.517	5
	40%	26.80	4.382	5
	control	29.40	0.894	5
	Total	20.88	6.597	25
Total	10%	13.40	1.350	10
	20%	15.60	1.075	10
	30%	18.20	1.229	10
	40%	26.70	3.020	10
	control	29.30	1.059	10
	Total	20.64	6.527	50

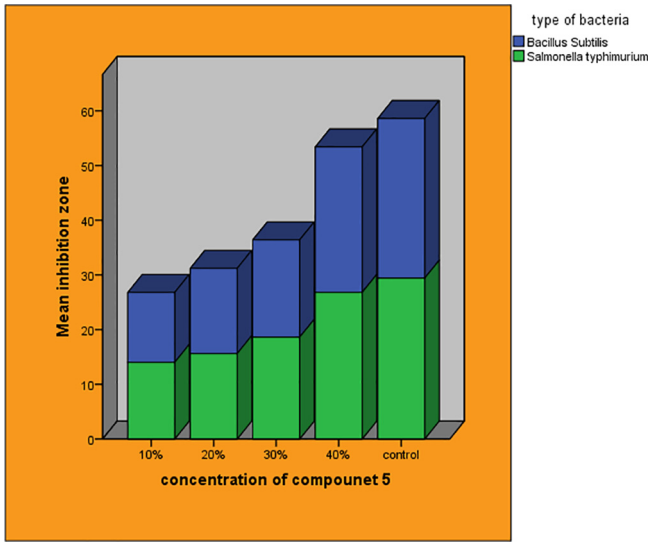

Fig. 2. effect of different concentrations of3-methyl-7-(5,6,7,8-tetra-hydronaphthalen-2yl)-4H-[1,2,4]triazino[3,4a]phthalazin-4one on inhibiting the growth of Bacillus Subtilis and Salmonella typhimurium.

C, 72.71; H, 5.49; N, 16.96; O, 4.84; found C, 72.69; H, 5.51; N, 16.94; O, 4.83.

2.3. *-methyl-7-(5,6,7,8-tetrahydronaphthalen-2yl)–2H- [1,2,4] triazino[3,4a] phthalazine (8)*

A compound 4 (0.01 mol ,2.9 g) and (0.01 mol, 0.9 g) Chloroacetone in dry xylene (40 mL) It has been heated for 8 h. under reflux. The solid which has been separated upon cooling has been filtered off and re-crystallized from the absolute ethanol to give **8**: White crystals; Yield 70%; m.p 205-206○C, (R_f = 0.60) ; ^{1}H NMR (DMSO d_6) δ: 2.350(s, 3H, CH3), 4.90 (s, 1H, CH of triazine moiety),07.16–08.21(m, 7H, Ar-H and NH of triazine); I.R. (KBr) v:3170 cm^{-1}(NH), 1620 cm^{-1}(C = N), 2895 cm^{-1}(C-Haliphatic); Anal. calcd. for $C_{21}H_{20}N_4$: C, 76.80; N, 17.06; H, 6.14; found: C, 76.79; H, 6.15; N, 17.02.

2.3.1. *6-(5,6,7,8-tetrahydronaphthalen-2yl)-[1,2,4]triazolo[3,4a] phthalazin-3(2H)- one (9)*

A compound 4 (0.01 mol, 2.9 g) and ethylchloroformate (0.02 mol, 2.1 g) in 20 mL of the pyridine has been heated for 12 h on water bath. Following the cooling, the reaction has been poured in ice water. The solid that has precipitated has been collected through by filtration, then it has been dried then crystallized from the ethanol in order to give **9**: pale yellow crystals; yield 60%; m.p 315-316○C; (R_f = 0.53). 1H NMR (DMSO d_6) δ: 6.93–7.90(m, 6H, Ar-H), 08.70 (s, 1H, NH); I.R. (KBr) v: 3220 cm^{-1}(NH), 1670 cm^{-1} (C = O), 1615 cm^{-1} (C = N); MS (70 eV) *m/z* (%): 317.14 (M+, 20). Anal. calcd. for $C_{19}H_{16}N_4O$: C, 72.13; H, 5.10; N, 17.71; O, 5.06; found C, 72.10; N, 17.60; H, 5.11; O, 5.04.

