ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 10, Issue 4, 2017

Online - 2455-3891
Print - 0974-2441

Research Article

SYNTHESIS, *IN SILICO* PHYSICOCHEMICAL PROPERTIES AND BIOLOGICAL ACTIVITIES OF SOME PYRAZOLINE DERIVATIVES

JAINEY P JAMES[1]*, ISHWAR BHAT K[1], NEETHU JOSE[2]

[1]Department of Pharmaceutical Chemistry, Nitte Gulabi Shetty Memorial Institute of Pharmaceutical Sciences, Nitte University, Deralakatte, Mangalore, Karnataka, India. [2]Department of Pharmaceutical Chemistry, Srinivas College of Pharmacy, Valachil, Mangalore, Karnataka, India. Email: jaineyjames@gmail.com

Received: 14 January 2017, Revised and Accepted: 25 January 2017

ABSTRACT

Objectives: Nitrogen-containing heterocyclic compounds play an important role in medicinal chemistry. Among them, five-membered ring pyrazolines have found to possess many biological and pharmacological activities such as anticancer, antitubercular, antimicrobial, anti-inflammatory. Objective is to determine the physicochemical and drug-like properties of the synthesized pyrazolines by *in silico* methods and to screen their antidiabetic and antioxidant activities.

Methods: Chalcones were synthesized from naphthaldehyde by condensing with various substituted acetophenones in ethanol and cyclized into pyrazolines using semicarbazides/thiosemicarbazides by conventional and microwave oven synthesis. The physicochemical and drug-like properties were determined using computational tools. Anti-diabetic activity was evaluated by alpha amylase inhibition assay method. Antioxidant activity studies were done by 2,2-diphenyl-1-picrylhydrazyl and nitric oxide method.

Results: Pyrazolines were synthesized from chalcones. Microwave irradiated synthesis of chalcone was carried out to get higher yield with less reaction period as compared to conventional method. The synthesized pyrazolines produce yield around 68% (conventional) and 85% (microwave). *In silico* studies showed considerable values satisfying all the parameters of physicochemical and Lipinski's Rule of Five properties. Among the compounds tested for antidiabetic and antioxidant studies, some showed promising activity.

Conclusion: Physiochemical and drug-like properties revealed that these compounds have good bioavailability and drug likeness properties. Hence, these compounds are found to be interesting lead molecules for further synthesis as antidiabetic and antioxidant agents.

Keywords: Chalcones, Pyrazolines, *In silico* physicochemical properties, Biological activities.

 DOI: http://dx.doi.org/10.22159/ajpcr.2017.v10i4.17093

INTRODUCTION

Pyrazoline derivatives are the electron-rich nitrogen heterocycles. They broadly exist in many natural alkaloids, vitamins, pigments, and synthetic derivatives possessing variant biological and pharmacological activities [1-3].

Degenerative processes related to aging and in diseases, namely, cancer, coronary heart disease, and Alzheimer's disease has been resulted from the oxidative and free radical mediated reactions [4]. It has been focused on the use of synthetic antioxidants to inhibit lipid peroxidation and to protect from damage due to free radicals [5]. 2-pyrazolines are capable of preventing oxidative damage as well as clastogenic effects [6] due to its significant antioxidant potential.

Good drug absorption and suitable drug delivery are very important in the development of drugs intended for oral use. Due to poor pharmacokinetics, about 30% of drugs fail in the initial stage of drug discovery and development. Hence, to minimize these failures, proper understanding of molecular properties is very essential. The crucial role played by small heterocyclic molecules in drug design cannot be denied. These molecules act as highly functionalized scaffolds [7].

In this work, pyrazoline, a five-membered heterocyclic ring, a prominent lead molecule, has played a vital role in the development of different medicinal agents. A variety of methods has been reported for the preparation of this class of compounds. In the present article, we report the reaction of naphthaldehyde with different aromatic ketones to form pyrazolines bearing a naphthyl moiety and studied their *in silico* molecular properties and *in vitro* antidiabetic and antioxidant activities.

