Journal of Medicinal and Chemical Sciences 6 (2023) 931-937

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Original Article

Antimicrobial and Antioxidant Activity of Heterocyclic Compounds Derived from New Chalcones

Raed Muslim Mhaibes*

Department of Biochemistry, College of Medicine, University of Misan, Misan, Iraq

ARTICLE INFO

Article history

Receive: 2022-07-25
Received in revised: 2022-08-14
Accepted: 2022-10-18
Manuscript ID: JMCS-2209-1761
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Fatimah Ramezani
Editor who approved publication:
Dr. Zeinab Arzehgar

DOI:10.26655/JMCHEMSCI.2023.4.25

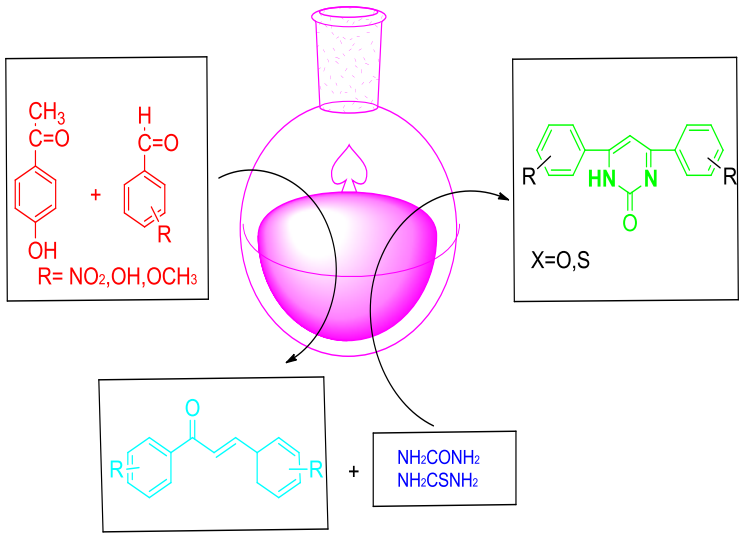
KEYWORDS

Chalcones
Pyrimidine derivatives
FTIR
^{1}H-NMR and biological activity

ABSTRACT

In this study, new chalcones was prepared from reaction of 4-hydroxy acetophenone with different aldehydes in a basic medium, then new pyrimidine derivatives were synthesized from reaction of prepared chalcones with urea and thiourea, the physical and chemical properties of synthesized compounds were studied using FT-IR, ^{1}H-NMR, melting points. Likewise, the possible biological and antioxidant activity of prepared compounds was studied.

GRAPHICAL ABSTRACT



* Corresponding author: Raed Muslim Mhaibes
✉ E-mail: Email: raid.mcm@uomisan.edu.iq

Introduction

Chalcone compounds, which derived from 1,3-diphenyl-2-propene-1-one, are possessing chromophore moiety in their structures such as ketoethylenic group (–CO–CH=CH-), usually exhibiting different colors [1]. Their abundance in edible plants and is considered as the flavonoids and iso-flavonoids precursors, give the chalcones their importance. This type of compound might be synthesized via the Claisen-Schmidt condensation reaction. They have various applications in terms of biological activities and industrial uses. The chalcones synthesis can be carried out by following the standard methods and microwave aided approach [2, 3]. On the other hand, pyrimidine heterocyclic compounds possess in their structures an unsaturated-six-membered ring with two nitrogen atoms located at the first and the third locations of the ring [4, 5]. The derivatives of pyrimidine play a significant role in medicinal chemistry as it is reported that they exhibit a wide range of biological activities, including anthelmintic, antimicrobial, and anti-inflammatory activities. Many other biological applications are shown in the literature belonged to this class of organic compounds such as being anti-tubercular, antimalarial, antiviral, anticancer, and analgesic. These reports and previous studies encourage the current research for synthesizing the novel derivatives of pyrimidine and investigating their biological activities such as analgesic and anti-inflammatory activities [6].

Materials and Methods

The solvents and reagents employed in this study were used with no further purification. The open-glass capillaries method was used to record the melting points of the prepared compounds with no correction. In addition, Affinity-1 Shimadzu model of FT-IR spectrometer was used to record the Infrared spectra in forms of KBr pellets. However, Brucker model of NMR instrument with spectrospin ultrashield magnet 300 MHz was used to scan the ^{1}H-NMR spectra. The internal reference was TMS and the solvent was DMSO-d_6 for identifying the organic inhibitor.

