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Preparation and characterization of some heterocyclic compounds derivatives as active hypoglycemic from Chalcones

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Abstract

This study aimed to synthesis and characterize heterocyclic compounds Pyrazolines and pyrimidine as hypoglycemic drugs. These compounds prepared by reacting hydrazine, urea, and thiourea with the appropriate Chalcones 2(a-f), using ethanol solvent and heated at temperature (78-80^{0}C) in moderate yields (58-86) %. The newly synthesized pyrazolines and pyrimidine have been characterized by element C.H.N analyzer, IR (Infrared Radiation) spectra and UV (Ultraviolet and Visible) spectra and ^{13}C-NMR (Carbon-13 Nuclear Magnetic Resonance) spectra. The activity of synthesized compounds (2c and 2f) hypoglycemic was tested in vivo. The results of this study approved the ability of these compounds to act significantly as hypoglycemic drugs and reduced the blood glucose level in hyperglycemic experimental animals. The author recommends to do another studies to investigate the antibacterial, antifungal and antioxidant activities of these compounds.

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Keywords: Chalcones, Thiourea, Urea, Heterocyclic, Antibacterial, Synthesis of Pyrazoline & Pyrimidine.

Introduction

The heterocyclic compound belongs to a major class of organic chemical compounds and identified by its unique feature. Some or all of the atoms in their molecules are connected in rings comprising at least one atom of an element other than carbon (C) (Bhat *et al.*, 2005). An example of these compounds is pyrazoline

and pyrimidines **Figure (1)**. Chalcone compounds from known compounds are used in the synthesis of heterocyclic compounds (Kalirajan *et al.,* 2007). Pyrazoline is a class of compounds (Sushama *et al.,* 2008), which has many applications in a different field (Harinadha *et al.,* 2007). Also, pyrazolines have played a crucial part in the development of theory in heterocyclic chemistry and used extensively in organic synthesis (Adel *et al.,* 2007). These compounds pyrazoline derivatives promise interesting in diverse pharmacological activities like antimicrobial, anti-inflammatory, analgesic, antidepressant, antitubercular and antimalarial activities (Sahu *et al.,* 2008). The antipyretic, anti-inflammatory and analgesic properties are expressed by many compounds like phenylbutazone, oxyphenbutazone, celecoxib that belongs to pyrazoles (Palaska *et al.,* 2001). Also, pyrimidine derivatives play essential roles and have many biological activities such as anticancer, antitubercular, antimalarial properties (Anupama *et al.,* 2012). This study designed to synthesize some new heterocyclic compounds Pyrazolines and pyrimidine in Iraq as hypoglycemic drugs.

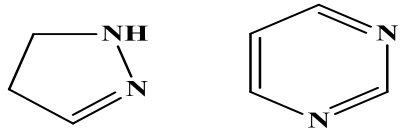


Fig (1): shows the chemical structure of pyrazoline and pyrimidine

Material and methods

Instrumentation

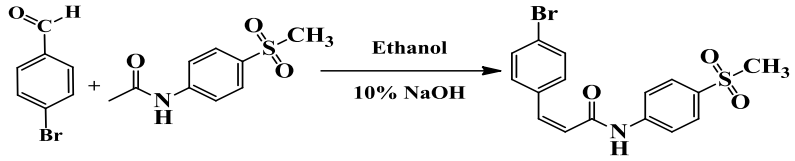
An open capillary is used to determine all melting points (**Tables 1, 2 and 3**). Also, element C.H.N analyzer was carried out on an EM-017. These instruments (Mth) are based in the Department of Chemistry laboratory / Faculty of Science / AL-Muthanna University. The FT-IR spectra in the range (4000-400)cm^{-1} was recorded as KBr disc on IR-Prestige-21(single beam path laser) / Shimadzu Fourier transform infrared spectrophotometer. UV-Visible spectra were measured using UV-1800PC Shimadzu, UV-Visible Spectrophotometer in range (200-800) nm. The ^{13}C-NMR using VARIAN spectrophotometer (75MHz) was also used / Chemistry, University of Technology Sharif, Tehran, Iran. The values of chemical transformation are expressed as δ (ppm), using TMS as reference and d_6DMSO as solvent. The reactions were followed and checked by TLC grade silica gel 'G' (Acme Synthetic Chemicals). The spots were made visible by exposing plates to iodine vapor, and eluted with hexane: ethyl acetate 7:3 mixtures unless otherwise stated. And all solvent extracts were dried over anhydrous sodium sulfate. All the chemicals supplied by BDH and Fluka and Sigma-Aldrich.