METHODS

General methods

All used materials were obtained commercially, mostly from Sigma-Aldrich, and were used without further purification. Melting points were found by capillary method and were uncorrected. Shimadzu Perkin Ekmer 8201 Pc infrared (IR) Spectrometer used in recording IR spectra (KBr pellets) and frequencies are expressed in cm^{-1}. Bruker Avance II 400 nuclear magnetic resonance (NMR) spectrometer recorded NMR spectra. All spectra were obtained in $CDCl_3$ and dimethyl sulfoxide (DMSO). Chemical shift values are reported as values in ppm relative to tetramethylsilane (δ=0) as internal standard. JEOL SX-102/DA-6000 mass spectrometer recorded fast atom bombardment **(**FAB) mass spectra using Argon/Xenon (6 KV, 10 Ma) as the FAB gas. The elemental analysis has been obtained using Vairo elementar model, CHN analyzer, and the results were found to be within ±0.4%. Cata-R, Catalyst Systems 140-700 W microwave reactor was used for microwave synthesis.

Synthetic methods

General methods of synthesis of pyrazolines

A mixture of chalcone (0.01 mol), semicarbazide/thiosemicarbazide (0.01 mol) in ethanol (30 ml) in the presence of acetic acid (2 ml) was subjected to microwave irradiation for 7-8 minutes. With constant stirring, the reaction mixture was poured into cold water. The product thus obtained was recrystallized from suitable solvents. Ethyl acetate:chloroform (8:2) is the solvent system for thin layer chromatography. The same reaction mixture was refluxed for 12-14 hrs under conventional heating [3].

Spectral data

3-(4-bromophenyl)-5-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (TP1)
Red crystals; m.p. 196-198°C; yield 76%; IR (cm^{-1}): 3431.1 (aromatic CH str), 3097.8 (thiocarbamoyl NH str), 1646.8 (C=N str), 1594.7 (C=C str), 1345.2 (C=S), 1385.0 (C-N), 544.7 (C-Br). ^{1}H NMR (δ ppm): 3.991-4.044 (dd, 1H, Ha), 3.212-3.214 (dd, 1H, Hb), 4.915-4.960 (dd, 1H, Hc), 8.108-8.700 (m, 11H, Ar-H), 7.834-7.875 (d, 2H, NH_2). Mass (m/z): (M^+) 460. Analytically calculated for C, 62.61; H, 3.94, found: C, 62.63; H, 3.91.

3-(4-chlorophenyl)-5-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (TP2)
Yellow crystals; m.p. 186-188°C; yield 77%; IR (cm^{-1}): 3440.2 (aromatic CH str), 3077.7 (thiocarbamoyl NH str), 1635.6(C=N str), 1522.5 (C=C str), 1336.7 (C=S), 1374.6 (C-N), 750.3 (C-Cl). ^{1}H NMR (δ ppm): 4.012-4.043 (dd, 1H, Ha), 3.423-3.456 (dd, 1H, Hb), 3.985-4.019 (dd, 1H, Hc), 7.910-8.073 (m, 11H, Ar-H), 8.312-8.415 (d, 2H, NH_2). Mass (m/z): (M^+) 416. Analytically calculated for C, 69.30; H, 4.36, found: C, 69.32; H, 4.38.

3-(4-fluorophenyl)-5-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (TP3)
Yellowish brown crystals; m.p. 169-171°C; yield 71%; IR (cm^{-1}): 3453.1 (aromatic CH str), 3025.5 (thiocarbamoyl NH str), 1643.6 (C=N str), 1545 (C=C str), 1351.3 (C=S), 1379.2 (C-N), 1423 (C-F). ^{1}H NMR (δ ppm): 4.657-4.683 (dd, 1H, Ha), 3.223-3.316 (dd, 1H, Hb), 4.112-4.208 (dd, 1H, Hc), 7.471-7.802 (m, 11H, Ar-H), 8.413-8.482 (d, 2H, NH_2). Mass (m/z): (M^+) 450. Analytically calculated for C, 72.16; H, 4.54, found: C, 72.14; H, 4.52.

3-(4-aminophenyl)-5-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (TP4)
Brown crystals; m.p. 163-165°C; yield 65%; IR (cm^{-1}): 3489.3 (aromatic CH str), 3031.8 (thiocarbamoyl NH str), 1641.4 (C=N str), 1521.1 (C=C str), 1362.8 (C=S), 1396.8 (C-N), 1423 (C-NH_2). ^{1}H NMR (δ ppm): 4.611-4.664 (dd, 1H, Ha), 3.167-3.190 (dd, 1H, Hb), 2.989-3.019 (dd, 1H, Hc), 7.325-7.762 (m, 11H, Ar-H), 8.182-8.254 (d, 2H, NH_2). Mass (m/z): (M^+) 396. Analytically calculated for C, 72.70; H, 5.08, found: C, 72.72; H, 5.05.

