International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2025: 7.089

Cu-Naringenin Complex Structural Understanding Pharmacological Uses and Electrochemical Behaviour: A Review

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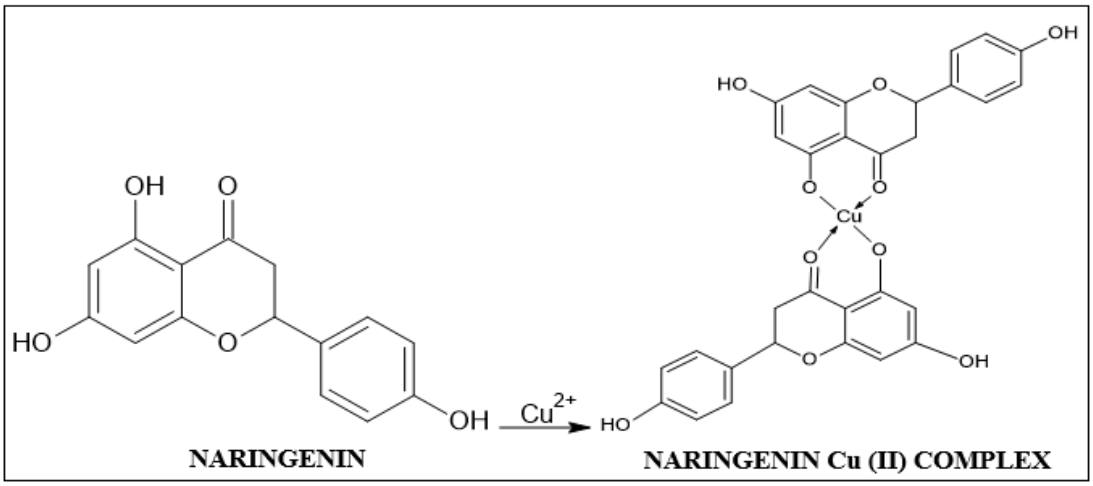
Abstract: ***Naringenin, a flavonoid with potent anti- inflammatory, anti-cancer, and antioxidant properties, is found naturally in citrus fruits. However, its therapeutic efficacy is limited by its poor bioavailability and solubility. To enhance its pharmacological potential, a naringenin-copper complex was prepared and investigated using FTIR, cyclic voltammetry, and UV-Vis (spectroscopic) techniques. The spectral data confirmed that the copper ion coordinated with the hydroxyl and carbonyl groups of naringenin. The complex Demonstrated enhanced redox stability, antioxidant capacity, and biological activity when compared to the free ligand. While antimicrobial and cytotoxic studies showed superior pharmacological action, antioxidant assays like DPPH and FRAP showed a higher capacity to scavenge radicals. These findings demonstrate that complexation with copper significantly improves the physicochemical and biological properties of Naringenin, suggesting potential therapeutic application***

Keywords: Naringenin-Cu complex; Antioxidant Activity; flavonoids; cyclic voltammetry; spectroscopic characterization; redox stability

1. Introduction

Naringenin is a naturally occurring flavonoid that is primarily found in citrus fruits [1]. Cardioprotective, anti-inflammatory [2], anticancer [3], antidiabetic, and antioxidant properties are just a few of its many pharmacological traits [4]. Despite these significant biological activity, naringenin's medicinal application is typically restricted by its poor water solubility, low stability, and limited bioavailability [5]. To get over these challenges, metal complexation has emerged as a viable technique for enhancing its physicochemical and pharmacological properties [6]. Because they can form stable complexes with bioactive ligands, transition metals like copper are crucial in biological systems. Copper is a necessary trace element for several enzymatic reactions, redox processes, and cellular Défense mechanisms [7]. The creation of a naringenin–copper complex may change the electronic structure of the ligand, improving its stability, redox behaviour, and biological efficacy [8]. According to studies, these metal–flavonoid complexes have better cytotoxic, antimicrobial, and antioxidant properties than free flavonoids [9]. Characterization using FTIR, cyclic voltammetry, and UV-Vis offers important information about the complex's structural characteristics and coordination mode [10]. Thus, in contemporary medicinal chemistry, the synthesis and assessment of naringenin–copper complexes hold significant promise for drug development and therapeutic applications [11]-[12].