2.3.2. *6-(5,6,7,8-tetrahydronaphthalen-2-yl)-[1,2,4]triazolo[3,4a] phthalazine-3(2H)-thione (10)*

Carbon sulfide (2 mL) has been added drop wise with the stirring to compound 4 (0.01 mol, 2.9 g) in the absolute ethanol (10 mL) containing potassium hydroxide (0.01 mol). The mix has been diluted with the absolute ethanol (20 mL) then refluxed for 8 h period. The reaction mix has been filtered, concentrated, diluted by the water, and then neutralized using the acetic acid. The product that has been precipitated has been crystallized from the dioxane for the purpose of giving **10** : yellow crystals; yield 40%; m.p 295-297○C (R_f = 0.74); 1H NMR (DMSO-d 6) δ: 07.1–07.95 (m, 6H, Ar-H), 9.70(s, 1H, NH); I.R. (KBr) v: 3316 cm^{-1} (NH), 1610 cm^{-1} (C = N), 1237 cm^{-1} (CS); MS (70 eV) *m/z* (%): 334.11 (M+, 5). Anal. calcd. for $C_{19}H_{16}N_4S$: C, 68.65; N, 16.85; H, 4.85; S, 9.64; found C, 68.60; N, 16. 78; H, 4.81; S, 9.61

3. Results and discussion

The key intermediate in the synthesis of new phthalazine (5–10) is 1-hydrazineyl-4-(5,6,7,8-tetra-hydronaphthalen-2-yl)-1,2-di-hydrophthalazine (4), Which was prepared beforehand [21]. The corresponding triazino derivative (5) were given by condensation of compound 4 with the pyruvic acid .(Scheme 1). The infrared spectra for compound 5 showed absorption band of (C = O) at (1660 cm^{-1}) and (C–H aliphatic) at (2920 cm^{-1}). The reaction of compound 4 in absolute ethanol with diethyl oxalate by ring closure given compound (6). The I.R. spectra of the compounds 6 has shown a new absorption bands at (1689–1676 cm^{-1}) as a

Table 3
. The effect of different concentrations of7-(5,6,7,8-tetrahydronaphthalen-2-yl)–2H-[1,2,4]triazineo[3,4a]phthalazine-3,4dione on inhibiting the growth of Rhodococcus Equi and Escherichia coli.

Descriptive Statistics				
Dependent Variable: inhibition zone				
type of bacteria	concentration of compounet 6	Mean	Std. Deviation	N
Rhodococcus Equi	10%	13.80	3.493	5
	20%	18.60	6.465	5
	30%	18.00	1.000	5
	40%	27.80	3.114	5
	control	29.20	1.304	5
	Total	21.48	6.953	25
Escherichia coli	10%	14.60	2.702	5
	20%	18.80	6.301	5
	30%	22.40	6.066	5
	40%	26.80	4.382	5
	control	29.40	0.894	5
	Total	22.40	6.850	25
Total	10%	14.20	2.974	10
	20%	18.70	6.019	10
	30%	20.20	4.709	10
	40%	27.30	3.622	10
	control	29.30	1.059	10
	Total	21.94	6.846	50