3-(4-nitrophenyl)-5-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (TP5)
Brownish yellow crystals; m.p. 163-165°C; yield 75%; IR (cm^{-1}): 3329.3 (aromatic CH str), 3026.2 (thiocarbamoyl NH str), 1653.7 (C=N str), 1536.6 (C=C str), 1357.3 (C=S), 1394.3 (C-N), 1333.4 (C-NO_2). ^{1}H NMR (δ ppm): 3.981-4.011 (dd, 1H, Ha), 3.321-3.343 (dd, 1H, Hb), 2.788-2.801 (dd, 1H, Hc), 7.02-7.661 (m, 11H, Ar-H), 8.231-8.267 (d, 2H, NH_2). Mass (m/z): (M^+) 426. Analytically calculated for C, 67.59; H, 4.25, found: C, 67.62; H, 4.23.

3-(4-chlorophenyl)-5-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carboxamide (SP1)
Red crystals; m.p. 127-129°C; yield 82 %; IR (KBr, cm^{-1}): 3444.01 (aromatic CH str), 3049.46, 3028.24 (carbamoyl NH_2 str), 1622.13 (C=N str), 1593.20 (C=C str), 1621.13 (C=O), 1384.89 (C-N), 732.95 (C-Cl). ^{1}H NMR (400 MHz, DMSO, δ/ppm): 3.71 (dd, 1H, HA), 3.93 (dd, 1H, HB), 4.95 (dd, 1H, Hx), 7.37-7.99 (m, 11H, Ar-H); Mass (FAB), m/z: (M^+) 399. Analytically calculated for C, 72.09; H, 4.54; found: C, 72.06; H, 4.52.

3-(4-bromophenyl)-5-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carboxamide (SP2)
Yellow crystals; m.p. 143-145°C; yield 72%; IR (KBr, cm^{-1}): 3456.56 (aromatic CH str), 3023.45, 3046.46 (carbamoyl NH_2 str), 1625.73 (C=N Str), 1556.29 (C=C Str), 1626.67 (C=O), 1356.45 (C-N), 656.45 (C-Br). ^{1}H NMR (400 MHz, DMSO, δ/ppm): 3.45 (dd, 1H, HA), 3.56 (dd, 1H, HB), 3.97 (dd, 1H, Hx), 7.21-7.96 (m, 11H, Ar-H); analytically calculated for C, 64.88; H, 4.08; found: C, 64.85; H, 4.06.

3-(4-fluorophenyl)-5-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carboxamide (SP3)
Red crystals; m.p. 169-171°C; yield 73 %; IR (KBr, cm^{-1}): 3567.40 (aromatic CH str), 3013.34, 3128.67 (carbamoyl NH_2 str), 1626.23 (C=N str), 1545.34 (C=C str), 16445.23 (C=O), 1373.38 (C-N), 1332.95 (C-F). ^{1}H NMR (400 MHz, DMSO, δ/ppm): 2.89 (dd, 1H, HA), 3.35 (dd, 1H, HB), 3.78 (dd, 1H, Hx), 7.25-8.09 (m, 11H, Ar-H); mass (FAB), m/z: (M^+) 383; %; analytically calculated for C, 75.18; H, 4.73; found: C, 75.16; H, 4.75.

3-(4-aminophenyl)-5-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carboxamide (SP4)
Red crystals; m.p. 168-169°C; yield 80%; IR (KBr, cm^{-1}): 3542.41 (aromatic CH str), 3056.34, 3056.67 (carbamoyl NH_2 str), 1667.56 (C=N Str), 1578.56 (C=C Str), 1634.23 (C=O), 1386.44 (C-N), 1332.95 (C-NH_2). ^{1}H NMR (400 MHz, DMSO, δ/ppm): 3.74 (dd, 1H, HA), 3.98 (dd, 1H, HB), 4.36 (dd, 1H, Hx), 7.78-8.47 (m, 11H, Ar-H); Mass (FAB), m/z: (M^+) 380; analytically calculated for C, 75.77; H, 5.30; found: C, 75.74; H, 5.34.