Synthesis of chalcones ($\mathbf{I_{a-c}}$) [7]

5 mmol of 4-hydroxyacetophenone and 5 mmol of aldehyde derivatives were mixed in 20 mL of EtOH in a round bottom flask, and then 6 mL of 40% NaOH solution was added dropwise and the reacting mixture was kept stirring and temperature under 10 °C for 12 hours. Thereafter, the mixture was kept for 24 hours at room temperature. Next, 1.5mL of 10% HCI was added dropwise to the mixture. The produced compound was then subjected to filtration and recrystallization from CH_3CH_2OH.

Synthesis of compounds ($\mathbf{I_{d-i}}$) [8]

A mixture of Chalcones ($\mathbf{I_{a-c}}$) (0.6 g, 0.01 mol), with NH_2CONH_2 and NH_2CSNH_2 (0.6 g, 0.01 mol) were dissolved in EtOH (10 mL). 40% aqueous NaOH (10 mL) was added slowly with constant stirring. The reaction mixture was stirred for 4 hours, and then 100 mL of cold H_2O was added with continuous stirring for two hours. After that, the mixture was kept in a cold place for 12 hours, and the product recrystallized was using C_2H_5OH as a solvent.

Biological activity [9]

The disk diffusion method was used to test the biological activity of the prepared compounds. The test was carried out against one strain of (*E.coli*), gram-negative bacteria, and one (*Staphylococcus Aurous*), gram-positive bacteria, as well as (*Aspergillus niger*), the fungi. The sterilization of the Petri dishes and prepared agar was conducted by autoclaving at 121 °C and for 15 min. The agar plates were uniformly surface inoculated from the broth culture of the tested microorganisms. 6 mm in diameter spaced apart holes were suitably made for the solidified medium and 100 µl of the synthesized compounds (0.025 mg of the produced material dissolved in DMSO solvent (1 mL)) was filled in. The prepared plates were subjected to 37 °C incubation for 24 hours to examine the inhibition zones that the compounds are causing on the bacteria. Table 1 presents the results of the preliminary screening test.

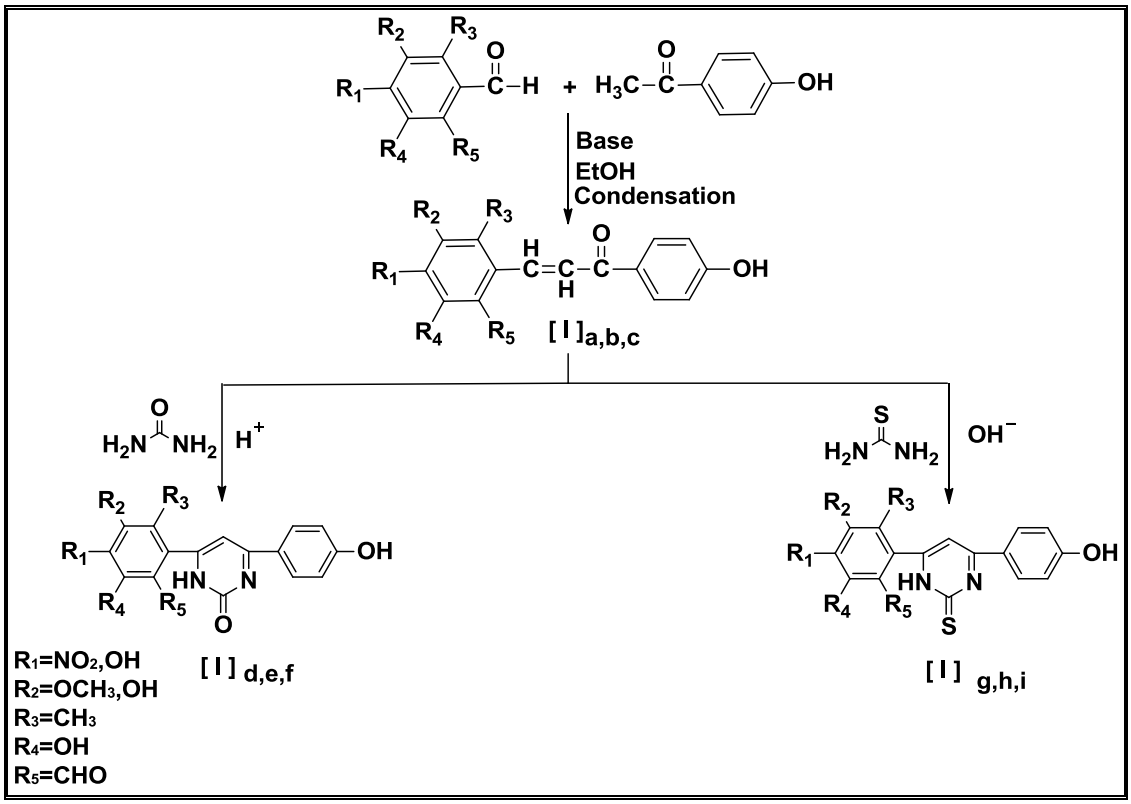
Antioxidant activity [10]