Experimental Approach Used in Studies

The copper (II)–naringenin complex was made using a simple complexation method. A precisely weighed naringenin (1 mmol, 272 mg) was dissolved in 25 mL of absolute ethanol, heated gradually to 35–40°C, and continuously stirred to ensure complete dissolution. To facilitate coordination, 0.1 M NaOH solution was added gradually until the pH reached approximately 7.5–8.0, deprotonating the phenolic hydroxyl group of naringenin. In a separate beaker, 10 mL of ethanol was used to dissolve 1 mmol (199 mg) of copper (II) acetate monohydrate. After that, the copper (II) solution was added dropwise while the ligand solution was constantly swirled at

room temperature. The reaction mixture was further stirred for another hour and then refluxed for two hours at 70°C to complete the complex formation. After cooling the reaction mixture to room temperature and then immersing it in an ice bath, a coloured precipitate of the copper (II)–naringenin complex was produced. The resulting solid was collected by vacuum filtration, thoroughly cleaned with cold ethanol to remove any remaining salt or unreacted ligand, cleaned with diethyl ether, and vacuum-dried at 40 to 50°C to obtain the pure complex. A range of analytical methods, including elemental analysis, cyclic voltammetry, Fourier Transform Infrared (FT-IR) spectroscopy, Electron Paramagnetic Resonance (EPR), and UV-visible spectroscopy, were used to characterize the obtained complex in to confirm its formation and determine its structural and electronic properties. The yield percentage was determined by the amount of naringenin used.

2. Result and Discussion

Spectroscopic Analysis:

UV-visible spectral analysis:

two distinctive π→π* transition bands can be seen in the ligands UV-visible spectrum in Dimethylformamide (DMF) a less intense band I in the 315-360 nm range that originates from the B ring and an intense and sharp band II at 218 nm that is attributed to the A and C ring π-system. For related flavanones, these assignments are consistent with TDDFT studies. Band I exhibits increased intensity and loss of symmetry with absorption extending beyond 360 nm upon Cu(II) complex formation in Dimethylformamide (DMF) indicating ligand- metal or metal- ligand charge transfer involving C4-O-Cu and C5-O-Cu bonds, while band II stays unchanged. The complex exhibits a weak d-d transition at 650 nm at higher concentration, which is not present in the free ligand. While solid-state spectra changes in water further validate coordination

Temperature-Dependent EPR for Weakly Coupled 1-Dimensional Cu(II) System:

The solid- state EPR spectra obtained between 120 K and room temperature show no significant change except for the expected decrease in signal intensity with increase temperature. Partial resolution of the hyperfine structure indicates very weak exchange coupling between Cu (II) ion, consistent with their 1-Dimensional arrangement linked by non-covalent interaction in the crystal lattice. Minimal magnetic exchange is further confirmed by the temperature dependent intensity, which exhibit Curie-Weiss behavior with a negligible Weiss constant. The complex maintains its solid-state structure when dissolved in DMSO, as evidenced by Similar g//- and A// values in both solid and solution states. Dipole- dipole interaction between Cu(II) ions in a 1-Dimensional system are also suggested by a weak broad resonance about 160 mT Albeit a thorough examination of this characteristic is outside the purview of this investigation.

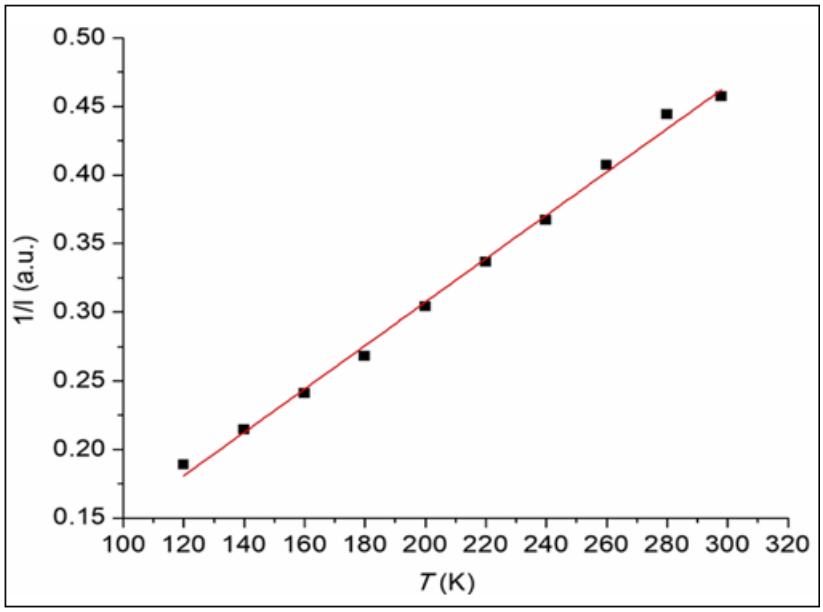


Figure 1: The 1/I vs T plot follows Curie–Weiss behavior with a good linear fit, indicating negligible exchange interaction between Cu(II) ions.