result the stretched bond (C = O) groups. The ^{1}H NMR spectrum of compound 6 has shown a signal at chemical shift (δ = 8.20 ppm) For NH Assigned. the reaction of compound 4 with ethyl-bromoacetate yielded 7-(5,6,7,8-tetra-hydronaphthalen-2yl)–2H-[1,2,4]triazino[3,4a]phthalazin-3(4H)-one (7). Compound7 has been produced through the nucleophilic attack of the NH_2 of the hydrazino moiety to the acyl carbon of ester group and ring closure through a mechanism of SN2. The compound 7 I.R. spectrum showed an absorption band for (C = O) group at (1650 cm^{-1}) and (C–H Aliphatic) at (2910 cm^{-1}). The ^{1}H NMR spectrum of compound 7 has shown a singlet signal at (δ = 4.30 ppm) is due to proton in the methylene group (–CH_2-). Compound (4) with chloroacetone in the dry xylene afforded matching hydrazine that has undergone 1,3-tautomerism that has been succeeded by the ring closure for producing 1,2,4-triazino[3,4-a] phthalazine derivative (8). The infrared spectra of compound 5; at (1,620 cm^{-1}) and (2,895 cm^{-1}), corresponding to the (C = N) and (C–H Aliphatic) Respectively. The ^{1}H NMR spectrum of the compound8 give a clear single signal at chemical shift (δ = 8.28 ppm) due to NH group and single signal at chemical shift (δ = 2.35 ppm) due to three protons in the methyl group (–CH_3). On the other hand, cyclization of 4 with the use of the ethyl-chloroformate in the pyridine has given the equivalent triazolo derivative (9). The I.R. spectrum of the compound 9 has shown thas there is a (C = O) group at (1670 cm^{-1}). The ^{1}H NMR spectrum of the compound9 give a clear single signal at chemical shift (δ = 8.70 ppm) due to NH group. Cyclization of compound 4 utilizing CS_2 in alcoholic potassium hydroxide has given the equivalent triazolo derivation (10). The I.R. spectrum of the compound 10 has shown the existence of an (NH)group at (3316 cm^{-1}) and (C = S) group at (1237 cm^{-1}). The ^{1}H NMR spectrum has shown a signal at chemical shift (δ = 9.70 ppm) for assigned NH group.

3.1. Antibacterial activity

Antimicrobial resistance appears when bacteria, viruses, fungi, and parasites change over time, and they become less responsive to drugs, making infections more difficult to treat and increasing the risk of disease, severe illness and death spread. Our ability to treat common infections continues to be threatened by the emergence and outbreaks of drug-resistant pathogens that create new resistance mechanisms and lead to the emergence of antimicrobial resistance. Of particular concern is the rapid global spread of bacteria that are resistant to multiple or all drugs (also known as "intractable germs") that cause infections that cannot be treated with the current presence of antimicrobial drugs, such as antibiotics. Hardly any new antimicrobials are in clinical development. In 2019, the organization identified 32 antibiotics under clinical development to treat pathogens on the organization's priority pathogens list, of which only six were classified as innovative. Moreover, difficulty in obtaining quality antimicrobials remains a major problem, and countries of all levels of development are affected by shortages of antibiotic supplies, particularly in health care systems.

Antimicrobial resistance seems naturally over time, generally thru genetic changes. Antimicrobial resistance is determined in humans, animals, food, plants, and the surroundings (in water, soil, and air), and can be transmitted from person to individual or between people and herds of animals, such as animal supply foods. The principal drivers of this resistance consist of misuse and overuse of antimicrobials. The lack of get entry to to easy water,

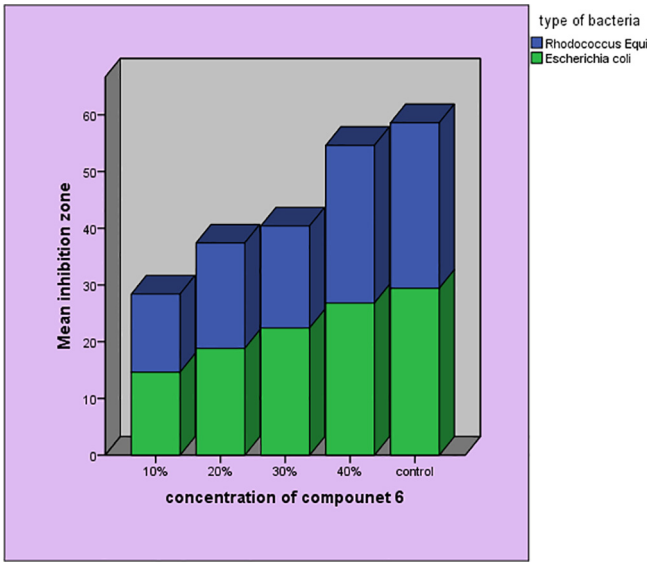

Fig. 3. effect of different concentrations of7-(5,6,7,8-tetrahydronaphthalen-2-yl)–2H-[1,2,4]triazineo[3,4a]phthalazine-3,4dione on inhibiting the growth of Rhodococcus equi and Escherichia coli.

sanitation, and hygiene offerings for each human beings and animals; Weak contamination and sickness prevention and manage in fitness care services and on farms; Insufficient get entry to to right and inexpensive medicines, vaccines, and diagnostics; Lack of cognizance and knowledge; The lack of enforcement of the legislation. Table 1 indicates the impact of compound 7 on some genera of poor and effective micro organism for the Gram stain, which ambitions the phone wall region of the micro organism fantastic for the Gram stain and inhibits the system of protein synthesis, the place 4 concentrations of this compound had been organized 10,20,30,40%, the place the excessive attention of this compound used to be forty p.c Better effects in inhibiting bacterial increase in contrast to different concentrations As proven in Fig. 1.