Procedure for the preparation of chalcones 1(a-f)

The chalcones **1(a-f)** prepared by the reaction of the mixture of 0.01 mole of acetone with 0.01 mole of aldehyde in ethanol (30ml) and a catalytic quantity of Sodium hydroxide (10%). The mixture was stirred for (3-6) hours at room temperature using magnetic stirrer. The reaction monitored by T.L.C, later on, the evaporation applied to remove the solvent. The product poured into a glass containing ice-water. Furthermore, the precipitate was collected by filtration. Finally, a suitable solvent used to recrystallize the products (Chanti *et al.*, 2015). The physical data of chalcones compounds **1(a-f)** is presented in **Table (1)**.
The following methods were used for chalcones preparations:

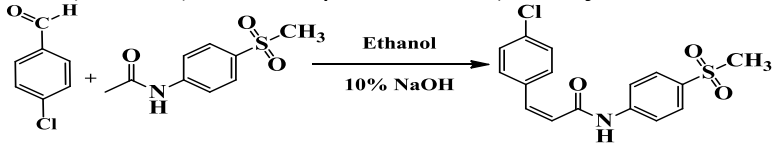
- **3-(4-Bromophenyl)-N-(4-(methylsulfonyl)phenyl)acrylamide(1a)**

It is prepared by reacting 4-(Methylsulfonyl) acetanilide (0.01mole, 2.13gm) with 4-bromobenz aldehyde (0.01 mole, 1.85gm). Yield 60%, m.p. 128-129 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 1651 (C=O of α,β-unsaturated). Recrystallize with methanol.



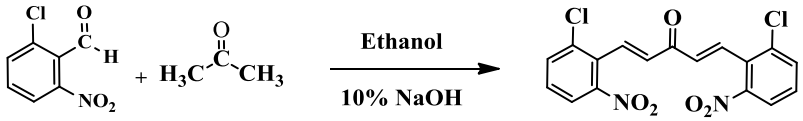
- **3-(4-Chlorophenyl)-N-(4-(methylsulfonyl) phenyl) acrylamide(1b).**

It is prepared by reacting 4-(Methylsulfonyl) acetanilide (0.01mole, 2.13gm) with 4-chlorobenzaldehyde (0.01mole, 1.40gm). Yield = 78%, m.p = 84-86 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 1644 (C=O of α, β-unsaturated). Recrystallize with methanol.



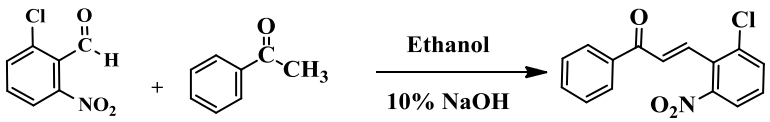
- **1,5-Bis(2-chloro-6-nitrophenyl)penta-1,4-dien-3-one(1c)**

It is prepared by reacting acetone (0.01 mole, 0.58gm, 1.07ml) with 2-chloro-6-nitrobenzaldehyde (0.02 mole, 3.71gm). Yield 82%, m.p. 210-211 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 1654 (C=O of α, β-unsaturated). Recrystallize chloroform.



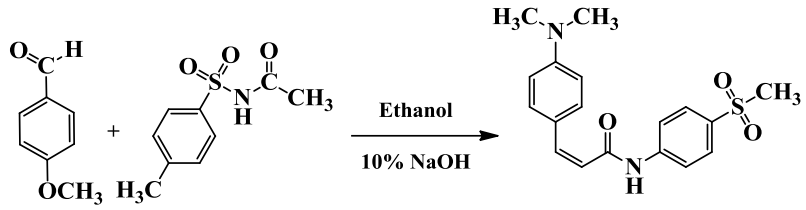
- **3-(2-Chloro-6-nitrophenyl)-1-phenylprop-2-en-1-one(1d)**

It is prepared by reacting acetophenone (0.01 mole, 1.20gm, 1.16ml) with 2-chloro-6-nitrobenzaldehyde (0.01 mole,1.85gm) Yield 89%, m.p. 196-197 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 1648 (C=O of α,β-unsaturated). Recrystallize with benzene.



❖ **3-(4-(Dimethylamino) phenyl)-N-(4-(methylsulfonyl)phenyl)acrylamide(1e).**

It is prepared by reacting 4-(methylsulfonyl) acetanilide (0.01 mole, 2.13gm) with 4-(dimethylamino) benzaldehyde (0.01mole, 1.49gm). Yield 91%, m.p. 95-97 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 1645 (C=O of α,β-unsaturated). Recrystallize with dimethyl ether.