The solution was prepared by dissolving 4 g of DPPH in 100 mL of MeOH. Different concentrations were prepared from the some of the synthesized compounds, including 25, 50 and 100 ppm, by dissolving 1 milligram of the compound in 10 mL of MeOH to achieve the 100 parts per million, followed by diluting the solution to 25 and 50 parts per million. The same way was used for the concentrations, 1 mL of normal, or diluted solution such as 25, 50, and 100 ppm was poured to the solution in the test-tube that contains 1 mL DPPH. Each solution was measured in terms of the absorbance using spectrophotometer at wavelength 517 nm after incubation for 1 hour and at 37 °C.

(Blank absorption - sample absorption/blank absorption) × 100 = 1 %

Results and discussion

In the current study, the new chalcones ($\mathbf{I_{a-c}}$) was synthesized from reaction of 4-hydroxyacetophnone with aldehyde derivatives, and then from reaction of prepared chalcones with urea and thiourea prepared compounds ($\mathbf{I_{d-i}}$), as indicated in Scheme 1. The vibration band of the (OH) group (stretch) appeared at (3458-3348) cm^{-1} and at (1315-1335) cm^{-1} for the (C=S) group, whereas, the (C=N) pyrimidine ring at (1610-1630) cm^{-1} [11]. The infrared spectra of compounds ($\mathbf{I_{a-c}}$) and ($\mathbf{I_{d-i}}$) are depicted in Figures 1, 2 and 3. ^{1}H-NMR spectrum compound ($\mathbf{I_c}$), δ 3.4 (s, 3H, OCH_3), 5.2 (s, 1H, CH,N), 6.6-8.3 (m, 8H, H_{arom}), 7.4 (s, 1H, H pyrimidine ring), and 9.2 (s, 1H, OH). [12]. The compounds ($\mathbf{I_b}$), ($\mathbf{I_e}$), and ($\mathbf{I_h}$) gives the best biological and antioxidant activity, as provided in Table 1 and Figure 4.



Scheme 1: Synthesis compounds $\mathbf{I_{a-c}}$ **and** $\mathbf{I_{d-i}}$

Compound (I_a)

Brown solid, yield 80%, mp 110-112 °C, IR (KBr) (ν_{max}/ cm^{-1}): 3358, 3109, 2927, 2854, 1620, 1577, 1517, 1348. *v*(OH), *v*(C-H) aromatic, *v*(C-H) aliphatic, *v*(C=C) aromatic, *v*(C=C) Chalcone and $\nu(NO_2)$ respectively. ^{1}H-NMR (300 MHz, DMSO): δ 8.4 (d, 2H, CH=CH), 7.6-8.3 (d, J=12 Hz, 8H, aromatic rings), and 9.5 (S, 1H, OH).

Compound (I_b)

Brown solid, yield 90%, mp 120-122 °C, IR (KBr) (ν_{max}/ cm^{-1}): 3458, 3100, 2927, 2854, 1654, 1600, 1577, 1560. *ν*(OH), *ν*(C-H) aromatic, *ν*(C-H) aliphatic,*ν*(CHO),*ν*(C=C) aromatic and Chalcone respectively.

