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## **BIOLOGICAL ADVANCEMENT OF Ni(II)** AMIDE COMPLEXES: A REVIEW

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**Abstract:** The biological activity of amide group containing ligands with their Ni(II) complexes against E. coli and S. aureus is described in this study. For the investigations, the usual disc diffusion method was used. The data collected throughout the investigation was correlated for structure-activity relationships and a tendency for a series of complexes was identified. The effect of four nickel complexes with ligands including against 33 pathogenic and control bacterial strains was studied in vitro. The complexes antifungal activity was also confirmed against four Candida species. In vitro antibacterial activity against the bacteria tested, particularly Gram-positive strains, as well as E. coli and S. aureus. The sensitivity of E. coli strains to the studied complexes was the lowest of all the microorganisms evaluated.

**Keywords:** Biological Advancement, E. coli and S. aureus.

#### **I.Introduction:**

One of the most prevalent chemical bonds is the amide bond, which is found in a variety of organic compounds and biomolecules. Because amide bonds are highly stable under a variety of reaction settings (including acidic and basic environments), at high temperatures, and in the presence of other chemicals, nature has exploited them to create these significant bio-molecules. The great stability of amide bonds is due to their propensity to create resonant structures, which give the amide CO-N bond a double bond nature. The most common types of bonding in organic molecules and other types of bio-molecules, including peptides, proteins, DNA, and RNA, are amide bonds. The ability of amide bonds to form resonant structures distinguishes them from other types of bonds. As a result, they are extremely stable and adopt certain three-dimensional forms, which in turn are in charge of their activities. Because of their great stability and propensity to form resonant structures, amide bonds are frequently found in proteins. This is one of the main reasons why proteins adopt secondary structures and how they function biologically. In order to regulate the functions of highly stable amide bonds, nature has created a few techniques. A common functional group that can be found in peptides, proteins, pharmaceuticals, natural products, and polymers is the amide. The traditional methods of synthesising amides include the interaction of a carboxylic acid with an amine in the presence of an activator. Due to their low electrophilic character and immunity to nucleophile assaults, amides are recognised as an inert functional group. The resonance stability of the amide bond, which causes this resistive behaviour, is the obvious cause. By selectively rupturing the nitrogen-carbon (N-C) bond of the amide, transition metal catalysis, however, avoids the critical parameter and promotes cross-coupling or other amide reactions. In the present paper review has been done about various process used in biological advancement of Ni(ii) amide complexes.

Ramakanth Pagadala et al conscious that microwave chemistry is a green chemical method that improves reaction conditions and product yields. The main aim is to synthesize the tetradentate N2O2 ligand [HO(Ar)CH<sup>1</sup>/4N–(CH2)2–N<sup>1</sup>/4CH(Ar)OH] and manganese(II), cobalt(II), nickel(II), and zinc(II) complexes of the type ML by classical and microwave techniques. The resulting Schiff base and its complexes are identify by 1H NMR, IR, elemental analysis, and electronic spectral data. The ligand and its Co(II) and Mn(II) complexes were further identified by X-ray diffraction and mass spectra to structure determination. They suggest that the metal is bonded to the ligand through the phenolic oxygen and the imino nitrogen.[1]

Zahra Piri et al deliberate that using ultrasonic irradiations, [ZnL2].CH3CN, [NiLCl] and [CoL2] (where L is 2-acetylpyridine -4N-p-chlorophenylthiosemicarbazone ligand) complexes were prepared and investigated using various spectroscopic methods. Crystal structures of ZnL2 and NiLCl complexes displayed distorted octahedral and square-planar coordination geometry around the central metal, respectively. The UV-Visible and mass spectroscopic analysis revealed 1:2 (metal:ligand) stoichiometry for

