Journal Name:	Journal of Pharmaceutical Research International
Manuscript Number:	Ms_JPRI_78008
Title of the Manuscript:	Preparation, analysis and antibacterial evaluation of some new 1,3,5-trisubstituted pyrazole derivatives
Type of the Article	Original research article

General guideline for Peer Review process:

This journal's peer review policy states that <u>NO</u> manuscript should be rejected only on the basis of '<u>lack of Novelty'</u>, provided the manuscript is scientifically robust and technically sound. To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<u>Compulsory</u> REVISION comments	Review of the article entitled Preparation, analysis and antibacterial evaluation of some new 1,3,5-trisubstituted pyrazole derivatives, Ms_JPRI_78008, for Journal of Pharmaceutical Research International	
	This article is a significant contribution to the research of new pyrazole derivatives with antibacterial activity, within the scope of the journal and suitable for publication after some revision.	
	The English language should be improved at some places, as well as the organization of the manuscript.	
	On page 1, in the abstract, the first sentence, lines 1 and 2, use plural for novel 1,3,5-trisubstituted-2-pyrazoline derivatives, as well as test their antibacterial activity	
	Line 7, state and two gramme negative bacterial strains (<i>Escherichia Coli, Klebsiella Penumoniae</i>), instead of (<i>Staphylococcus aureus, S. Faecalis, Bacillus Substilis, P. Vulgaris, and B. Pumilus</i>)	
	Lines 8 and 9, delete repeated part of the sentence and two gramme negative i.e.	
	Lines 12 and 13, use italic for (Staphylococcus Aureus, Staphylococcus Faecalis, Bacillus Substilis, Pseudomonas Vulgaris, and B. Pumilus) or state against the mentioned gramme positive bacterial strains	
	Line 21, use the first small letter for fifth position Line 22, use the first small letter for methyl	
	On page 2, in the Introduction, paragraph 1, line 2, state the numbers of references before the sign of punctuation, as well as in the rest of the manuscript Paragraph 2, line 8, use small letter for scientists	
	Lines 9 and 10, state the expensive costs of clinical research, instead of expensive expense, preferably Lines 13 and 14, use italic for <i>Trypanosoma</i> , <i>Plasmodium</i> , <i>Toxoplasma gondii</i> , <i>Leishmania</i> , and <i>Entamoeba</i>	
	Line 15, use the first small letter for the isolation Line 16, state synthetic medical molecules, instead of synthetic medicine molecules, preferably	
	On page 3, paragraph 1, lines 11 and 12, state The reaction of chalcone derivatives with succinic hydrazide in the presence of	

pyridine was used to create novel pyrazoline derivatives

Paragraph 2, in Materials and methods, lines 1 and 2, use italic for *p*-chloroacetophenone, *p*-bromoacetophenone, and *p*-methylacetophenone Lines 3 and 4, 4-nitrobenzaldehyde should be placed in the same row, preferably Line 9, use superscript for ¹HNMR

Line 11, use the first small letter for spectra and end the sentence with electron spin ionization (ESI).

On page 4, paragraph 2, line 1, use italic for *p*-chloro acetophenone and *p*-methyl acetophenone

Line 3, delete repeated word added, before 50 % aqueous solution of potassium hydroxide was added

Line 4, use the abbreviation 24 h for hours, instead of hrs, preferably

Lines 5 and 6, state

When the synthesis was completed, instead of

Then the synthesis is completed

Line 8, use the same formatting of reference numbers within the entire manuscript, without subscript and before the sign of punctuation, according to the style of the journal

Paragraph 3, the grammar of the first sentence should be improved, for example, as follows

Succinic acid (0.05 M) was easily converted to succinichydrazide by reaction with hydrazine hydrate (0.05 M) in alcohol, then the reaction mixture was cooled to room temperature and succinichydrazide separated as solid, which was recrystallized using ethanol.

Line 5, use the first small letter for hexane: ethyl acetate

Line 6, state ¹HNMR, instead of 1HNMR

Paragraph 4, line 1, use plural for were mixed, instead of was mixed The last sentence of this paragraph should be modified

The synthesized compounds were purified by the column chromatography and were obtained as pale yellow colored solid powder.

On page 5, the quality of Image 2 can be improved.

Paragraph 1, the first and the second sentence should be improved, as follows The synthesized compounds were tested against five gram positive (*Staphylococcus Aureus, Staphylococcus Faecalis, Bacillus Substilis, P. Vulgaris and B. Pumilus*) and two gram negative (*Escherichia coli and Klebsiella penumoniae*) organisms using the Agar diffusion method. Norfloxacin and Ciprofloxacin were used as standard drugs for comparison of the efficacy of synthesized compounds against gram positive and gram negative bacteria, respectively [28].

