**Synthesis and efficacy of copper(II) complexes bearing *N*(4)-substituted thiosemicarbazide and diimine co-ligands on plasmid DNA and HeLa cell lines**

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**Response to reviewers comment**

**Reviewer: C**

1. Full names of ligands L1-L3 should be given in the Abstract

As per the suggestion by the reviewer, full names of the ligands L1-L3 were included in the abstract (Page no. 1)

1. There is no reference to Supplementary Data from the text of the manuscript

As per the suggestion, it was included in the manuscript (Page no.7)

**Reviewer: F**

1. Keyword “N(4)-substituted thiosemicarbazide” should be changed because  
   it already appears in the title

As per the comment, Keyword “N(4)-substituted thiosemicarbazide was changed from the manuscript (Page no.1)

1. line 9: it should be “nine novel

As per the reviewer suggestion, the sentence was changed (Page no. 1)

1. line 56: it should be “characterize”

As per the reviewer suggestion, the sentence was changed (Page no.2)

1. line 193: it should be “are assigned to”

As per the reviewer suggestion, the sentence was changed (Page no.8)

1. line 278: There should be reference for “chelation theory”

As per the suggestion by the reviewer, the reference was included in the manuscript (Page no. 11)

1. line 341: “except for mixed ligand…” instead of except it should be “while” or something similar.

As per the suggestion by the reviewer, the sentence was reframed (Page no. 13)

1. Scheme 2 - in the formula I believe it should be NHR not NH2

Instead of NHR it was given as NH2 by mistake. It was changed in the present manuscript (Page no.6)

1. Scheme 3 - There should be what are the chelate rings (in the legend).

As per the reviewer suggestion, chelate rings of the ligands were included in the scheme 3 (Page no.6)

1. Why are almost all the Figures in Supp info? Where are NMR spectra for H(L2)  
   and H(L3)? I believe authors should decide what to put in the main text and  
   what in Supp info. And this should be clearly stated in the man text, e.g.  
   “as an example we present NMR spectra of HL(1) in Fig 1, while data (or  
   spectra) for other compounds are given in Supp info.” This is also related  
   to other spectra presented in Suppinfo.

As per the suggestion by the reviewer, the data of ligands H(L2) and H(L3) included in the supplementary information. (Page no. 7)

1. Line 190. In caption of the Figure it is written that it is complex C5 while  
   in the text it is written C9

Instead of C5 it was given as C9 by mistake. It was changed in the present manuscript (Page no. 8)

1. The authors did not show 3-4 bands in Figure 4. This should be commented

The electronic spectra of thiosemicarbazone copper(II) complex C5 in DMF displayed three intense absorption bands near 295, 415 and 725 nm.

**Reviewer: G**

1. Introduction: the authors should also mention that the aim of their study  
   was to examine the antibacterial activity of compounds against Gram-positive  
   (B.thuringiensis) and Gram-negative (E.coli) bacteria (line 62‒63).

As per the suggestion, the sentence was reframed (Page no. 3)

1. Experimental: The data of 13C NMR experiments are missing (Material and  
   methods, line 81).

As per the reviewer suggestion, the sentence was corrected (Page no.3)

1. The characteristic 13C NMR resonances of ligands should be listed in the  
   Supplementary materials (after 1H NMR data).

It was already listed in the same format (Supplementary information Page no. 1)

1. Scheme 1 is missing in the manuscript (line 151).

As per the suggestion, scheme 1 was included in the manuscript (Page no. 6)

1. Due to the lack of crystal structures of the complexes, the authors  
   should record ESI-MS of complexes, if it is possible, with the aim to  
   complete the characterization of the compounds.

In the absence of X-ray single crystal, the geometric shape of the copper(II) complexes have been elucidated using high resolution mass spectrometry. It was included in the result and discussion section, page no.10).

1. The authors should compare their results of the anticancer activity with  
   those previously published for the structurally similar metal complexes.

As per the reviewer suggestion, anticancer activity of the synthesized copper(II) complexes compared with structurally similar metal complexes and included in the manuscript (Page no. 13)

1. Suggestion: In my opinion, it is more appropriate to put Copper(II)  
   complexes or Antibacterial activity as Keyword than Ascorbic acid (line  
   24‒25).

As per the suggestion by the reviewer, keyword was changed in the manuscript (Page no. 1)

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