Table 2 shows the effect of different concentrations of compound 5 on inhibiting the growth of both positive and negative bacteria for the Gram stain, as multiple concentrations of this compound were prepared, which are 10, 20, 30, 40%, as there were no significant differences between the concentrations prepared from this compound. There are significant differences between each concentration and control, as the concentration of 40% gave the best inhibition of the growth of positive and negative bacteria for the Gram stain compared with the rest of the concentrations as shown in Fig. 2.

Table 3 shows the effect of different concentrations of compound 6 on inhibiting the growth of both positive and negative bacteria for the Gram stain, as multiple concentrations of this compound were prepared, which are 10, 20, 30, 40%, as there were no significant differences between the concentrations prepared from this compound. There are significant differences between each concentration and control, as the concentration of 40% gave the best inhibition of the growth of positive and negative bacteria for the Gram stain compared with the rest of the concentrations as shown in Fig. 3

4. Conclusion

The reactions were monitored by TLC technique and determination of retention factor (R_f) for some compounds. The structure formula of these compounds were confirmed by using physical and spectral data (FT-IR, ^{1}H NMR, GC–MS). The multiple concentrations of this compound were prepared, which are 10, 20, 30, 40%, as there were no significant differences between the concentrations prepared from this compound. There are significant differences between each concentration and control, as the concentration of 40% gave the best inhibition of the growth of positive and negative bacteria.

CRediT authorship contribution statement

Mohammed Abed Kadhim: Conceptualization, Methodology, Software, Data curation, Writing - original draft. **Saddam Mohammed Abed:** Visualization, Investigation, Supervision. **Najeeb Mohammed Hussein:** Software, Validation, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] F Al'-Assar, KN Zelenin, EE Lesiovskaya, IP Benzhan, BA Chakchir. Synthesis and pharmacological activity of 1-hydroxy-, 1-amino-, and1-hydrazino-substituted 2,3-dihydro-1H-pyrazolo[1,2-a]pyridazine-5,8-diones and 2,3-dihydro-1H-pyrazolo[1,2-b]phthalazine-5,10- diones. Pharm. Chem. J. 2002. 36, 598–603

[2] R.P. Jain, J.C. Vederas, Structural variations in keto-glutamines for improved inhibition against hepatitis A virus 3C proteinase, Bioorg Med. Chem. Lett. 14 (14) (2004) 3655–3658.

[3] R.W. Carling, K.W. Moore, L.J. Street, D. Wild, C. Isted, P.D. Leeson, S. Thomas, D. O'Connor, R.M. McKernan, K. Quirk, S.M. Cook, JRAtack, K.A. Wafford, S.A. Thompson, G.R. Dawson, P. Ferris, J.L. Castro, 3-Phenyl-6-(2-pyridyl) methyloxy-1,2,4-triazolo[3,4-a]phthalazines and analogues: high-affinity gamma-aminobutyric acid-A benzodiazepine receptor ligands with alpha 2, alpha 3, and alpha 5-subtype binding selectivity over alpha 1, J. Med. Chem. 47 (2004) 1807–1822.

[4] S. Demirayak, A.C. Karaburun, R. Beis, Some pyrrole subst ituted aryl pyridazinone and phthalazinone derivatives and their antihypertensive activities, Eur. J. Med. Chem. 39 (2004) 1089–1095.

[5] G.R. Madhavan, R. Chakrabarti, S.K.B. Kumar, P. Misra, R.N.V.S. Mamidi, V. Balraju, K. Kasiram, R.K. Babu, J. Suresh, B.B. Lohray, V.B. Lohrayb, J. Iqbal, R. Rajagopalan, Novel phthalazinone and benzoxazinone containing thiazolidinediones as antidiabetic and hypolipidemic agents, Eur. J. Med. Chem. 36 (2001) 627–637.