Compound (I_c)

White solid, yield 70%, mp 170-172 °C, IR (KBr) (ν_{max}/ cm^{-1}): 3348, 3090, 2945, 2837, 1662, 1583, 1232. *ν*(OH), *ν*(C-H) aromatic, *ν*(C-H) aliphatic, *ν*(C=C) chalcone, *ν*(C-O-C) respectively.

Compound (I_d)

Yellow solid, yield 70%, mp 205-207 °C, IR (KBr) (ν_{max}/ cm^{-1}): 3360, 3080, 2955, 2850, 1645, 1625, 1580, 1507, 1350. *ν*(OH), *ν*(C-H) aromatic, *ν*(C-H) aliphatic, *ν*(C=O)amid, *ν*(C=N)and *ν*(NO_2) respectively . ^{1}H NMR (300 MHz, DMSO): *δ* 3.30 (s, 1H, -CH of pyrimidine ring), 7.5-8.28 (m, 9H, Ar-H), 8.4 (s, 1H, NH), and 10.5 (s, 1H, OH).

Compound (I_e)

Yellow solid, yield 60%, mp 220-222 °C, IR (KBr) (ν_{max}/ cm^{-1}): 3340, 3065, 2959, 2870, 1650, 1630, 1615, 1600. *ν*(OH), *ν*(C-H) aromatic, *ν*(C-H) aliphatic, *ν*(CHO),*ν*(C=O)amide, *ν*(C=N) and *ν*(C=C) chalcone respectively.

Compound (I_f)

White solid, yield 65%, mp 210-212 °C, IR (KBr) (ν_{max}/ cm^{-1}): 3420, 3050, 2970, 2840, 1640, 1620, 1570, 1240. *ν*(OH), *ν*(C-H) aromatic, *ν*(C-H) aliphatic, *ν*(C=O)amide, *ν*(C=N), *ν*(C=C) Chalcone and *ν*(C-O-C) respectively.

Compound (I_g)

Brown solid, yield 55%, mp 260-262 °C, IR (KBr) (ν_{max}/ cm^{-1}): 3380, 3040, 2980, 2850, 1630, 1510, 1345, 1320. *ν*(OH), *ν*(C-H) aromatic, *ν*(C-H) aliphatic,*ν*(C=N), *ν*(NO_2 and *ν*(C=S) respectively.

Compound (I_h)

Green solid, yield 70%, mp 280-282 °C, IR (KBr) (ν_{max}/ cm^{-1}): 3360, 3080, 2950, 2866, 1625, 1620, 1600, 1315. *ν*(OH), *ν*(C-H) aromatic, *ν*(C-H) aliphatic, *ν*(C=N), *ν*(CHO), *ν*(C=C) chalcone and *ν*(C=S) respectively.

Compound (I_i)

Milky solid, yield 80%, mp 270-272 °C, IR (KBr) (ν_{max}/ cm^{-1}): 3420, 3050, 2945, 2838, 1670, 1610, 1595, 1335. *ν*(OH), *ν*(C-H) aromatic, *ν*(C-H) aliphatic, *ν*(CHO), *ν*(C=N), *ν*(C=C) chalcone and *ν*(C=S) respectively. ^{1}H NMR (300 MHz, DMSO): *δ* 3.50 (s, 1H, -OCH_3), 7.0-8.20 (m, 9H, Ar-H), 8.5 (s, 1H, NH), and 10 (s, 1H, OH).