Cu(II)-Naringenin coordination: FT-IR and Raman:

FT-IR and Raman spectroscopy were used to characterize the Cu(II)-Naringenin complex and compare it with free Naringenin. Assignments of vibrational bands were based on previous theoretical and experimental research. Coordination effect is indicated by the phenolic O-H stretching band shifting from 3290 cm^{-1} in Naringenin to 3201 cm^{-1} in the complex and the presence of coordination water is confirmed by an additional band at 3412 cm^{-1}. Both species exhibit C-H stretching vibration in the 3200-2800 cm^{-1} region, which are better resolve in Raman spectra. Consistent with earlier reports on Cu(II) flavonoid complexes the carbonyl (C=O) stretching band shifts from 1635 cm^{-1} in Naringenin to 1615 cm^{-1} in the complex, indicating Weakening of the C=O bond due to metal coordination. Complex formation is further supported by changes in C=C stretching bands. Strongs evidence for coordination through the C4-O and C5-O sites is provided by the disappearance of the 1316 cm^{-1} band, which is attributed to C5-OH deformation. Furthermore, the formation of Cu-O bonds is definitively confirmed by the appearance of a new low intensity band at 596 cm^{-1}, which is attributed to M-O stretching.

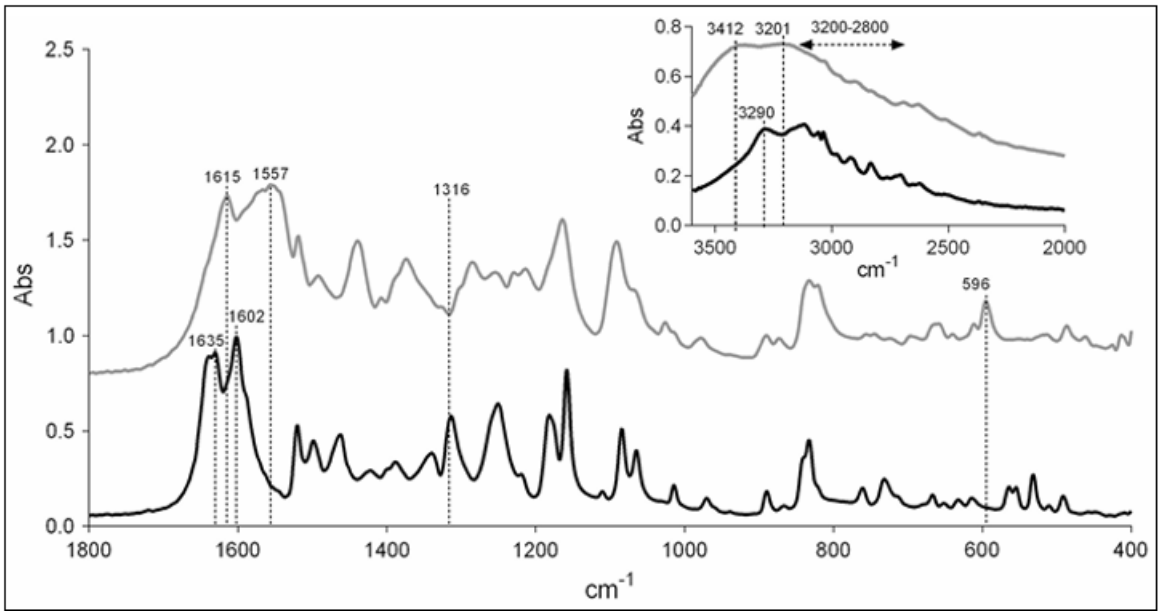


Figure 2: IR spectra for Cu(II)-Naringenin complex

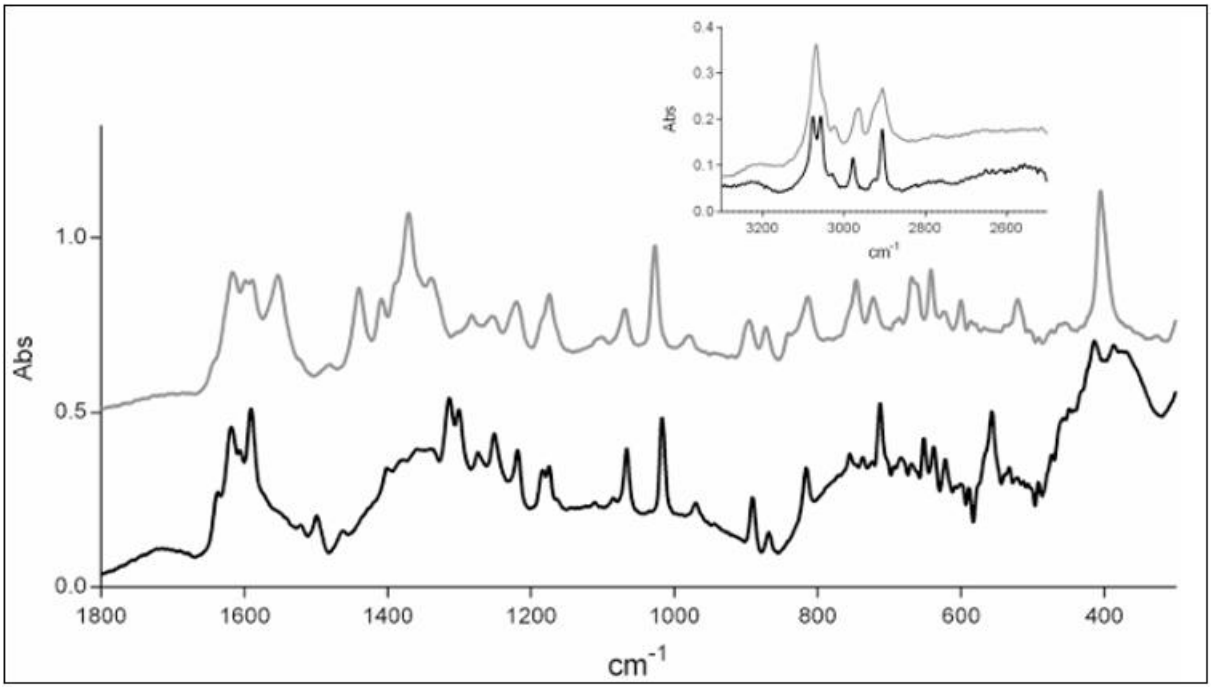


Figure 3: Raman spectra for Cu(II)-Naringenin complex

Naringenin And its Cu(II) Complex Scavenging properties:

Because electron delocalization is limited by the lack of conjugation between rings A and B to sp3 hybridization at C2 and C3, flavanones typically have lower antioxidant activity than other flavonoids. As a result, the antiradical activity of free naringenin is moderate. However experimental findings show that when naringenin is chelated with Cu(II), its capacity to scavenge radicals is increased. For other flavonoid- metal complexes, comparable gains have been documented. Cu(II) coordination redistributes electron density within the molecule, according to theoretical Mulliken population analysis, even though complex formation has no effect on the primary reactive