❖ ***N*-(4-hydroxyphenyl)-5-phenylpenta-2,4-dienamide (1f).**

It is Prepared by reacting N-(4-hydroxyphenyl)acetamide (0.01 mole,1.51gm) with cinnamaldehyde (0.01 mole, 1.32gm). Yield 57%, m.p. 138-140 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 1647 (C=O of α, β-unsaturated). Recrystallize with benzene.

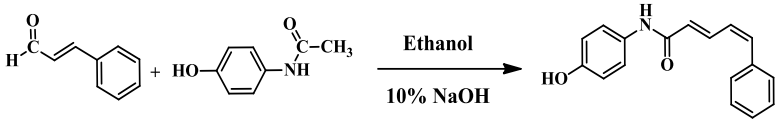


Table (1): Physical properties of the chalcone compounds.

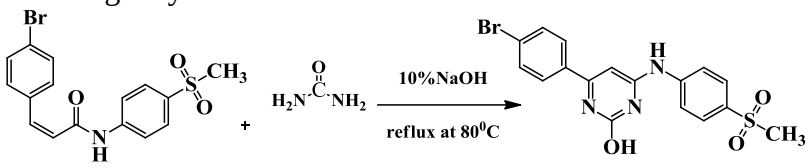
NO	Color	M.P. ˚C	Yield %	Recrystallization Solvent	Stirring (hr).
1a	white	128-129	60%	methanol	4
1b	white	84-86	78%	methanol	6
1c	yellow	210-211	82%	chloroform	3.30
1d	yellow	196-197	89%	benzene	6
1e	Light gray	95-97	91%	dimethyl ether	3
1f	gray	138-140	57%	benzene	5

Procedure for the preparation of pyrimidine 2(a-d)

The Pyrimidine compounds **2(a-d)** prepared by the reaction of the mixture of 0.01 mole of chalcones **1(a-d)** with 0.01 mole of urea and thiourea in Ethanol (15ml) and a catalytic quantity of (10%). Sodium hydroxide refluxed with stirring for (9-16) hours. The reaction monitored by T.L.C. and the product was cooled and poured into cold water. The product was filtered dried and recrystallized in a suitable solvent (Arunlal *et al.*, 2015). The physical data of Pyrimidine **2(a-d)** is shown in **Table (2).** The following methods are used for Pyrimidine preparations including:

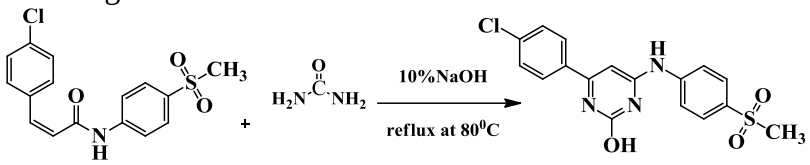
❖ **4-(4-Bromophenyl)-6-((4-(methylsulfonyl)phenyl)amino)pyrimidin-2-ol(2a).**

It is prepared by reacting (1a) (0.01mole, 3.80gm) with urea (0.01mole, 0.6gm). Yield = 65%, m.p = 159-161 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 3288 (OH). Recrystallized using ethyl acetate.



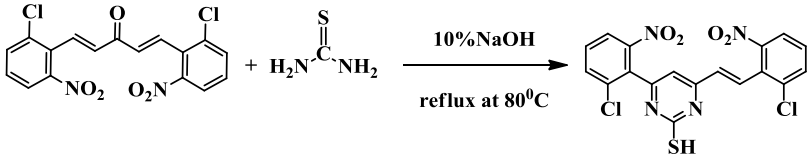
❖ **4-(4-Chlorophenyl)-6-((4-(methylsulfonyl)phenyl)amino)pyrimidin-2-ol (2b).**

It is prepared by reacting (1b) (0.01mole, 3.35gm) with urea (0.01mole, 0.6gm). Yield = 58%, m.p = 164-165 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 3353 (OH). Recrystallized using chloroform.



❖ **4-(2-Chloro-6-nitrophenyl)-6-(2-chloro-6-nitrostyryl) pyrimidine-2-thiol(2c).**

It is prepared by reacting (1c) (0.01mole, 3.93gm) with thiourea (0.01mole, 0.7gm). Yield = 77%, m.p = 246-247 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 2363 (SH). Recrystallized using methanol.