On page 6, paragraph 2, use plural for Norfloxacin solutions were also prepared

On page 7, paragraph 4, line 1, the unite of measure can be stated for Molecular

weight (g/mol), as well as in the rest of the manuscript Lines 1 and 2, Element (Found/Calc.(%)) can be replaced, instead of Element (Found/Calc.)%, in line 4, replace ¹HNMR, instead of 1HNMR, as well as in the rest of the manuscript

On page 8, in paragraph 1, lines 3 and 5 and in paragraph 3, line 3, delete the additional space, as well as on pages 9 -13, where it appears, similarly Move to the next page subtitle

Compound CL-5: 1-(5-(4-chlorophenyl)-3-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-

1-yl)-3-(hydrazinyloxy)propan-1-one

On page 13, use subscripts in the Molecular formula: C₂₀H₂₄N₄O₃

Within the paragraph Antibacterial activity, after the second sentence, line 4, and before the third sentence, which should be moved to separate paragraph, add subtitle Antibacterial activity against gram positive bacteria Present Table 1 after the last sentence of this paragraph The compounds series BR-1 to BR-4 have shown the highest activity (Table 1).

Move from the last paragraph on page 14, and place after Table 1, the next sentence The graphical representation of antibacterial activity on gram positive bacterial strains is shown in zone of inhibition in Figures 1 to 5.

Present Figures 1 to 5 after that sentence

After Figure 5, state subtitle

Antibacterial activity against gram negative bacteria

Place the second and the third paragraph from page 14 after this subtitle Move the last sentence from the first paragraph, currently on page 21, after the aforementioned two paragraphs

The graphical representation of zone of inhibition is shown in Figures 6 and 7.

Paragraph of the text on page 20 and its end on page 21, should be deleted, as it is the same as the second paragraph on page 14, currently

On page 15, the entire Figure 1 should be seen, move the second part of the figure to the left side

On page 17, BR-3, as well as BR-4 should be stated in one row The entire Figure 2 should be seen, move the second part of this figure to the left side

On page 18, BR-3, and BR-4 should be stated in one row The entire Figure 3 should be seen, move the second part of this figure to the left side

In the legend of Figure 3, state in italic Bacillus Substilis

On page 19, the entire Figure 4 should be seen, move the second part of this figure to the left side

	On page 20, the entire Figure 5 should be seen, move the second part of this figure to the left side	
	Put dots after the legends of Figures $1-5$.	
	In conclusion, paragraph 1, line 1, state All the synthesized 2-pyrazolines have been evaluated for their antibacterial activity Line 3, use italic for <i>Escherichia coli</i> , <i>Proteus vulgaris</i> Lines 5 and 6, the name of the compound, 2-pyrazolines should be in the same row,	
	preferably Line 7 and 8, the number and the unit of measure, 0.1 ml, should be in the same row	
	Line 10, use the past tense for thus revealed	
	Paragraph 2, lines 1 and 3, use the first small letter for fifth position Line 3, replace may be necessary, instead of may necessary Use comma before, the addition of F, NO ₂ has shown moderate activity , whereas in the case of -CH ₃ -OCH ₃ substitution may diminish activity	
	Paragraph 3, line 2, replace This is the evidence that, or ihis evidences that, instead of This evident	
	Use the first small letter for the fifth position Line 6, use the first small letter for methyl	
	The last two sentence of the conclusion should be modified, as follows This is the evidence that the presence of bromine at the third and the fifth position of pyrazole is essential for the antimicrobial activity, whereas chlorine, bromine, fluorine and nitro group attached at the phenyl ring enhance the antimicrobial activity. The obtained results for antimicrobial activity suggest that Cl, Br, F, and nitro substitution at the third and the fifth position may enhance the antimicrobial activity of the compounds, whereas methyl and methoxy substitution may result in reduction of the activity.	
	Add issue numbers to references 1-4, 6-16, 18-22, 25-27 and 29-31, wherever available	
	Format the entire manuscript according to the style of the journal.	
Minor REVISION comments		
Optional/General comments	This article is a significant contribution to the research of new pyrazole derivatives with antibacterial activity, within the scope of the journal and suitable for publication after some revision.	

PART 2:

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Are there ethical issues in this manuscript?	(If yes, Kindly please write down the ethical issues here in details) There are no ethical issues in this manuscript	
Are there competing interest issues in this manuscript?	There are no competing interest issues in this manuscript	
If plagiarism is suspected, please provide related proofs or web links.	There is no plagiarism suspected in this manuscript	

PART 3: Declaration of Competing Interest of the reviewer:

Here reviewer should declare his/her competing interest. If nothing to declare he/she can write "I declare that I have no competing interest as a reviewer"

I declare that I have no competing interest as a reviewer

PART 4: Objective Evaluation:

Guideline	MARKS of this manuscript
Give OVERALL MARKS you want to give to this manuscript	
(Highest: 10 Lowest: 0)	
Guideline:	
Accept As It Is: (>9-10)	Major Davision (57.9)
Minor Revision: (>8-9)	Major Revision: (>7-8)
Major Revision: (>7-8)	
Serious Major revision: (>5-7)	
Rejected (with repairable deficiencies and may be reconsidered): (>3-5)	
Strongly rejected (with irreparable deficiencies.): (>0-3)	

PART 5: Reviewer Details:
This information is mandatory to prepare the Reviewer Certificate properly.
Certificate prepration will not be possible if incomplete information is received.

Name of the Reviewer	Tamara Jovanovic
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5-8 Keywords regarding expertise of Reviewer | Materials, chemistry, medicinal and pharmaceutical chemistry, chemical technologies, nanotechnologies, biomedical engineering, spectroscopy