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Urease inhibition activity of Transition metal chelates: *anti – ulcer agents*

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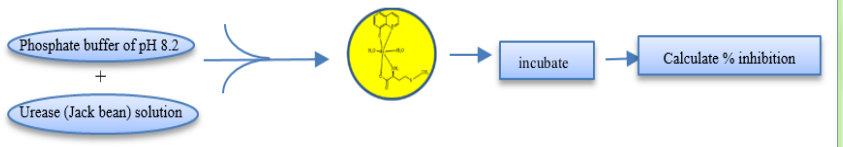
Objective & Background

In the current work, in-vitro urease inhibition activity of metal Heterochelates of Cr (III), Mn (II), Fe (III), Co (II), Ni (II), Cu (II), Zn (II), Cd (II) and Pb (II) with 8-hydroxyquinoline and *DL*-methionine has been presented with their docking study. These complexes were already reported for their excellent anti-oxidant activity. All the complexes showed urease inhibition activity, while thiourea was the standard having IC_{50} value 21.6 ± 0.12 µM. Among the nine complexes, it was found that Cu (II) complex showed potent inhibitory activity (22.6 ± 0.72 µM) comparable with the standard thiourea (21.6 ± 0.12 µM).

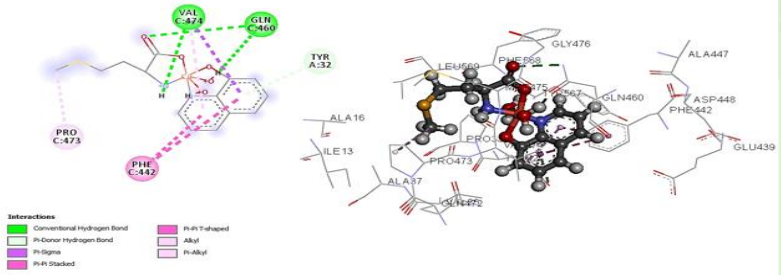
A gram negative bacteria Helicobacter pylori produce urease enzyme and cause urinary tract stones and peptic ulcer by using urease mechanism. Urease inhibitors are used to reduce the activity of Urease enzyme by decreasing the hydrolysis of urea. This inhibition results in the decrement of H. Pylori survival inside the mucosa of stomach. Discovery of new urease inhibitors are the active area of research to overcome all the losses and health problems. A number of urease inhibitors have been reported which includes heavy metal ions . This research is interesting in studying the urease inhibition activity and chemical docking of new complexes.



Molecular docking study

Autodock was used to perform the docking simulations employing the 3D structure of bacillus pasteurii urease (PDB code: The following parameters were used to perform the docking simulation: size x = 82.6443; size y = 86.0453.2962; size z = 67.2583; center x = 15.5310; center y = 94.9548; center z = 74.2453

Results



2D and 3D depiction of docking of (6) in active site of bacillus pasteurii urease.

The IC_{50} values of both ligands compared with a standard Thiourea (IC50 =21.6 ± 0.12) displayed urease inhibition activity. All metal Compounds are found to be active except 1 and 7 (IC50>200 µM). While compound 6 containing Cu metal (IC_{50} =22.6 ± 0.72) exhibited significant inhibitory potential

The inhibitory activity of metal compounds with has been the subject of interest of current study. The IC_{50} of all heterochelates were compared with standard. And it was found that copper compound exhibited significant urease inhibition activity. The docking study of these heterochelates also showed that the compound containing copper as its center metal found to have greater potential in inhibiting effect of Urease enzyme as compare to all synthesized hetero chelates. It has an ability to act as potent anti-ulcer agents in future.

References

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