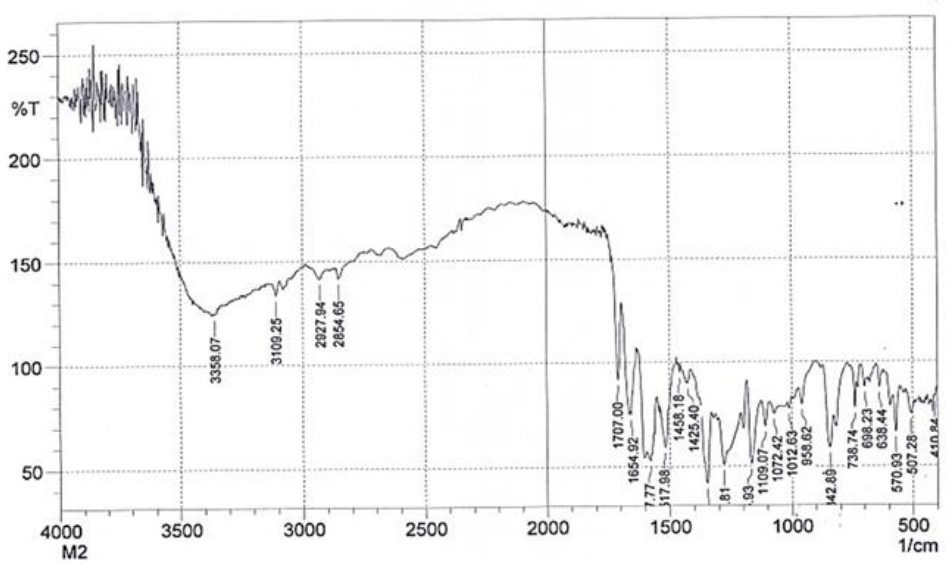


Figure 1: FT-IR spectrums of chalcones (**I_a**)

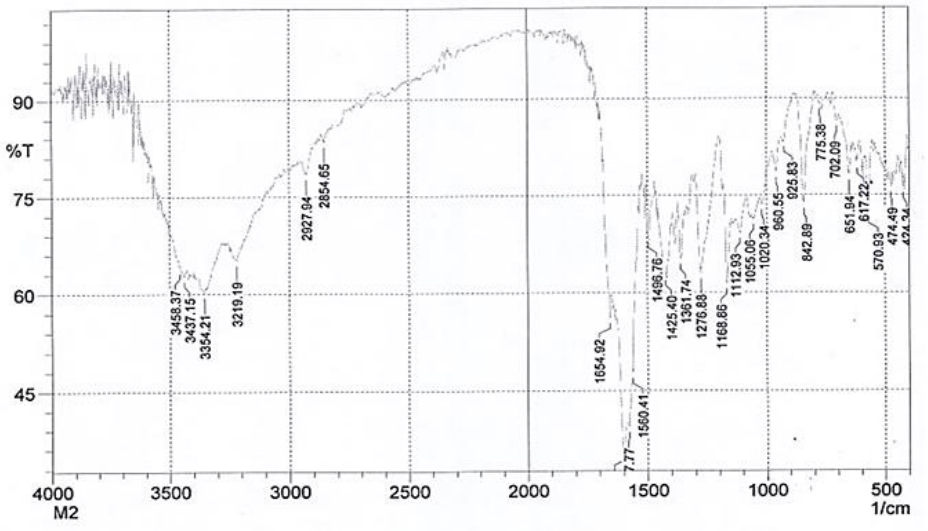


Figure 2: FT-IR spectrums of chalcones (**I_b**)

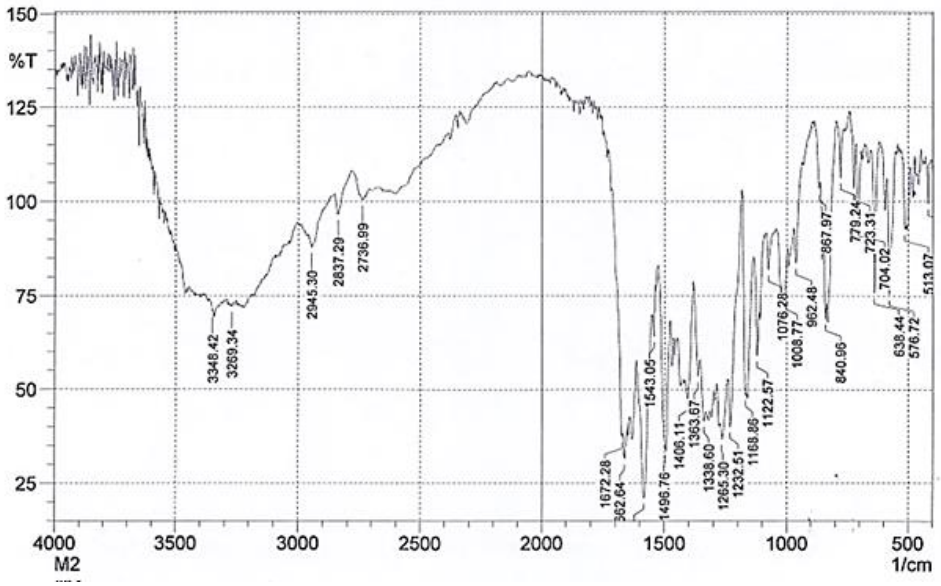


Figure 3: FT-IR Spectrums of Chalcones (**I_c**)