Co(II) complex. The synthesized complexes were used as precursors for preparing their corresponding nano-sized metal oxides via thermal decomposition. The nanostructures of metal oxides were characterized by scanning electron microscope (SEM), energy dispersive X-ray (EDX), X-ray diffraction (XRD) and Fourier transform infrared (FT-IR). The in vitro antibacterial activity of thiosemicarbazone complexes and their corresponding nano-sized metal oxides were studied against a series of gram positive and gram negative bacteria, using the zone inhibition methods. While NiLCl complex was shown to possess more antimicrobial activity than its nano-sized metal oxide, the prepared nano-sized zinc and cobalt oxides have shown the highest activity. [2]

N. Sreeju et al deliberate that transition metals which known for mankind, the synthesis of Cu has remains a major challenge owing to their instinctive oxidative power under ambient conditions. They introduces a microwave-assisted one-pot method of synthesis of highly stable copper nanoparticles (CuNPs) in aqueous medium using hydrazine as reducing agent and leaf extract of Psidium guajava as the stabilizer. The effects of different synthesis parameters like precursor pH, temperature, quantity of stabilizing and reducing agent, power level and time of microwave irradiation on the formation of nanoparticles have been investigated. UV-vis spectra of the colloid display Surface Plasmon Resonance bands centered around 561-572 nm, characteristic of copper nanoparticles. Comparative studies of FTIR spectra of the extract and copper nanoparticles reveal the involvement of different functional groups in stabilization. TEM micrographs and XRD patterns show the formation of nearly spherical nanoparticles of size around 15 nm with face centered cubic structure. The catalytic efficiency of the synthesized copper nanoparticles has been represent through the degradation of the organic pollutants methylene blue, methyl red, methyl orange, eosin yellow, 2-nitrophenol and 3-nitrophenol. The in vitro cytotoxic effect of CuNPs on L929 fibroblast cells has been evaluated and found to be surprisingly small. Dose dependent antibacterial activity of the synthesized CuNPs against pathogenic gram negative Escherichia Coli and gram positive Staphylococcus aureus has been investigated through agar - well diffusion method. Anti- oxidant potential has been depicted through DPPH, OH- and NO radical scavenging assays. Superior enhancement of thermal conductivity observed in CuNPs-water and CuNPs-ethylene glycol nanofluids promises their unambiguous exploitation as heat transfer fluids.[3]

Manas Sutradhar et al conscious that one-dimensional (1D) polynuclear Cu(II) complex derived from (5-bromo-2hydroxybenzylidene)-2-hydroxybenzohydrazide (H2L) is synthesized and characterized by elemental analysis, IR spectroscopy, ESI-MS, and single crystal X-ray crystallography. Its catalytic performance towards the solvent-free microwave-assisted peroxidative oxidation of hydrocarbons under mild conditions is compared with that of dinuclear Cu(II) complexes of the same ligand, previously reported as antiproliferative agents. Polymer 1 exhibits the highest activity, either for the oxidation of cyclohexane (leading to overall yields, based on the alkane, of upto 39% of cyclohexanol and cyclohexanone) or towards the oxidation of toluene (selectively affordingbenzaldehyde up to a 44% yield), after 2 or 2.5 h of irradiation at 80 or 50 \_C, respectively.[4]

Kiyohisa Ohta et al deliberate that the determination of Cu and Mn in biological materials and river waters by sequential metal vaporelution analysis (SMVEA) using an atomic absorption detector (AA) is reported. An improved Mo column (open column, i.d. 1.22 mm) with three ring supporters was developed for SMVEA. An optimum flow rate of carrier gas (pure argon) for separation of metal vapors was 4.0 ml min\_1. Cu and Mn peaks separated from Al,Ca, Cd, Fe, K, Mg, Na, Pb, and Zn peaks at a vaporization temperature of 1950°C and a column temperature of 1900°C. The appearing order of these metals was Cd, Zn, Pb, Cu, Na and Mn. It was understood by considering the boiling points of these metals or chlorides. The delay of appearing time is due to an interaction between the metal vapors and inside surface of the column. Under the experimental conditions, the number of theoretical plates was 11.3 for Cd, 89.6 for Cu, 160 for Na, and 258 for Mn in the improved column. Under the optimal experimental conditions, NIST biological standards and river waters were analyzed for copper and manganese. The analytical results agreed well with the certified values and the recoveries were in the range of 94 to 109%.[5]