❖ **4-(2-Chloro-6-nitrophenyl)-6-phenylpyrimidine-2-thiol (2d).**

It is prepared by reacting (1d) (0.01mole, 2.87gm) with thiourea (0.01mole, 0.7gm). Yield = 86%, m.p = 119-120 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 2358 (SH). Recrystallized using chloroform.

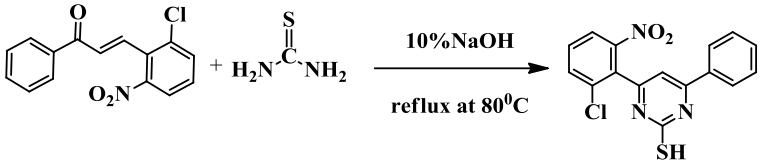


Table (2): Physical properties of the pyrimidine compounds.

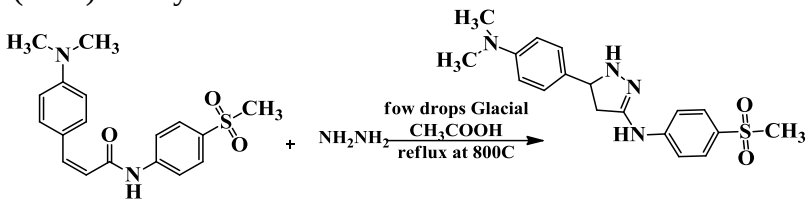
NO	Color	M.P.˚C	Yield %	Recrystallization Solvent	Reflux time (hr.)
2a	Earthy color	159-161	65%	ethylacetate	10
2b	Earthy color	164-165	58%	chloroform	14
2c	Light orange	247-248	77%	methanol	16
2d	Light orange	119-120	86%	chloroform	9

Procedure for the preparation of Pyrazoline 2(e-f)

The Pyrazoline compounds **2(e-f)** were prepared by the reaction of the mixture of 0.01 mole of chalcones **1(e-f)** with 0.01 mole of hydrazine hydrate in Ethanol (20ml) and add by few drops of glacial acetic acid were refluxed with stirring for (19-20) hours. The reaction observed by T.L.C, later on, evaporation of the solvent was done. Then, the compounds were re-crystallize in a suitable solvent. The physical data was determined in a suitable solvent (Saravanan *et al.*, 2010). The physical data of Pyrazoline **2(e-f)** is presented in **Table (3).** The following methods were used for Pyrazoline preparations:

- **5-(4-(Dimethylamino) phenyl)-*N*-(4-(methylsulfonyl) phenyl)-4, 5-dihydro-1*H*-pyrazol-3-amine (2e).**

It is prepared by reacting (1e) (0.01mole, 3.44gm) with hydrazine hydrate (0.01 mole, 0.5gm, 0.48 ml). Yield = 63%, m.p = 185-187 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 1625 (C=N). Recrystallize benzene.



- **4-(5-Styryl-4, 5-dihydro-1*H*-pyrazol-3-yl) amino)phenol (2f).**

It is prepared by reacting (1f) (0.01mole, 2.65gm) with hydrazine hydrate (0.01mole, 0.5gm, 0.48ml). Yield = 78%, m.p = 223-225 ^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 1621 (C=N). Recrystallize diethylether.

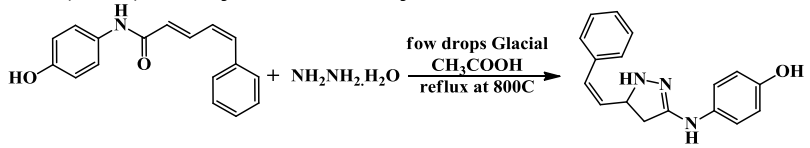


Table (3): Physical properties of the Pyrazoline compounds

NO	Color	M.P. ˚C	Yield %	Recrystallization Solvent	Reflux time (hr.)
2e	Brown	185-187	63%	benzene	20
2f	Brown	223-225	78%	diethylether	19

In vivo evaluation of the hypoglycemic activity of the prepared compounds

Forty-two, adult healthy male rats, (MOS Maussollos, BLP / c) weight (g 25-35) of 8 weeks of age were used in this study. Animals were acclimatized in the animal house. The animals were divided and six rats were kept in each box under standard laboratory conditions according to instruction (Coskun *et al.*, 2004 &, Al-Salman, 2004).