[6] E.M. Lenz, L.D. Wilson, B. Wright, E.A. Partridge, C.T. Rodgers, P.R. Haycock, J.C. Lindon, J.K. Nicholson, A comparison of quantitative NMR and radiolabelling studies of the metabolism and excretion of Statil (3-(4-bromo-2-fluorobenzyl)-4-oxo-3H-phthalazin-1-ylacetic acid) in the rat, J. Pharm. Biomed. Anal. 28 (2002) 31–43.

[7] S. Grasso, G. De Sarro, A. De Sarro, N. Micale, M. Zappalà, G. Puja, M. Baraldi, C. De Micheli, Synthesis and anticonvulsant activity of novel and potent 6,7-methylenedioxyphthalazin-1(2H)-ones, J. Med. Chem. 43 (2000) 2851–2859.

[8] Milind. Rane and Umesh. Bhadade, "Multimodal Biometric Identification using Feature Fusion", Test Engineering and Management, Page No. 29604 – 29614, 2020.(Scopus Published)

[9] Milind. Rane and Umesh. Bhadade, "Face and Palmprint Biometric Recognition by using Weighted Score Fusion Technique", IEEE International Conference in Information Processing, PuneCon 2020.

[10] Milind. Rane and Umesh. Bhadade, "Dual Palm print based Human Recognition using Fusion", International Conference on Innovations in Information and Communication Technologies,

[11] S.R. Sivakumar, Kishore Guanasam, S. Ramachandran, JT Leonard, Pharmacological evaluation of some new 1-substituted-4-hydroxyphthalazines Eur, J. Med. Chem. 37 (2000) 793–801.

[12] J. Munín, L. Santana, F. Eu Uriarte, E Quezada Borges, A compara tive synthesis of 6-benzyl-2,3-dihydroimidazo[2,1-a]phthalazine and 2H-7-benzyl-3,4-dihydropyrimido[2,1-a]phthalazine, Tetrahedron Lett. 56 (2015) 828–830.

[13] Milind E. Rane, Umesh S Bhadade. Multimodal System using Radon-Gabor Transform. International Conference on Energy, Communication, Data Analytics and Soft Computing (ICECDS-2017).

[14] Milind Rane, Tejas Latne, Umesh Bhadade, Biometric Recognition Using Fusion, ICDSMLA 2019 (2019) 1320–1329.

[15] Y. Nomoto, H. Obase, T.H. Takai, M. Teranishi, J. Nakamura, K. Kubo, Studies on cardiotonic agents. II. Synthesis of novel phthalazine and1,2,3-benzotriazine derivatives, Chem. Pharm. Bull. 38 (1990) 2179–2183.

[16] Bilal Alhayani, Husam Jasim Mohammed, Ibrahim Zeghaiton Chaloob, Jehan Saleh Ahmed, Husam Jasim Mohammed, Ibrahim Zeghaiton Chaloob, Jehan Saleh Ahmed, Effectiveness of artificial intelligence techniques against cyber security risks apply of IT industry, Mater. Today: Proc. (2021), https://doi.org/10.1016/j.matpr.2021.02.531.

[17] Milind E. Rane, Umesh S. Bhadade, Comparative Study of ROI Extraction of Palmprint, IJCSN Int. J. Comput. Sci. Network 5 (2) (2016).

[18] M. Johensen, K. Rehse, H. Pertz, J.P. Stasch, E. Bischoff, New antithrombotic1-phthalazinamines with serotonin antagonistic properties, Arch. Pharm. 336 (2012) 591–597.

[19] B. Alhayani, A.A. Abdallah, Manufacturing intelligent Corvus corone module for a secured two way image transmission under WSN, Eng. Comput. 37 (9) (2020) 1–17.

[20] Bilal Alhayani, Sara Taher Abbas, Dawood Zahi Khutar, Husam Jasim Mohammed,Best ways computation intelligent of face cyber attacks, MaterialsToday Proceedings,2021,https://doi.org/10.1016/j.matpr.2021.02.557

[21] A. Pramanik, Synthesis of biologically important phthalazinones, 2,3-benzoxazin-1-ones and isoindolinones from ninhydrin and their antimicrobial activity, Tetrahedron Lett. 54 (24) (2013) 3137–3143.