C4'-OH group. Homolytic cleavage of the C7-O-H bond is facilitated by an increased negative charge on the C4-O and C7-O groups. Cu(II) functions as an electrons acceptor and stabilizes radical intermediates as evidence by the partial transfer of unpaired electron density to the Cu centre during radical formation. This trend is confirmed by solvent simulation. Cu(II)/Cu(I) redox cycling and decreased metal redox potential may also improve antioxidant efficiency, indicating that Cu(II)-naringenin complexes have better biological and therapeutic potential.

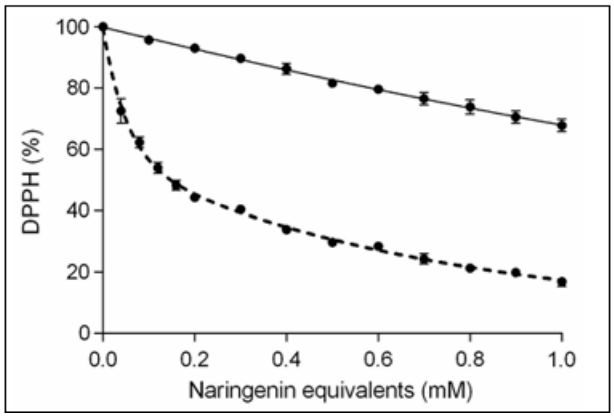


Figure 4: DPPH Scavenging by Cu(II)-Naringenin complex

3. Conclusion

The Cu-naringenin complex's structural characteristics, characterization, pharmacological potential, and electrochemical behavior are all methodically summarized in this review. The successful coordination of naringenin to Cu(II), primarily through the 5-hydroxyl and 4-carbonyl groups is confirmed by spectroscopic characterization using FT-IR, Raman, EPR, UV-visible, and NMR techniques as well as thermal and elemental analyses. This coordination is frequently accompanied by coordinated water molecules. The ligand physicochemical characteristics are greatly impacted by these structural changes. Because of enhanced redox activity and metal- assisted biological interaction, pharmacological studies show that Cu complex improves antioxidant, antiradical, anticancer, and antimicrobial activities when compared to free naringenin. Well define Cu(II)/Cu(I) redox couples are revealed by electrochemical studies suggesting effective electron-transfer behavior pertinent to catalytic and biological applications. All things considered the Cu-naringenin complex show promise as a Metallo flavonoids requiring additional in vivo, toxicity, and structure activity relationship research for more advanced therapeutic development.

Acknowledgement
The author is grateful to Department of Chemistry, PMCoE Government J.S.T. PG College Balaghat for support and thankful to Dr. Rakesh Choure for his advice and encouragement throughout preparation of this manuscript.

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