Table 1: Biological study of prepared compounds

Code	*E.Coli*	*Staphylococcus aureus*	*Aspergillus niger*
I_a	-	-	25 mm
Ib	14 mm	19 mm	25 mm
Ic	10 mm	15 mm	20 mm
Id	-	-	25 mm
Ie	16 mm	22 mm	22 mm
If	5 mm	15 mm	20 mm
Ig	5 mm	10 mm	15 mm
Ih	13 mm	18 mm	27 mm
Ii	10 mm	15 mm	15 mm
Ofoxacin	29 mm	-	-
Penicillin	-	27 mm	-
Fluconazole	-	-	28 mm

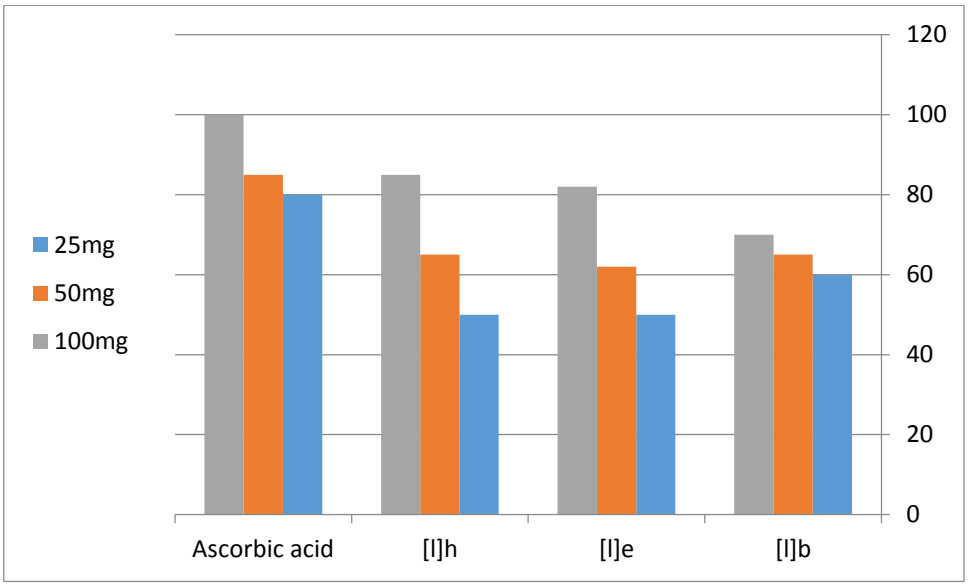


Figure 4: Antioxidant activity I_b, I_e and I_h

Conclusion

The new prepared compounds were synthesized from reaction of Chalcones with urea, thiourea, and the new prepared Chalcones have a lot of an electron-donating group. This donating group gave more activity for the prepared compounds against ant-bacterial and anti-fungal. The prepared compounds were characterized using spectroscopic techniques (FT-IR and ^{1}H-NMR). The biological and antioxidant activity of three prepared compounds I_b, I_e, and I_h were better than another prepared compounds because they have more an electron donating groups.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

The author declared that they have no conflict of interest.

ORCID

Raed Muslim Muhiebes

https://orcid.org/0000-0002-4835-0873

References

[1]. Kachroo M., Panda R., Yadav Y., Synthesis and biological activities of some new pyrimidine derivatives from chalcones, *Der Pharma Chemica*, 2014, **6**:352 [Google Scholar]

[2]. Ahmad M.R., Sastry V.G., Bano N., Anwar S., Synthesis of novel chalcone derivatives by conventional and microwave irradiation methods and their pharmacological activities, *Arabian Journal of Chemistry*, 2016, **9**:S931 [Crossref], [Google Scholar], [Publisher]