Kalpanadevi, K. and R. Manimekalai conscious that nickel oxide (NiO) nano-particles have been produced microwave method from the Ni(OH)2 precursor, which was obtained by slow drop-wise addition of 0.1M sodium hydroxide to 0.1M nickel nitrate. The mixture have been vigorously stirred until the pH reached 7.2. after that irradiated with microwave to deposit Ni(OH)2 at a better precipitation rate. Drying the precipitate at 320°C resulted in formation of NiO nanoparticles. High Resolution Transmission Electron Microscope (HRTEM), Scanning Electron Microscope (SEM) and X-ray diffraction (XRD), employed for the structural characterization of the as-prepared NiO nanoparticles, revealed their good crystallinity and high-purity. Microwave irradiation increased homogeneity and decreased the mean particle size of the produced NiO particles.[6]

B. Lal and P. K. Rastogi studied that microwave assisted combustion approach is utilized for synthesis of nano-sized Cr substituted Ni ferrites (NiCrxFe2-xO4). The as obtained materials were further sintered at 450°C in air and then utilized for physicochemical and electrochemical characterizations. X-ray diffraction (XRD) patterns showing sharp peaks confirmed the formation of single phase cubic spinel structure. TEM image reveals the formation of nanocrystalline particles having size in range of 10-20 nm. Further, the electrocatalytic oxygen evolution reaction (OER) of as-synthesized materials was studied by linear sweep voltammetry in alkaline solution. The OER results showed that co-substitution of Cr in NiFe2O4 matrix improved the electrocatalytic activity of the oxides towards OER. The NiCr0.5Fe1.5O4 shows the best OER performance in 1.0 M KOH solution. It achieved a low overpotential of about 320 mV at 10 mA/cm2 current density, which is comparable to other reported electrocatalysts.[7]

Ramakrishnan Azhagu Raj conscious that using Coriandrum sativum L., a leaf-extracted, assisted microwave method (MM) was used to synthesize nickel oxide formation. They synthesized nickel oxide nanoparticles (NiO) with a crystal size in the range of 15–16 nm by Coriandrum sativum leaf-assisted microwave method (LAMM). The synthesized materials show that an X-ray diffraction (XRD) study confirmed the formation of a single phase structure exhibiting a crystallite size in the range of 15–16nm using Scherrer's method. The NiO prepared by the MM had a surface area of 60.35 m2/g, pore volume of 0.9427 cm3/g and an average pore diameter of 13.27 Å. Surface morphology was analyzed by the scanning electron microscope (SEM), X-ray photoelectron spectroscope, Brunauer-Emmett-Teller (BET) analysis, and the vibrating sample magnetometer (VSM). Catalytic activity (CA) tended toward the oxidation of styrene to benzaldehyde. The inexpensive catalyst tested is likely effective as a catalyst due to synergistic interactions between metal oxides with high dispersion. In comparison with other findings, LAMM is easy and eco-friendly. The current study obtained nanocrystalline NiO that was suitable for potential applications in catalysis. [8]

A. Bello O et al deliberate that hydrothermal Microwave Irradiation were used to deposit manganese oxide on nickel foam-graphene. The 3D graphene was synthesized using nickel foam template by chemical vapour deposition (CVD) technique. The structure & surface morphology of the composite has determined from Raman spectroscopy, X-ray diffraction (XRD), scanning electron and transmission electron microscopies (SEM and TEM). The Raman spectroscopy measurements on the samples reveal that 3D graphene consists of mostly few layers with low defect density. The composite was tested in a three electrode configuration for electrochemical capacitor, and exhibited a specific capacitance of 305 F g-1 at a current density of 1 A g-1 and showed excellent cycling stability. The results demonstrate that microwave irradiation technique could be a promising approach to synthesis graphene based functionalmaterials .[9]