3-(4-hydroxyphenyl)-5-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carboxamide (SP5)
Brown crystals; m.p. 172-175°C; yield 83%; IR (KBr, cm^{-1}): 3448.43 (aromatic CH str), 3032.14, 3064.32 (carbamoyl NH_2 str), 1628.23 (C=N str), 1585.34 (C=C str), 1632.33 (C=O), 1356.67 (C-N), 3209.43 (C-OH). ^{1}H NMR (400 MHz, DMSO, δ/ppm): 3.25 (dd, 1H, HA), 3.47 (dd, 1H, HB), 3.95 (dd, 1H, Hx), 7.22-7.81 (m, 11H, Ar-H); Mass (FAB), m/z: (M^+) 381; analytically calculated for C, 75.57; H, 5.02; found: C, 75.58; H, 5.00.

***In silico* studies**

Physicochemical properties

Physiochemical properties and the presence of various pharmacophoric features, influence the behaviors of molecules in a living organism, including bioavailability. Good intestinal absorption, molecular flexibility (measured by the number of rotatable bonds), low polar surface area or total hydrogen bond count (sum of donors and acceptors), are important predictors of good oral bioavailability [8]. Thus, to achieve good oral drugs, we have investigated a series of pyrazoline derivatives bearing a anthracenyl moiety for the prediction of their molecular properties, Lipinski's "Rule of Five" [9] and drug likeness properties. High oral bioavailability is an important factor for the development of bioactive molecules as therapeutic agents.

Rule of Five properties

Lipinski [9] used various molecular properties in formulating his "Rule of Five." The rule states that most molecules with good membrane permeability have log P ≤5, MW≤500, the number of hydrogen bond acceptors ≤10, and the number of hydrogen bond donors ≤5. The rule is widely used as a filter for drug-like properties. A compound that fulfills at least three out of the four criteria is said to adhere to "Lipinski's Rule of Five." A poor permeation or absorption is more likely when there are more than five H-bond donors and ten H-bond acceptors [10].

The compounds that were drawn using ChemDraw software were initially screened for Lipinski's rule of 5 using Molinspiration server.

Biological activities

Evaluation of antidiabetic activity [11]

The compounds were tested for *in vitro* alpha-amylase inhibition assay. Preincubation of starch azure (substrate) and TrisHCL buffer was done at 37°C for 5 minutes. To this mixture, the test sample along with porcine pancreatic amylase in TrisHCL buffer was added and then incubated for 10 minutes at 37°C. The absorbance was measured at 595 nm using microplate reader BMG, Germany. The inhibitory concentration was calculated and reported.

Evaluation of antioxidant activity

2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity
The stable radical DPPH was used as the reagent in this spectrophotometric assay [12]. 3 ml of 0.1 mM solution of DPPH and 1 ml of the compounds bearing different concentrations (10-200 μM)

was mixed was kept in the dark for 30 minutes. It was incubated for 30 minutes at room temperature, and the absorbance was read against blank at 517 nm.

Nitric oxide (NO) free radical scavenging method
NO radicals were generated from sodium nitroprusside. 1 ml of sodium nitroprusside (10 mM) and 1.5 ml of phosphate-buffered saline (0.2 M, pH 7.4) were added to the various test concentrations (10-200 µM). These mixtures were incubated for 150 minutes at 25°C. Moreover, 1 ml of Griess reagent was added, and absorbance was read against 546 nm [13].

For both antioxidant determination methods, the percentage of inhibition was computed from the following equation:

$$\text{Inhibition level, } \% = \frac{\text{Control absorbance} - \text{Test absorbance}}{\text{Control absorbance}} \times 100$$

RESULTS AND DISCUSSION

Cyclization of chalcone with thiosemicarbazide/semicarbazide in conventional and microwave methods has been described in the Scheme 1. Comparison of conventional and microwave techniques, in terms of time and yields, have been described in Table 1. Spectral and elemental analysis data confirmed the structure of the compounds.