Induction of Diabetes

Diabetes induced experimentally in the laboratory animal (mice). The animals were withholding food for approximately 12 hours and injected with single dose of alloxane monohydrate (125 mg / kg BW) dissolved into distilled water (D.W) directly before injection subcutaneously. Controlled animals received only normal saline solution (Nimenibo-Vadia, 2003). Alloxan treated animals allowed to drink from D-Glucose 5% overnight to prevent the shortage of sugar in the blood that usually occurred as a result of the release of huge insulin from the pancreas. Seven days after injection, the animals revealed extreme fatigue and frequency of urination, which was the indication of diabetic signs (Alarcon-Aguilara *et al.,* 2002).

Administration of Laboratory Animals

Experimental animals were divided into six groups (6 mice in each Group) as follow:
Group (A): positive control that treated only with alloxan (**125 mg/kg**) B.W.
Group (B): alloxan-induced diabetes mice that treated with (**50 mg/kg**) of compound pyrimidine (**2c**).
Group (C): alloxan-induced diabetes mice that treated with (**50 mg/kg**) of compound pyrazoline (**2f**).
Group (D): alloxan-induced diabetes mice that treated with (**100 mg/kg**) of compound pyrimidine (**2c**).
Group (E): alloxan-induced diabetes mice that treated with (**100 mg/kg**) of compound pyrazoline (**2f**).
Group (F): negative control (normal) that is treated orally with distilled water D.W.
All mice were treated for two weeks.

Determine the blood glucose level

The colorimetric method is used to determine the level of serum glucose by the spectrophotometer.

Solution	Blank	Standard	Sample
Standard	--	µl10	--
Sample	--	--	µl 10
Working reagent	ml1	ml1	ml1

Sample and working reagent were mixed and let about 10 minutes at 37°C, the estimated absorption of sample and standard, measured at a wavelength 505 nanometer.

Calculation:

$$[\text{Glucose}] = \frac{\text{Absorption of sample}}{\text{Absorption of standard}} \times \text{conc. of standard (n)}$$

n = 5.56 mmol /L (100mg/dl).

Statistical analysis

Blood glucose levels are expressed in mg/dl as mean ± SD and determination of LSD. The data are statistically analyzed using ANOVA. Values of $p \leq 0.05$ or less are taken as significant.

Results and Discussion

Characterization of the chalcone compounds

The analytical data for compounds including the calculated values of C.H.N analysis, UV and IR spectra (Lacroix *et al.*, 2003) revealed the following values for the prepared compounds as follows:

- **3-(4-bromophenyl)-N-tosylacrylamide(1a).** λ_{max} = 306nm and R_f = 0.65. Elemental analysis ($C_{16}H_{14}BrNO_3S$); (M.Wt:380.26). **Calc**. C, 50.54; H, 3.71; N, 3.68%. **Found**. C, 50.81; H, 2.88; N, 3.09. **FT-IR** [cm^{-1}]: *υ* (Conj C=O) 1651*s*; *υ* (Conj. C=C) 1619*s*; *υ* (C=C stret.) 1524*s*, 1455*m;* *υ* (NH Stret.) 3240*m*; *υ* (NH Bend) 1569*s*; *υ* (O=S=O) 1153*s*; *υ* (C-Br) 802*s*.

- **3-(4-Chlorophenyl)-N-tosylacrylamide(1b).** λ_{max} = 326.18nm and R_f = 0.69. Elemental analysis ($C_{16}H_{14}ClNO_3S$); (M.Wt: 335.81). **Calc**. C, 57.23; H, 4.20; N, 4.17%. **Found.** C, 57.57; H, 4.87; N, 3.99. **FT-IR** [cm^{-1}]: *υ* (Conj. C=O) 1644*s*; *υ* (Conj. C=C) 1611*s*; *υ* (C=C stret.) 1534*m*,1524*m*; *υ* (NH Stret.) 3094*m*; *υ* (NH Bend) 1568*s*; *υ* (O=S=O) 1149*s*; *υ* (C-Cl) 812*s*.

- **1,5-Bis(2-chloro-6-nitrophenyl)penta-1,4-dien-3-one(1c).** λ_{max} = 310nm and R_f = 0.71. Elemental analysis ($C_{17}H_{10}Cl_2N_2O_5$); (M.Wt: 393.18). **Calc**. C, 51.93; H, 2.56; N, 7.12%. Found. C, 52.99; H, 2.61; N, 7.01. **FT-IR** [cm^{-1}]: *υ* (Conj. C=O) 1654*s*; *υ* (Conj. C=C) 1614s*;* *υ* (C=C stret.) *υ* 1562*s*, 1529*m*; *υ* (C-NO_2) 1316*s*; *υ* (C-Cl) 815*s*.

