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COUMARIN DERIVATIVES, METAL COMPLEXES, PHYSICOCHEMICAL STUDIES AND THEIR IMPORTANCE IN VARIOUS FIELD: A LITERATURE REVIEW

Mr. Sopan T. Adhao, Dr. Rahul R. Wagh

Department of Chemistry, Patkar-Varde College, S.V.Road, Goregaon (W), Mumbai-400104.

ABSTRACT

So far several research papers, articles and abstracts have been published on coumarin derivatives synthesis and transition metal complexes synthesis with these compounds. However not much work is done and published on physicochemical studies. In recent years, attention has increasingly been given to the synthesis of coumarin derivatives as a source of new photochemical and biochemical agents. The synthesis of novel coumarin derivatives remain a main focus of medicinal research. Coumarin derivatives been reported to possess antifungal, antibacterial, anticoagulant and anti-tumor activities. The transition metal (II) ions such as Co(II), Ni(II), Cu(II), Zn(II), Pd(II) and Cd(II) complexes are prepared by refluxing metal salt solution and the alcoholic solution of these ligands [1]. The structures of organic ligands and their metal complexes synthesized are analyzed by Elemental Analysis, IR, 1H NMR, UV–Vis spectroscopy and Mass Spectrometry from recognized institutions. Physicochemical studies on metal complexes with coumarins are carried out by using various classical and instrumentation techniques. A coumarin derivative forms stable metal chelates with bivalent transition metal ions. The complexes so formed have square planar, tetrahedral or octahedral geometries [2-3]. The coumarin moiety may or may not take part in coordination bond formation, which is confirmed by structural analysis. The physicochemical studies will predict the stability of the complexes along with their analytical applications.

Keywords: Transition metals, Complexation, Physicochemical studies, Metal Complexes, Coumarin Derivatives

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INTRODUCTION

It is well known fact that metal complexes of O, N-donor ligands have an important role in coordination chemistry. A good deal of research has been carried out on synthesis and structure of metal complexes with O, N-donor ligands [4-5]. This can be achieved by using synthetic organic compounds bearing O, N-donor functional groups. The best suitable ligands known are heterocyclic compounds. As an important group of organic heterocyclic compounds, coumarin (2H-1-benzopyran-2-one) and its derivatives, have been extensively use in biological, chemical and physical fields. Coumarin derivatives have found extensive applications in medicine and biology and they are also known for their tendency to give coordination compounds with different transition metal ions. The complexation behaviour of the transition metal ions with O, N- donor ligands is the interest of many chemists [6].

The Schiff base ligands between acetyl coumarin and amino aliphatic or aromatic compounds can be readily prepared by convenient methods. The chelating ligands are polyfunctional molecules which can trap transition metal ions in an organic cluster. Many types of Schiff base ligands containing coumarin moiety [5] are known and the properties of their metal chelates have been investigated.

The study of recent year's literature reveals that coumarin Schiff base derivatives shows activity such as anticoagulant, antibacterial and insecticidal. This prompted chemist to synthesize some Schiff bases containing coumarin moiety. It can be achieve by condensation of acetyl coumarin with different aliphatic or aromatic amines. The metal (II) complexes can be prepared by refluxing metal salt solution and the alcoholic solution of these ligands [1].

Coumarin derivatives are known for their physiological, photodynamic, anti- coagulant, bacteriostatic and antitumor activity. Recently, coumarin derivatives have been evaluated in the treatment of human immunodeficiency virus, due to their ability to inhibit human immunodeficiency virus *integrase.* The coumarin derivatives play the vital role in designing of new cytotoxic agents [20].

The biological activity of coumarin derivatives has great importance in medicine like antibacterial, insecticidal, anti-tumor and vasodilatory. Several research articles reported advances in various medicinal applications of metal complexes of coumarins [2,7,20]. The biological activity of some coumarin derivatives significantly enhances by binding to metal ions.

A broad array of medicinal applications of metal complexes of coumarins has been investigated. It was found that in some cases the metal complexes obtained revealed higher biological activity than their ligands [7.]

The transition metal ions have good capacity to form coordination compounds with O, N-donor ligands which are able to donate an electron pair. Some of the coumarins show distinct physiological, photodynamic and bacteriostatic activities and placed for many diverse uses. Their chelating characteristics have long been observed and the bacteriostatic activity seems to be due to chelation. The physicochemical studies of the coumarins with chelating group at appropriate position and their metal complexes reveal that the ligand can be used as potential analytical reagents [8].

The complexes of these ligands with some transition metal ions like Co(II), Ni(II), Pd(II), Zn(II), Cd(II), Cu(II) will have a better choice for this study [3,5,6,16]. Since complexes formed by these metal ions plays an important role in enhancing the biochemical and catalytic activities of the compounds [7-8].

On the basis of literature survey made on metal complexes of coumarin derivatives, it was found that the study of the structure, biological activities and synthesis of these compounds has been the aim of many researchers in this field [1-20]. So it is necessary to do some physicochemical studies on the metal complexes of these compounds.