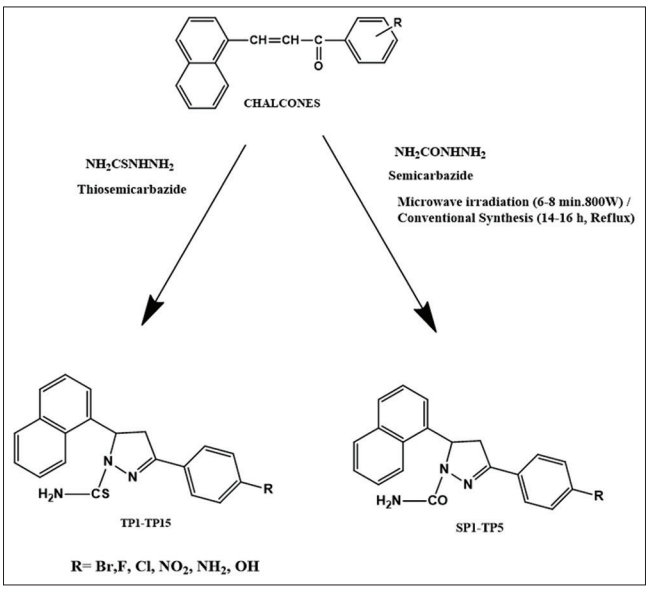
In IR spectra an absorption band in TP1 afforded pyrazoline C-N stretching 1646.8 cm^{-1} and C=S bands at 1345.2 cm^{-1}. In ^1H NMR spectra of TP1, the CH_2 protons of the pyrazoline ring resonated as a pair of doublets of doublets at 3.991 ppm (HA), 3.212 ppm (HB). The CH (Hx) proton appeared as a doublet of doublets at 4.915 ppm. This confirmed the cyclization of chalcones to 2-pyrazolines. Mass spectra of compounds were collected and the molecular ion peak was found correct according to the molecular formula.

Physicochemical properties

The analogs possessed desired physicochemical properties with no violations from the standard ranges and are tabulated in Table 2. The number of the rotatable bond must be <10. Drugs that penetrate central nervous system should have lower polar surface areas <140 than other kinds of molecules. The results showed that all the compounds have a promising oral bioavailability.

Rule of five properties

Based on the experimental values, it was inferred that all the compounds successfully satisfied all the parameters of Lipinski's Rule of Five. Compounds with log P values <5, mean that they can readily get pass ester/phosphate groups in skin membranes. The results obtained are given in Table 2. The calculated values of log P for the derivatives ranged from 2.72 to 4.7. The lipophilic aptitude of a compound increases with the increasing log P. The C log P values of all the compounds show variation which can be attributed to the presence and position of different substituents on the phenyl ring. The series under investigation has not only the most of the compounds possessing less number of hydrogen bond donors (<5) but also does possess considerable number of acceptors (<10).



Scheme 1: Synthesis of pyrazolines

All the pyrazolines tested for antidiabetic and antioxidant studies showed promising activity when compared with the standard. Among that, compounds TP1 and TP3 showed anti-diabetic activity equivalent to standard acarbose as given in Table 3.

Table 4 exhibited the radical scavenging activity results in DPPH and NO methods, stating that compounds TP1 and TP5 proved to as good scavengers from both methods.

CONCLUSION

The present study has achieved the efficient synthesis of pyrazoline bearing a naphthyl moiety and examined their preliminary *in vitro* antidiabetic and antioxidant activities. The molecular properties were predicted, which showed that these active compounds can be used as templates for development of new drugs. In addition, it was found

Table 1: Reaction time and yield of conventionally and microwave assisted synthesis of pyrazolines

Compounds	Conventional synthesis		Microwave assisted synthesis	
	Time (hrs)	Yield (%)	Time (minutes)	Yield (%)
Pyrazolines	12-14	54-73	7-8	65-83

Table 2: Physicochemical properties of pyrazoline derivatives

Compound code	tPSA	nrobs	Molecular weight	Log P	nONs	nOHNHs
TP1	41.62	3	410.33	4.7	3	2
TP2	41.62	3	365.88	4.62	3	2
TP3	41.62	3	349.42	4.23	4	4
TP4	67.64	3	346.45	3.27	4	3
TP5	61.85	3	347.43	3.69	4	3
SP1	58.69	2	349.81	4.07	4	2
SP2	58.69	2	394.26	4.34	4	2
SP3	58.69	2	333.36	3.67	4	2
SP4	84.75	2	330.38	2.71	5	4
SP5	96.94	2	331.37	3.13	5	3