- **3-(2-Chloro-6-nitrophenyl)-1-phenylprop-2-en-1-one(1d).** λ_{max} = 327nm and R_f = 0.68. Elemental analysis ($C_{15}H_{10}ClNO_3$); (M.Wt: 287.70). **Calc**. C, 62.62; H, 3.50; N, 4.87%. **Found**. C, 62.68; H, 4.45; N, 5.68. **FT-IR** [cm^{-1}]: *υ* (Conj. C=O) 1648*s;* *υ* (Conj. C=C) 1615*s;* *υ* (C=C stret.) *υ* 1569*s*, 1524*s*; *υ* (C-NO_2) 1442*s*; *υ* (C-Cl) 812*s*.

- **3-(4-(Dimethylamino)phenyl)-N-(4-(methylsulfonyl)phenyl)acrylamide(1e).** λ_{max} = 329nm and R_f = 0.73. Elemental analysis ($C_{18}H_{20}N_2O_3S$); (M.Wt: 344.43). **Calc**. C, 62.77; H, 5.85; N, 8.13%. Found. C, 61.87; H, 5.97; N, 9.08. **FT-IR** [cm^{-1}]: *υ* (Conj C=O) 1645*m*; *υ* (Conj. C=C) 1615*s*; *υ* (C=C stret.) 1540*m*, 1438*m*; *υ* (NH Stret.) 3324*m*; *υ* (NH Bend) 1569*s*; *υ* (O=S=O) 1150*s*; *υ* (C-N) 1360*m*.

- ***N*-(4-Hydroxyphenyl)-5-phenylpenta-2,4-dienamide(1f).** λ_{max} = 285nm and R_f = 0.64. Elemental analysis ($C_{17}H_{15}NO_2$); (M.Wt: 265.31). **Calc**. C, 76.96; H, 5.70; N, 5.28%. **Found.** C, 77.68; H, 6.61; N, 5.88. **FT-IR** [cm^{-1}]: *υ* (Conj C=O) 1647*s;* *υ* (Conj. C=C) 1615*s;* *υ* (C=C stret.) 1525*m*,1457*m;* *υ* (NH Stret.) 3107*m;* *υ* (NH Bend) 1575*s;* *υ* (C-OH) 3357*m*.

Characterization of the heterocyclic compounds

The analytical data of the compounds **for** C.H.N analysis, UV, IR and ^{13}C-NMR spectra (Ragini *et al.,* 2010) revealed the following values

- ***N*-(6-(4-Bromophenyl)-2-hydroxypyrimidin-4-yl)-4-methylbenzenesulfonamide(2a).** λ_{max} = 329nm and R_f = 0.81. Elemental analysis ($C_{17}H_{14}BrN_3O_3S$); (M.Wt: 420.28). **Calc.** C, 48.58; H, 3.36; N, 10.00%. **Found**. C, 47.68; H, 3.38; N, 10.01. **FT-IR** [cm^{-1}]: *υ* (C=N) 1619*s*; *υ* (OH) 3288*m*; *υ* (NH Stret.) 3291*m*; *υ* (NH Bend) 1576*s*; *υ* (Aromatic C=C) 1517*m*, 1537*s*; *υ* (O=S=O) 1146*s*; *υ* (C-Br) 815*s*. ^{13}C-NMR (DMSO-d_6), [δ/ ppm]: C(CH_3-SO_2) 45.94, C(Pyrimidine), (N-C_2-N) 139.63, (N-C_4) 152.10, (C_5) 110.44, (N-C_6-NH) 148.29, C(benzene) 116.54-130.25.

- ***N*-(6-(4-Chlorophenyl)-2-hydroxypyrimidin-4-yl)-4-methylbenzenesulfonamide(2b).** λ_{max} = 304nm and R_f = 0.85. Elemental analysis ($C_{17}H_{14}ClN_3O_3S$); (M.Wt: 375.83). **Calc.** C, 54.33; H, 3.75; N, 11.18%. **Found**. C, 54.63; H, 3.75; N, 11.36. **FT-IR** [cm^{-1}]: *υ* (C=N) 1615*s*; *υ* (OH) 3353*m*; *υ* (NH Stret.) 3265*m*; *υ* (NH Bend) 1566*s*; *υ* (Aromatic C=C) 1534*m*,1506*m;* *υ* (O=S=O) 1150*s;* *υ* (C-Cl) 812*s*. ^{13}C-NMR (DMSO-d_6), [δ/ppm]: C(CH_3-SO_2) 48.58, C(Pyrimidine), (N-C_2-N) 148.72, (N-C_4) 161.59, (C_5) 119.19, (N-C_6-NH) 154.75, C(benzene) 120.44-139.80.