[3]. Maleki A.R., Nateghi L., Rajai P., 'The Effect of Microwave Pretreatment on the Extraction Rate of Flavonoid, Anthocyanins, Antioxidant Compounds and Antimicrobial Activity of Punica Granatum Var. Pleniflora (Persian Golnar)', *Chemical Methodologies*, 2022, **6**:280 [Crossref], [Google Scholar], [Publisher]

[4]. Sharma V., Chitranshi N., Agarwal A.K., Significance and biological importance of pyrimidine in the microbial world, *International journal of medicinal chemistry*, 2014, **2014**:202784 [Crossref], [Google Scholar], [Publisher]

[5]. Rehan T.A., Lami N., Khudhair N., 'Synthesis, Characterization and Anti-corrosion Activity of New Triazole, Thiadiazole and Thiazole Derivatives Containing Imidazo[1,2-a]pyrimidine

Moiety', *Chemical Methodologies*, 2021, **5**:285 [Crossref], [Google Scholar], [Publisher].
[6]. Misra A., Jain S., Kishore D., Dave V., Reddy K.R., Sadhu V., Dwivedi J., Sharma S., A facile one pot synthesis of novel pyrimidine derivatives of 1, 5-benzodiazepines via domino reaction and their antibacterial evaluation, *Journal of microbiological methods*, 2019, **163**:105648 [Crossref], [Google Scholar], [Publisher]
[7]. Adam R.W., Al-Labban H.M.Y., Kadhim I.N., Aljanaby A.A.J., Synthesis, characterization, and antibacterial activity of some new pyrimidine derivatives from chalcone derivatives, *Drug Invention Today*, 2019, **11**:1732 [Google Scholar], [Publisher]
[8]. Tomma J.H., Khazaal M.S., Al-Dujaili A.H., Synthesis and characterization of novel Schiff bases containing pyrimidine unit, *Arabian Journal of chemistry*, 2014, **7**:157 [Crossref], [Google Scholar], [Publisher]
[9]. Jasim S., Mustafa Y., 'New fused-coumarin composites: synthesis, anticancer and antioxidant potentials evaluation', *Eurasian Chemical Communications*, 2022, **4**:607 [Crossref], [Google Scholar], [Publisher]
[10]. Muhiebes R.M., O Al-Tamimi E., 'Modification of Creatinine to Form New Oxazepane Ring and Study Their Antioxidant Activity', *Chemical Methodologies*, 2021, **5**:416 [Crossref], [Google Scholar], [Publisher]
[11]. Al-Haidari A.S., Al-Tamimi E.O., 'Synthesis of new derivatives of 1,3,4-thiadiazole and 1,3,4-oxadiazole on cyclic imides and studying their antioxidant', *Eurasian Chemical Communications*, 2021, **3**:508 [Crossref], [Google Scholar], [Publisher]
[12]. Hussien H.A.K., Al-Messri Z.A.K., 'Synthesis, characterization and evaluation of 5-alkylidene meldrum's acid derivatives as multifunction lubricating oil additives', *Eurasian Chemical Communications*, 2021, **3**:598 [Crossref], [Google Scholar], [Publisher].
[13]. Al-Noor T.H., Ali A.M., Al-Sarray A.J., Al-Obaidi O.H., Obeidat A.I., Habash R.R., A Short Review: Chemistry of Curcumin and Its Metal Complex Derivatives, *Journal of University of Anbar for Pure Science,* 2022, **16**:20 [Google Scholar], [Publisher]
[14]. Al-Sarray A.J., Al-Mussawi I.M., Al-Noor T.H., Abu-Zaid Y., Organo-Clay Composites of Intercalated 4-Methylaniline and Its Schiff Base Derivative: Preparation and Characterization, *Journal of Medicinal and Chemical Sciences*, 2022, **5**:1094 [Crossref], [Google Scholar], [Publisher]

HOW TO CITE THIS ARTICLE
Raed Muslim Mhaibes. Antimicrobial and Antioxidant Activity of Heterocyclic Compounds Derived from New Chalcones. *J. Med. Chem. Sci*., 2023, 6(4) 931-937
https://doi.org/10.26655/JMCHEMSCI.2023.4.25
URL: http://www.jmchemsci.com/article_159207.html