Role of Schiff Bases Metal Complexes in Agriculture as Urease Inhibitors

Sonu Chauhan[1]*, Suman[1], Anushree[1] and Poonam Ranga[2]

[1]Department of Chemistry, [2]Department of Microbiology, COBS&H, CCS Haryana Agricultural University, Hisar-125004, Haryana, India

Corresponding Author
Sonu Chauhan
Email: chauhansonu7777@gmail.com

OPEN ACCESS

Keywords

Urease, Inhibitors, Schiff bases, Metal complexes, Agriculture

How to cite this article:

Chauhan, S., Suman., Anushree, and Ranga. P. 2026. Role of Schiff Bases Metal Complexes in Agriculture as Urease Inhibitors. *Vigyan Varta* 7 (02): 147-150.

ABSTRACT

Schiff bases demonstrate biological activities and are unexacting to synthesize, which makes them attractive platform for drug discovery. This article, includes synthesizing and assessing urease inhibitory activity of Schiff base metal complexes. The Schiff base ligands were synthesized by condensing ketones or aldehydes (carbonyl compound) with specified amines and thereafter coordinating them with transition-metal ions like as nickel(II), cobalt(II), copper(II), and zinc(II), followed by their spectroscopic characterization. *In vitro*, evaluation of Schiff base and their complexes was done using thiourea as the reference. Many of the synthesized metal complexes demonstrated marked suppression of urease activity, emphasizing their promise for pharmaceuticals. Incorporation of electron-withdrawing substituents, results in enhancement of inhibitory potency of these complexes. These outcomes indicate that Schiff base metal complexes are promising lead structures for the development of new urease inhibitors aimed at managing urease-mediated conditions, including gastric ulceration and urinary tract infections.

INTRODUCTION

Urease belongs to the large superfamily of amidohydrolase and phosphotriesterase enzymes, all of which contain catalytically important metal ion(s) at their active centers. It functions as a nickel-dependent metalloenzyme and historically was the first enzyme successfully obtained in crystalline form, a milestone that helped establish that enzymes are proteins. The natural substrate of urease is urea, which itself was the earliest organic compound synthesized in the laboratory in 1828. In biological systems, urease has a relatively short lifetime because it is quickly degraded and turned over through microbial metabolic processes. Urease is synthesized by a variety of organisms, including higher plants, numerous bacterial species, and many fungi, where it plays a key role in nitrogen metabolism by converting urea into ammonia and carbon dioxide.

$$H_2O + H_2NCONH_2 \xrightarrow{\text{urease}} 2\,NH_3 + CO_2$$

In kinetic terms, it is an exceptionally powerful biocatalyst: the enzyme-catalyzed hydrolysis of urea proceeds roughly 10^{14} times prompter than the non-catalyzed reaction, demonstrating urease efficiency to stabilize the transition state and reducing the energy of activation for this transformation. In depths of soil, diverse life flourishes, as fungi, bacteria, and plants each bestow to the ecosystem. Among these organisms, *Helicobacter pylori* stands out as a remarkable urease, crucial for breakdown of urea. Also, Jack bean's urease is particularly indelible; it is the first metalloenzyme known to require nickel for its activity. This extraordinary enzyme quickly catalyzes the conversion of urea into ammonia and carbon dioxide, illustrating a profound transformation pivotal for nutrient cycling. It has molecular mass of 480 kDa, and is most effective at a pH 7.4, unveiling a balanced enzymatic performance. Furthermore, its optimal activity is displayed at temperature 60˚C , accentuating its unique prowess in the sophisticate dance of enzymatic reactions within the soil ecosystem.

1. **Structure of urease enzyme:** The active site of urease consists of two nickel ions which are interconnected by a hydroxyl group and lysine-derived oxygen atoms. Each nickel atom is connected with a water molecule and two histidine residues, while the coordination sphere of the second nickel Ni(2) is completed by an aspartate residue. Ni(1) displays a penta-coordinated, distorted square-pyramidal geometry, whereas Ni(2) exhibits a distorted octahedral geometry with six coordinating atoms (Acar *et al*., 2025).

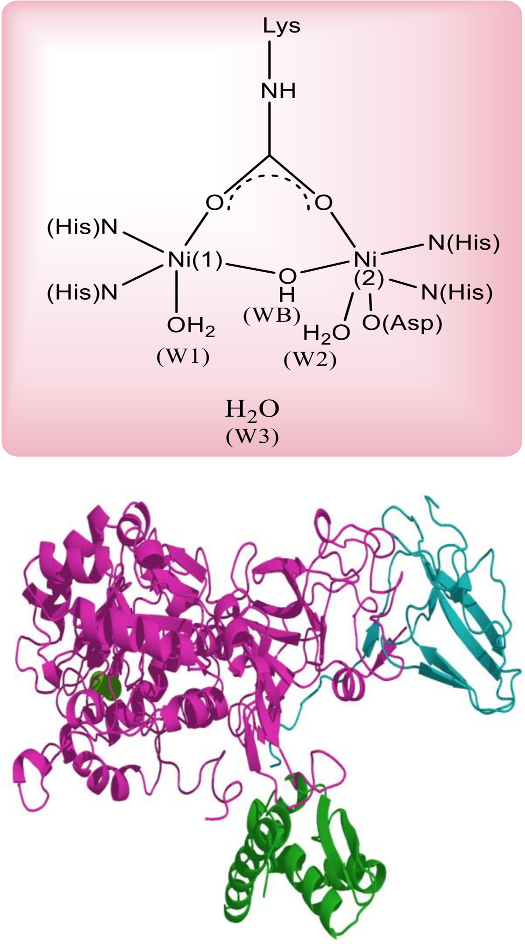


Figure 1: Structure of urease enzyme

2. **Ammonia Volatilization:** Urea granules readily pull in moisture from the air due to their hygroscopic properties. Once spread on soil, they dissolve and seep into the ground, mixing with existing soil water. This sets off urease enzymes, which speed up urea's breakdown into ammonium ions.