- **4-(2-Chloro-6-nitrophenyl)-6-(2-chloro-6-nitrostyryl)pyrimidine-2-thiol(2c).** λ_{max} = 308nm and R_f = 0.91. Elemental analysis ($C_{18}H_{10}C_{l2}N_4O_4S$); (M.Wt: 449.27). **Calc.** C, 48.12; H, 2.24; N, 12.47 %. **Found**. C, 47.82; H, 2.27; N, 12.49. **FT-IR** [cm^{-1}]: *υ* (C=N) 1612*s*; *υ* (SH) 2363*s*; *υ* (Aromatic C=C) 1566*m*, 1524*s*; *υ* (C-NO_2) 1483*s*; *υ* (C-Cl) 809*s*. ^{13}C-NMR (DMSO-d_6), [δ/ppm]: C(C=C) 113.31, 123.08, C(Pyrimidine), (N-C_2-N) 171.20, (N-C_4) 165.15, (C_5) 105.98, (N-C_6-NH) 154.72, C(benzene) 116.54-152.10.

- **4-(2-Chloro-6-nitrophenyl)-6-phenylpyrimidine-2-thiol(2d).** λ_{max} = 282nm and R_f = 0.89. Elemental analysis ($C_{16}H_{10}ClN_3O_2S$); (M.Wt: 343.79). **Calc.** C, 55.90; H, 2.93; N, 12.22%. **Found**. C, 56.65; H, 2.78; N, 11.82. **FT-IR** [cm^{-1}]: *υ* (C=N) 1609*s*; *υ* (SH) 2358*s*; *υ* (Aromatic C=C) 1566*s*, 1520*s;* *υ* (C-NO_2) 1455*s*; *υ* (C-Cl) 814*s*. ^{13}C-NMR (DMSO-d_6) [δ/ppm]: C(Pyrimidine), (N-C_2-N) 183.92, (N-C_4) 163.25, (C_5) 106.59, (N-C_6-NH) 164.02, C(benzene) 119.25-146.62.

- **5-(4-(dimethylamino)phenyl)-N-(4-(methylsulfonyl)phenyl)-4,5-dihydro-1H-pyrazol-3-amine(2e).** λ_{max} = 303nm and R_f = 0.78. Elemental analysis ($C_{18}H_{22}N_4O_2S$); (M.Wt: 358.46). **Calc.** C, 60.31; H, 6.19; N, 15.63%. **Found**. C, 61.45; H, 6.08; N, 14.77. **FT-IR** [cm^{-1}]: *υ* (C=N) 1625*s*; *υ* (NH Stret.) 3231*m*; *υ* (NH Bend) 1569*s*; *υ* (Aromatic C=C) 1524*s*, 1458*s;* *υ* (O=S=O) 1153*s*; *υ* (C-N) 1320*s*. ^{13}C-NMR (DMSO-d_6), [δ/ppm]: C(CH_3-SO_2) 48.32, C(CH_3-N-CH_3) 40.83, C(Pyrazoline), (C=N) 152.08, (CH_2) 45.92, (CH) 50.10, C(benzene) 117.99-147.45.

- **4-((5-Styryl-4,5-dihydro-1H-pyrazol-3-yl)amino)phenol(2f).** λ_{max} = 304nm and R_f = 0.93. Elemental analysis ($C_{17}H_{17}N_3O$); (M.Wt: 279.34). **Calc.** C, 73.10; H, 6.13; N, 15.04%. **Found**. C, 74.30; H, 5.88; N, 15.38. **FT-IR** [cm^{-1}]: *υ* (C=N) 1621s; *υ* (NH Stret.) 3110*m*; *υ* (NH Bend) 1563*s*; *υ* (Aromatic C=C) 1543*s*, 1458*s;* *υ* (O=S=O) 1153*s*; *υ* (C-OH) 3356*m*. ^{13}C-NMR (DMSO-d_6), [δ/ppm]: C(C=C) 129.12, 139.23, C(Pyrazoline), (C=N) 157.70, (CH_2) 41.47, (CH) 45.95, C(benzene) 116.99-152.14.