Tejpal Singh Chundawat et al studied that highly efficient microwave assisted synthesis of 2,4,5-trisubstituted imidazoles using a newly developed Schiff's base complex nickel catalyst (Ni-C) is described. The approach involves the reaction of various aldehydes with benzil and ammonium acetate in the presence of the Ni-C catalyst to furnish cyclized products in excellent yields. The Ni-C catalyst exhibited remarkable catalytic activity with respect to the reaction time in the microwave reactor. The catalyst can easily recovered by simple filtration and reused.[10]

Gopal Carpenter et al conscious that Nickel ferrite nanoparticles (NiFe2O4) were successfully produce by microwave-assisted combustion method (MWAC) using citric electron acid as a chelating agent. This were characterized by X-ray diffraction (XRD) pattern, Scanning Microscopy (SEM), Fourier transform infrared (FTIR) and UV-Visible techniques. XRD analysis revealed that NiFe2O4 nanoparticles have spinel cubic structure with the average crystalline size of 26.38 nm. SEM analysis revealed random and porous structural morphology of particles and FTIR showed absorption bands related to octahedral and tetrahedral sites, in the range 400–600cm-1 which strongly favor the formation of NiFe2O4 nanoparticles. The optical band gap is determined by U.V Visible method and found to be 5.4 eV.[11]

Chundawat et al conscious that N-(4-Bromophenyl)salicylidenimine-derived nickel catalyst is used in the novel microwave-assisted 3-component reaction of benzil, arylaldehydes, and ammonium acetate to furnish the title compounds in high yields. The catalyst can be recycled and reused for 3 times with a slight drop in yields.[12]

Keith P. Donegan et al deliberate that nickel nanocrystals with icosahedral morphologies have been successfully synthesised using a microwave-assisted irradiation method. Nickel acetylacetonate was used as the metal precursor, while sodium formate & trioctylphosphine oxide were employed as the reducing agent and capping ligands, respectively. The nanocrystals, with a mean diameter of 237 \_ 43 nm, exhibited enhanced ferromagnetic behaviour at room temperature compared to bulk nickel, with coercivities of up to 164 Oe and saturation magnetisation values of up to 46 emu g\_1, due to their icosahedral morphologies.[13]

Soren Dresp et al studied that Nickel-Iron layered double hydroxides (NiFe-LDH), a known highly active material for the oxygen evolution reaction (OER) in alkaline media, needs better synthesis. Due to high energy efficiency of microwave heating, microwave assisted solvothermal synthesis can play major role in environmental friendly synthesis routes. This approach could also be a key step for sustainable production of highly active materials like electrocatalysts. Therefore, they developed a simplified and shortened solvothermal microwave assisted one pot synthesis to produce highly active NiFe-LDH supported on Vulcan XC-72R. The synthesis was studied by Inductively coupled plasma optical emission spectrometry (ICP-OES), X-ray diffraction and rotating ring disk electrodes (RDE) in a three electrode set-up.[14]

K. K. Narang & Meena Singh conscious that bi metallic tetrathiocyanate complexes of the type MM' (SCN)4.L, hi = Z n (II), C u (II), N i (II), Co(II), hl' = Hg and L = benzoylhydrazide (BH), oxaldihydrazide (OM) and malondihydrazide (MDd) have synthesize in dilute ethanolic medium. The 1:1 meta: ligand complexes, which have been studided by elemental analysis, magnetic moment data, electronic and IR are in soluble in water and common organic solvents and decompose above 250°C without melting. The ligands act as bidentate coordinating species in the complexes. Some of these bimetallic complexes have been tested on microorganisms and were found to be biologically active.[15]

Ravi Eluri, Brian Paul deliberate that nickel nanoparticle (NiNP) were synthesized by reduction of less toxic nickel acetate tetrahydrate (Ni(CH3CO2)2·4H2O) precursor, using sodium hypophosphite monohydrate (NaPH2O2·H2O) under microwave irradiation. By varying the molar ratio of [Ni+2]/[NaPH2O2]/[NaOH], NiNP of 3.8 to 7.1 nm was obtained. Increasing NaOH concentration resulted in morphological change from isolated spherical particles (7.2±1.5 nm) to agglomerated nano flowers (72±14 nm). Phase analysis and interplanar spacing measurements confirmed the particles as fcc-Ni. Quantitative analysis showed

the presence of P and O due to HPO2- radical in reaction product. Addition of small amounts of polyvinylpyrolidone (PVP) or cetyltrimethylammonium bromide (CTAB) resulted in slight increase in particle size.[16]