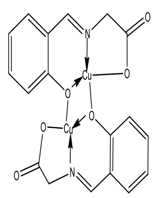
The release of ammonium ions causes a short-term pH spike nearby, forming alkaline hotspots that promote ammonia gas release. As a result, ammonia drifts off into the air, wasting nitrogen from the soil. Grasping this mechanism helps farmers fine-tune nitrogen application, cut losses, and reduce environmental harm.

3. **Overuse of urea:** Healthy soils rely on a balanced mix of nutrients to promote robust plant growth and sustain ecosystem health. The optimal ratio of nitrogen, phosphorus, and potassium (N: P: K) is generally 4:2:1, which supports thriving crops and vibrant soil microbes and organisms that boost overall fertility. Yet, heavy reliance on urea has drastically altered this essential nutrient equilibrium (Motasim *et al*., 2024).

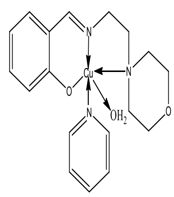
This shift creates a nitrogen overload while often starving the soil of phosphorous and potassium. Too much nitrogen harms soil structure, stifles microbial life, and disrupts nutrient recycling, gradually eroding fertility and threatening farm output. To protect soil vitality and food production, farmers must shift to balanced fertilizer strategies that restore all key nutrients, not just nitrogen-heavy ones like urea.

4. **Urease inhibition:** Increased ammonia levels impact medicine and agriculture profoundly. In farming, ammonia assists plant growth and breakdown of urea for seed germination, but excessive amount of ammonia disrupts soil balance, results in harming of crops by favouring of pathogens. Medically, formation of urinary stone is promoted by it *via* precipitation of crystal from uplifted kidney concentrations. Nitrogen issues were effectively tackled by urease inhibitors. Along with fertilizers, they muffle urea hydrolysis, boosting yields, crop uptake, and soil health by reducing volatilization losses. Therapeutically, they slow ammonia release from ureolytic bacteria, offering treatment potential for related infections (Cantarella *et al*., 2018).

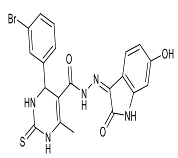
5. **Schiff base metal complexes as urease inhibitors:** Schiff base ligands result from condensation of primary amines with carbonyls like aldehydes or ketones- a method pioneered by Hugo Schiff in 1864. To synthesize metal complexes, reflux metal salts with pre-made Schiff bases in an appropriate solvent, then wash the products with alcohol and dry them (Dalia *et al*., 2018). Metal complexes inhibit urease uniquely, unlike organic inhibitors alone, and are classified by metal type: Cu/Zn/Co/Ni, other transition metals, or non-transition metals/metalloids. The great interest in copper complexes as urease inhibitors might be due to the strong Lewis acid properties of its metal ions. Zhu and co-workers (2007) synthesized copper complexes, derived from different Schiff bases and evaluated their activities against urease, among these a mononuclear complex **2** ($IC_{50} = 0.43$ μM) was found to be more potent than a binuclear complex **1** with IC_{50} value of 2.25 μM (de Fátima *et al*., 2018). Iftikhar and co-workers (2017) described dihydropyrimidine (DHPM) **3** as the most potent jack bean urease inhibitor ($IC_{50} = 0.23$ μM) (de Fátima *et al*., 2018). Thus, in agriculture, urease inhibitors paired with fertilizers boost nitrogen use efficiency.



1 (IC_{50} = 2.25 μM)



2 (IC_{50} = 0.43 μM)



3 (IC_{50} = 0.23 μM)

CONCLUSION:

Metal complexes inhibiting enzymes is an emerging research field with therapeutic potential and broader uses. The activity of enzyme can be synchronized by preferring different metals and altering their coordination sphere, including oxidation state, coordination number, ligand type, and geometry. The tunable structures of Schiff bases and their metal complexes boost efficiency, cut nitrogen loss, and safeguard soil health without harming crops. Moving forward, these compounds offer a wise path to better yields, greener fertilizers, and lasting agricultural systems.

REFERENCES:

Acar, M., Tatini, D., Romani, V., Ninham, B. W., Rossi, F., & Nostro, P. L. (2025). Curious effects of overlooked aspects on urease activity. *Colloids and Surfaces B: Biointerfaces*, *247*, 114422.

Cantarella, H., Otto, R., Soares, J. R., & de Brito Silva, A. G. (2018). Agronomic efficiency of NBPT as a urease inhibitor: A review. *Journal of advanced research*, *13*, 19-27.

Dalia, S. A., Afsan, F., Hossain, M. S., Khan, M. N., Zakaria, C., Zahan, M. E., & Ali, M. (2018). A short review on chemistry of Schiff base metal complexes and their catalytic application. *Int. J. Chem. Stud*, *6*(3), 2859-2867.

Motasim, A. M., Samsuri, A. W., Nabayi, A., Akter, A., Haque, M. A., Abdul Sukor, A. S., & Adibah, A. M. (2024). Urea application in soil: Processes, losses, and alternatives-A review. *Discover Agriculture*, *2*(1), 42.

de Fátima, Â., de Paula Pereira, C., Olímpio, C. R. S. D. G., de Freitas Oliveira, B. G., Franco, L. L., & da Silva, P. H. C. (2018). Schiff bases and their metal complexes as urease inhibitors-a brief review. *Journal of advanced research*, *13*, 113-126.