MEDICINAL CHEMISTRY

Manuscript Evaluation Form

Editor-in-Chief: Dr. Dimitra Hadjipavlou-Litina, Aristotle University of Thessaloniki, Thessaloniki, Greece

PAPER TITLE	Design, synthesis, and evaluation of isoquinoline ureas as TRPV1 antagonists
AUTHOR(S) NAME	Nehaben A. Gujarati, Bradley J. Undem and Vijaya L. Korlipara

Sec. A: REFEREE'S ASSESSMENT *(cross as appropriate)*

Criterion	Excellent	Good	Fair	Poor
Originality of the topic	x			
Technical Quality		x		
Importance in its Field	x			
Style & Overall Representation		x		
Readily Understandable	x			
Suitability for the Journal	x			
Adequate Illustrations or Drawings	x			
English language		x		

Description	Yes	No	Comments/ Suggestions
Does the title represent manuscript's contents?	x		
Is the Abstract accurate and concise?	x		
Are the approach/ methods properly described?	x		
Are the conclusions and interpretations sound?	x		
Are the references properly cited?	x		
Is this a new/ original/ contribution?	x		
Is it within the scope of the journal?	x		

Overall the Paper is Rated:	**(Excellent 8---------- Poor)** 10 9 **8** 7 6 5 4 3 2 1

Sec. B: REFEREE'S RECOMMENDATIONS

Accept with minor changes	x
Accept with major changes	
Reject in current form, but may be resubmitted	
Reject, with no resubmission	

OTHER SPECIFIC CRITICISMS

Imperfect style	x
Too long	
References incorrectly presented	
Typographical and Grammatical errors	x

PAPER TYPE: **Research article** ☐ **Review article** ☐ **Letter article** ☐

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Confidential Comments to the Editor (not for Transmission to Authors):

Comments for the Authors *(continue on another sheet, if necessary)*:

Review of the article entitled
Design, synthesis, and evaluation of isoquinoline urease as TRPV1 antagonists, by Nehaben A. Gujarati, Bradley J. Undem and Vijaya L. Korlipara

In this study, a series of analogues derived from the modification of the phenyl moiety of the isoquinoline urea lead compound A-425619 has been successfully synthesized. Their antagonist potency against transient potential vanilloid receptor 1 (TRPV1) has been evaluated using smooth muscle assay using guinea pig trachea, along with the evaluation of the molecular properties and molecular modeling using CoMFA studies. Inhibition of TRPV1, with the new potent and selective antagonists, has emerged as a novel approach in the treatment of various pain states.

The theme of this article is within the scope of the journal and it is suitable for publication after some revision.

The English language, spelling and grammar at some places have to be improved.

In the first sentence of the 2.2 Biological activity section it can be stated
The target compounds, presented in Schemes 2 and 3
Figure 2 can also be added, with the general formula of the target compounds, currently presented in the caption of Table 1, optional

All the superscripts in Table 1 should be at the right side.

State the complete names of the compounds in one row, wherever it is possible, preferably. For example,
5-aminoisoquinoline, 5-isoquinoline urea derivatives,
Para-trifluoromethyl derivative, *m*-isothiocyanate

In the section 2.3. Molecular Modeling,
CoMFA studies should be replaced instead of COMFA studies

In the reference 25, move 0.001 to the next row, beside kcal/mol Å, as follows
0.001 kcal/mol Å. The numbers and the units of measure should be in the same row.

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FIELD OF EXPERTISE OF REFEREE: Materials and chemical technologies, nanotechnologies, biomedical engineering, chemistry**,** medicinal chemistry

Name & Affiliation of referee: Tamara Jovanović, Department of Biomedical Engineering, Faculty of Mechanical Engineering, University of Belgrade, Kraljice Marije 16, 11120 Belgrade, Serbia

Dr Tamara Jovanović / November 24, 2018
SIGNATURE OF REFEREE / DATE