Thierry Besson and Christopher T. Braiconscious that Microwave-assisted technique has only recently received widespread global acceptance. This is a consequence of the recent availability of commercial microwave systems specific for synthesis, which offer improved reproducibility, rapid synthesis, rapid reaction optimisation and the potential discovery. The beneficial effects of this technique are finding an increased role in process chemistry. Since a large number of natural products and target drug compounds contain an aromatic heterocyclic core, synthetic routes usually quite challenging. The various opportunities by this technology are particularly attractive for the synthesis of aromatic heterocycles implied in drug discovery strategies, where fast high-yielding protocols and the avoidance or facilitation of purification are highly desirable. This chapter aims to review recent developments in the synthesis of heteroaromatic compounds under conditions that include the application of microwave heating in the ring-formingstep. However, functionalisation of pre-formedhetero aromatic core structures (e.g., N-alkylation of nitrogen heterocycles, heteroaromatic substitution) and the generation of heteroaromatic species from existing non-aromatic ring systems (e.g., by dehydrogenation) are not included. Microwave heating has been either synthetically enabling or has provided a key advantage over conventional thermal methods. Microwave-promoted synthesis, early examples relied on the expedient use of microwave equipment designed for non-laboratory applications, in particular domestic microwave ovens. Custom-designed microwave instruments for laboratory use are now commercially available and these offer superior control of the reaction conditions and enhanced reproducibility whilst also providing a key safety advantage. The use of microwaves in conjunction with synthetic technologies is emphasised.[17]

T. Sujeshwari, E. Akila & P. Maheswaran told that four new Cu(II), Ni(II), Co(II) and Mn(II) metalloinsertors were synthesized by using a Schiff base, formed by condensation reaction of isatin, p-chloroaniline with 1, 10-phenanthroline. They have been structurally identify by IR, UV-vis, NMR, EPR, elemental analyses, molar conductivity and magnetic susceptibility studies. The molar conductance data of the complexes indicate that they are non-electrolytes in nature. The spectral and analytical data reveal that the complexes have distorted octahedral geometry. They have been examined for their antibacterial activities against few pathogens. The data reveal that the complexes exhibit better biocidal activities against bacteria than the free Schiff base ligand.[18]

Xianluo Hu et al conscious that rapid and economical route based on an efficient microwave assisted process were developed to synthesize Ni nanowires in large quantities. The Ni nanostructures can be tuned by altering capping agents and solvents. Microwave-induced reaction of Ni with TOP can transform Ni nanowires into porous Ni3P nanowires. The products were characterized by using X-ray diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM), energy-dispersive X-ray (EDX) spectroscopy, elemental mapping, and magnetic characterization. This study an efficient and cost-effective approach that is potentially competitive for scaling-up industrial production. The as-formed Ni and Ni3P nanowires not only provide flexible building blocks for advanced functional devices but also are ideal candidates for fundamental studies and potential magnetic, electronic, and catalytic applications.[19]

K.S. Hui et al Xu-Rong Liu Spinel told that cobalt oxide (Co3O4) nanowires grown on Ni foamare synthesized using a novel microwave-assisted template-free method. The effect of reaction temperature, concentration of reactants and reaction time on them orphology and crystalline structures of the prepared nanowires is studied. They demonstrated that uniform Co3O4 nanowires with diameters of 500–580 nm and lengths of 6–8 mm can be synthesized proper reaction condition. Moreover, the proposed microwave-assisted template-free method can reduce reaction time, increase reaction efficiency and provide good control over the geometry of the nanostructures. [20]