In vivo study

The concentration of serum glucose in experimental mice groups (**A, B, C, D, E and F**) are presented in **Table (4)** and **Figure (2).** A significant decrease in Serum glucose concentration was observed among (**B, C, D and E**) groups as compared with group (**A**) after (**2 week**) treatment with (**50mg/kg**) and (**100mg/kg**) respectively of pyrimidine compound [**2c**], and also treatment with (**50mg/kg**) and (**100mg/kg**) of pyrazoline compound [**2f**]**.** The results of this study revealed a significant increase (**P≤0.05**) in the serum concentration of glucose in a group (**F**) as compared with other groups. The levels of blood glucose decreased significantly in (**B, C, D, and E**) groups as compared to group (A) after 2 weeks treatment with (**50 mg/kg**) and (**100 mg/kg**) from pyrimidine compound [**2c**] and treatment with (**50 mg/kg**) and (**100 mg/kg**) pyrazoline compound [**2f**].

Fig (2): Serum glucose levels after treatment with pyrimidine [2c] and pyrazoline [2f].

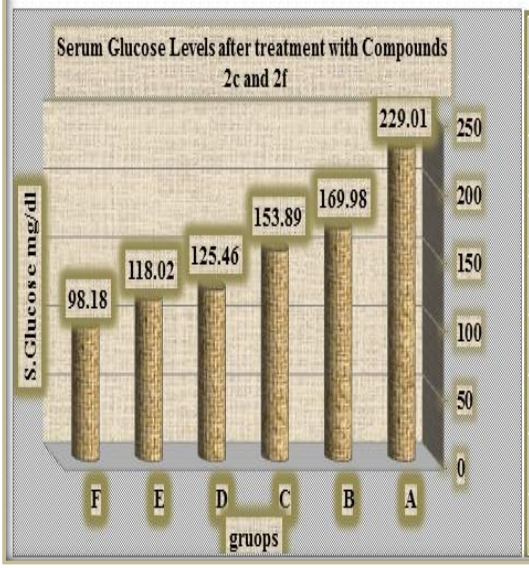


Table (4): Serum glucose levels after treatment with pyrimidine [2c] and pyrazoline [2f].

Glucose conc. mg/dl		
Groups	N	Mean ± S.D
Group A (Positive control)	6	229.01^{a}±18.01
Group B (comp. 2c 50 mg/kg)	6	169.98^{b}±18.04
Group C (comp. 2f 50 mg/kg)	6	153.89^{b}±11.26
Group D (comp. 2c 100 mg/kg)	6	125.46^{c}±3.23
Group E (comp. 2f 100 mg/kg)	6	118.02^{c}±7.00
Group F (Negative control)	6	98.18^{d}±8.01
L.S.D		23.53

Fig. (2): Shows the serum levels after treated with pyrimidine **2c** and pyrazoline **2f**.
Table. (4): Shows serum levels after treatment with pyrimidine **2c** and pyrazoline **2f.**

Note: Each value represents (mean ± SD) values with non-identical superscript (a, b or c …etc.) were considered significantly different ($p \leq 0.05$), n=no. of animals

The previous researcher approved that Alloxan, abeta-cytotoxin can induce chemical diabetes through damage of insulin-secreting cells (Nelson *et al.,* 2000). In the current study, the experimental animals that treated with a test prepared compounds (**2c** and **2f**) in (**100mg/kg**) concentration, showed a significant decreased in the serum glucose levels. This is compatible with a previous study (Jelodar *et al.,* 2003) and it is indicating the anti-hyperglycemic activity of the prepared compounds. The diabetic rats, revealed an elevated glucose and depression in the levels of hepatic glycogen contents, which could be attributed to the availability of less active form of enzyme glycogen synthase (Grover *et al.,* 2000). Moreover, in turn, it has been reported to be responsible for incorporation of glucose moieties in pre-existing glycogen chain (DeCarvalho *et al.,* 2003). The activities of the test compounds (2c and 2h) might be related to the elevation in the utilization of glucose. These observations are supported by the decreased in serum glucose levels and the increase in the activity of glycogen synthase enzyme as evidenced by the rise in liver glycogen contents in test groups (Stanely *et al.,* 2000). Moreover, the pyrimidine and pyrazoline treated group with a concentration of (**100 mg/kg**) acted to lowering the levels of high blood glucose in compare to the group that treated with (**50 mg/kg**).

In conclusion, this study revealed the ability of the prepared compounds in the lowering of blood glucose levels in the experimentally induced diabetic rats. The author recommends doing more future studies to test the prepared compounds in different types of diabetes to determine the mechanism of its action as hypoglycemic compounds.

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