Further Reading

[22] N.P. Shetgiri, B.K. Nayak, Synthesis and antimicrobial activities of oxadiazoles, phthalazines and indolinones, Indian J. Chem. 44B (2005) 1267–1272.

[23] A.K. Chakraborti, B. Gopalakrishnan, M.E. Sobhia, A. Malde, Comparative molecular field analysis (CoMFA) of phthalazine derivatives as phosphodiesterase IV inhibitors, Bioorg. Med. Chem. Lett. 13 (2003) 2473–2479.

[24] X. Cockcroft, K.J. Dillon, L. Dixon, J. Drzewiecki, F. Kerrigan, V.M. Loh Jr, N.M.B. Martin, K.A. Menear, G.C.M. Smith, Phthalazinones 2: Optimisation and synthesis of novel potent inhibitors of poly(ADPribose) polymerase, Bioorg. Med. Chem. Lett. 16 (2006) 1040–1044.

[25] B. Al Hayani, H. Ilhan, Image transmission over decode and forward based cooperative wireless multimedia sensor networks for Rayleigh fading channels in medical internet of things (MIoT) for remote health-care and health communication monitoring, J. Med. Imag. Health Info. 10 (1) (2020) 160–168.

[26] B.S.A. Al Hayani, H. Ilhan, Visual Sensor Intelligent Module Based Image Transmission in Industrial Manufacturing for Monitoring and Manipulation problems, J. Intell. Manufact. 4 (2020) 1–14.

[27] V.M. Jr Loh, X. Cockcroft, K.J. Dillon, L. Dixon, J. Drzewiecki, P.J. Eversley, S. Gomez, J. Hoare, F. Kerrigan, I.T. Matthews, K.A. Menear, N.M. Martin, R.F. Newton, J. Paul, G.C. Smith, J. Vile, A.J. Whittle, Phthalazinones. Part 1: The design and synthesis of a novel series of potent inhibitors of poly(ADP-ribose) polymerase, Bioorg. Med. Chem. Lett. 15 (2005) 2235–2238.

[28] B. ALhayani, H. Ilhan, Efficient cooperative imge transmission in one-Way mult-hop sensor network, Int. J. Elect. Eng. Edu. 57 (2) (2020) 321–339.

[29] B. .Alhayani and Milind Rane,"face recognition system by image processing" International journal of electronics and communication engineering & technology (IJCIET),vol.5, no.5, pp. 80–90. 2014.

[30] W.M. Eldehna, H.S. Ibrahim, H.A. Abdel-Aziz, N.N. Farrag, M.M. Youssef, Design, synthesis and in vitro antitumor activity of novel Nsubstituted-4-phenyl/benzylphthalazin-1-ones, Eur. J. Med. Chem. 89 (2015) 549–560.

[31] N. Haider, T. Kabicher, J. Käferböck, A. Plenk, Synthesis and in-vitro antitumor activity of 1-[3-(indol-1-yl)prop-1-yn-1-yl]phthalazines and related compounds, Molecules. 12 (2007) 1900–1909.

[32] J.S. Kim, H.J. Lee, M.E. Suh, H.Y. Choo, S.K. Lee, H.J. Park, C. Kim, S.W. Park, C.O. Lee, Synthesis and cytotoxicity of 1-substituted 2-methyl-1H-imidazo[4,5-g] phthalazine-4,9-dione derivatives, Bioorg. Med. Chem. 12 (2004) 3683–3686.

[33] S. Demirayak, A.C. Karaburun, I. Kayagil, K. Erol, B. Sirmagul, Some pyridazinone and phthalazinone derivatives and their vasodilator activities, Arch. Pharm. Res. 27 (2004) 13–18.

[34] M.A. El-Hashash, D.B. Guirguis, A.M. Nayera, M.A. Kadhim, Org. Lett. 3 (2014) 1701–1705.

[35] C.S. Leifert, H.L. Chidburee, S. Hampson, S. Workman, D. Sigee, H.A.S. Epton, A. Harbour, J. Appl. Bacteriol. 78j (1995) 1365–2672.