Murugaiyan Manimohan et al studied of new N, N, O tridentate donor water soluble isoniazid based biopolymer Schiff base ligand and their transition metal complex were prepared. The compounds have been designed for potential biological application such as antibacterial, antifungal, anti-inflammatory, total antioxidant, antidiabetic and DNA binding studies. Thermal degradation, thermal stability and percentage of mass loss for the prepared compounds were investigated through thermo gravimetric and differential thermal (TGA-DTA) analyses. Crystalline structure of synthesized biopolymer derivatives were explored by X-ray diffraction (XRD) studies, the crystallinity of chitosan is gradually decreased after the Schiff base and complex formation. Surface morphology and structures of the prepared compounds were examined using SEM analysis. Antidiabetic studies of Biopolymer Schiff base and metal complexes were carried out by  $\alpha$ -amylose inhibitory method. DNA nuclease activities of synthesized metal complexes were investigated by Ultra-Violet (UV) and viscometry methods. The Cu (II) complexes showed better DNA binding results than Co (II) and Zn (II) complexes.[21]

Dimitar Radev et al studied the mechanically-assisted synthesis of mixed nickel-copper oxides at the temperature range of 600–1000 °C. Nickel and copper oxalates were used as starting materials and the mechanical treatment has been prolonged up to 5 h using planetary ball mill. The XRD analysis shows for-mation of NiO-CuO and CuO-NiO solid solutions. As a result, the lattice parameter of the cubic bunsenite (NiO) increases due to the bigger ion radii of Cu2+. It was found that the formation of solid solutions is favoured by the intense mechanical treatment of reagents and the rise of the synthesis temperatures. An anomalous change of the lattice parameters of CuO obtained from mechanically untreated precursors is observed at 1000 °C which is not detected in tenorite, obtained by mechanically-assisted synthesis.[22]

Xu-Rong Liu et al conscious that mixed ligand approach was applied to design coordination polymers with diversiform architectures. They studied that , two novel mixed-ligand Zn(II)-based coordination polymers [Zn(bdc)(bib)](H2O)3 (1,

H2bdc<sup>1</sup>/<sub>4</sub>1,4-dicarboxybenzene, bib<sup>1</sup>/<sub>4</sub>1,3-bis(imidazol-1-yl)benzene) and [Zn(NH2-bdc)(bib)](H2O)2 (2, NH2-H2bdc<sup>1</sup>/<sub>4</sub>2-amino-1,4-dicarboxybenzene) have been successfully prepared based on zinc nitrate, N-containing ligand and linear carboxylate ligand at the same hydrothermal condition. The anti-viability of compounds 1 and 2 against SMMC-7721 liver cancer cells was assessed with CCK-8 detection kit. Besides, the cell apoptosis and ROS detection experiments were also performed to study the related mechanism about the anticancer activity of compounds 1 and 2.[23]

Chrisoula Kakoulidou et al studied novel zinc coordination compounds of gatifloxacin (Hgati), a third-generation quinolone, with a N, N0-donor heterocyclic ligand, such as 2,20-bipyridylamine, 1,10-phenanthroline or 2,20-bipyridine, were characterized with physicochemical & spectroscopies techniques. The antimicrobial activity of the compounds against the microorganisms was similar or better than that of free Hgati. The complexes may bind to calf-thymus DNA via intercalation as concluded via a series of studies employing DNA-viscosity measurements, UV–Vis spectroscopy and competition with ethidium bromide. The complexes may bind to albumins in order to get transferred through the bloodstream.[24]

Nashwa M. El-Metwally et al studied and complexes was prepared using optically active compound as ephedrine. Previously Cu(II)-ephedrine complex was prepared and completely different from that prepared in the study concerning the structural and molecular formula. The mode of coordination was discussed based on IR and Raman spectra and suggested a neutral bidentate. The electronic spectra and magnetic measurements are coinciding for proposal geometry. The EPR spectral parameters confirm the square-pyramidal geometry of Cu(II) complex; the mass and 1HNMR spectra of Cu(II) and Zn(II) complexes, respectively, support the molecular formula. The thermogravimetric analysis and the kinetic parameters were carried out for most complexes. The effect on DNA degradation was discussed on all prepared complexes in comparing with the free organic compound.[25]

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