PSA: Polar surface area

Table 3: Antidiabetic activity by alpha-amylase method

Compound	R	IC_{50}
TP1	4-Br	9.18
TP2	4-Cl	12.34
TP3	4-F	9.10
TP4	4-NH_2	10.6
TP5	4-NO_2	10.34
SP1	4-Cl	10.16
SP2	4-Br	12.34
SP3	3-F	11.1
SP4	4-NH_2	11.11
SP5	4-OH	12.68
Standard	Acarbose	9.14

IC_{50}: Inhibitory concentration 50%

Table 4: Antioxidant activity of pyrazolines

Compound	R	DPPH method	NO method
Inhibition level, % at 200 μM			
TP1	4-Br	89	80
TP2	4-Cl	67	75
TP3	4-F	79	63
TP4	4-NH_2	78	65
TP5	4-NO_2	84	80
SP1	4-Cl	65	72
SP2	4-Br	67	75
SP3	3-F	73	74
SP4	4-NH_2	67	63
SP5	4-OH	61	63
Standard	Ascorbic acid	90	90

DPPH: 2,2-diphenyl-1-picrylhydrazyl, NO: Nitric oxide

that all the compounds followed Lipinski's Rule of Five. Thus, the idea of appending the naphthyl moiety to the pyrazoline nucleus so as to combine the beneficial effects in a single structure proved to be successful. In conclusion, the present study showed that synthesized compounds can be used as template for future development through modification and derivatization.

ACKNOWLEDGMENTS

The authors are grateful to IISc - Bengaluru for ^{1}H NMR and CDRI - Lucknow for Mass spectroscopic analysis, Mangalore University for elemental analysis. The authors are highly grateful to Nitte University for providing all the necessary research facilities and financial assistance.

REFERENCES

1. Bhat KI, Jainey PJ. Antimicrobial studies of some substituted pyrazoline derivatives derived from acetyl hydrazines. Asian J Pharm Clin Res 2014;7(4):237-9.
2. Reddy LS, Raju MB, Sridhar C. Novel pyrazolines: Synthesis and evaluation of their derivatives with anticancer and anti-inflammatory activities. Int J Pharm Pharm Sci 2016;8(1):247-54.
3. Jacob KS, Ganguly S. A battle against aids: New pyrazole key to an older lock-reverse transcriptase. Int J Pharm Pharm Sci 2016;8(11):75-9.
4. Taj T, Kamble RR, Gireesh TM, Hunnur RK, Margankop SB. One-pot synthesis of pyrazoline derivatised carbazoles as antitubercular, anticancer agents, their DNA cleavage and antioxidant activities. Eur J Med Chem 2011;46(9):4366-73.
5. Kumar A, Bhat G, Varadaraj BG, Rajeev K, Singla RK. Synthesis and evaluation of antioxidant activity of novel 3, 5-disubstituted-2-pyrazolines. Bull Fac Pharm Cairo Univ 2013;51(2):167-73.
6. Babu VH, Sridevi CH, Joseph A, Srinivasan KK. Synthesis and biological evaluation of some novel pyrazolines. Indian J Pharm Sci 2007;69(3):470-3.
7. Lone IH, Khan KZ, Fozdar BI. Synthesis, physicochemical properties, antimicrobial and antioxidant studies of pyrazoline derivatives bearing a pyridyl moiety. Med Chem Res. DOI: 10.1007/s00044-013-0643-z.
8. Veber DF, Johnson SR, Cheng HY, Smith BR, Ward KW, Kopple KD. Molecular properties that influence the oral bioavailability of drug candidates. J Med Chem 2002;45(12):2615-23.
9. Lipinski CA. Lead-and drug-like compounds: The rule-of-five revolution. Drug Discov Today Technol 2004;1(4):337-41.
10. Muegge I. Selection criteria for drug-like compounds. Med Res Rev 2003;23(10):302-21.
11. Eichler HG, Korn A, Gasic S, Pirson W, Businger J. The effect of a new specific alpha-amylase inhibitor on post-prandial glucose and insulin excursions in normal subjects and Type 2 (Non-insulin-dependent) diabetic patients. Diabetologia 1984;26(4):278-81.
12. Chanda S, Dave R. *In vitro* models for antioxidant activity evaluation and some medicinal plants possessing antioxidant properties: An overview. Afr J Microbiol Res 2009;3(13):981.
13. Jainey PJ, Bhat KI. Microwave assisted synthesis of novel pyrimidines bearing benzene sulfonamides and evaluation of anticancer and antioxidant activities. Asian J Pharm Clin Res 2014;7(4):111-4.