In this literature review, some coumarin derivatives, their complexes form and physicochemical studies of their transition metal complexes and their importance in various fields will be discussed.

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Coumarin Derivatives and Their Importance:

Coumarins are fragrant chemical compounds in the benzopyrane chemical class found in many plants[5], notably in high concentration in the tonka bean, vanilla grass, sweet wood stuff, sweet grass, cassian cinnamon and sweet clover. It has sweet odour and has been used in perfumes since 1882. Coumarin is used in the pharmaceutical industries as a precursor molecule in the synthesis of a number of synthetic anticoagulant pharmaceuticals. Coumarin has clinical medicinal values by itself as a modifier, along with other biological activities that may lead to other medicinal uses have been suggested with varying degree of evidences. Coumarin is also used as a gain medium in some dye lasers and as a sensitizer in older photovoltaic cells. The coumarin nucleus is very interesting chromospheres due to its photochemical and photo physical properties [3,9.] Coumarins are widely used as flash pumpable laser dyes or for photographic purposes because the triplet excited state often occurs in high yield [10.]

Coumarin can be synthesized in the laboratory by Perkin reaction between salicyldehyde and acetic anhydride. The Pechmann condensation provides another synthesis of coumarin and its derivatives [11]. Coumarins have shown some evidence of many biological activities although they are approved for few medicinal uses as pharmaceuticals. The activities reported for coumarin and its derivatives include anti-HIV, anti-tumor, antifungal and antibacterial [11,12,13,14]. It is also used in the treatment of asthma. Coumarin is moderately toxic to the liver and kidneys. Although only somewhat dangerous to human. Coumarin is potent rodenticide.

One can prepare a ligand by the reaction of acetyl coumarins with amino aliphatic or aromatic compounds. A multi-dentate organic ligand will be prepared using organic synthetic methods provided in the literature and will be characterized using elemental analysis and various physicochemical techniques.

The ligands so obtained will then be used to synthesize complexes with various metal ions. These complexes will then be characterized to deduce the coordination structure. The chelation properties and stability constants of synthesized ligands and metal complexes will be determined using suitable methods.

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Physicochemical Studies on Some Transition Metal Complexes and Origin of This Work:

In recent years, attention has increasingly been given to the synthesis of Schiff base coumarin derivatives as a source of new photochemical and biochemical agents. The synthesis of novel Schiff base coumarin derivatives remain a main focus of medicinal research. Coumarin derivatives been reported to posses antifungal, antibacterial, anticoagulant and anti-tumor activities.

K.B.Vyas et al. [1] in 2009 synthesized and studied antimicrobial activities of coumarin derivatives of metal complexes of Cu(II), Ni(II), Fe(II), Co(II) & Mn(II). Complexes of 3-[{-(3',4'-di methoxy phenyl) }-prop-2-enoyl]-4-hydroxy-6- methyl-2H-chromene-2-one with Cu(II), Ni(II), Fe(II), Co(II) and Mn(II) had been synthesized and characterized using elemental analysis, IR spectra and conductivity measurements. These studies revealed that they are having octahedral geometry. In vitro antimicrobial activity of all synthesized compounds and standard drugs had been evaluated against four strains of bacterial culture and one fungus, which includes two gram +ve bacterial culture and two gram -ve bacterial culture. The compounds show net enhancement in activity on coordination of metals with ligand but moderate activity as compared to standard drugs.

E.S. Aazam et al. [3] in 2012, synthesized and studied photo-luminescent properties of a Schiff-base Ligands containing coumarin moiety and its mononuclear Zn(II), Cd(II), Cu(II), Ni(II) and Pd(II) metal complexes. They prepared mononuclear Zn(II), Cd(II), Cu(II), Ni(II) and Pd(II) metal complexes of Schiff-base ligand (HL1) derived from 8-acetyl-7-hydroxycoumarin and p-phenylenediamine and characterized it by micro analytical, mass, UV–Vis, IR, 1H NMR, 13C NMR, ESR, conductance and fluorescence studies. The measured low molar conductance values in DMSO indicate that the complexes were non-electrolytes. The established structures of the solid complexes by using IR, electronic and ESR spectroscopy suggesting that Zn(II) and Ni(II) complexes were octahedral, Cd (II) complex was tetrahedral, Cu(II) and Pd(II) complexes were square planar geometries. The ESR spectrum of the Cu (II) complex in DMSO at 298 and 150 K was recorded and its salient

features were reported, it supports the mononuclear structure. The Schiff base exhibited photoluminescence originating from intra ligand (p–p*) transitions. Metal-mediated enhancement was observed on complexation of HL with Zn (II) and Cd (II), whereas metal-mediated fluorescence quenching occurs in Cu (II), Ni(II) and Pd(II).

V.K. Revankar et al. [5] in 2008, synthesized and studied antitumor activities on novel Co(II), Ni(II) and Cu(II) metal complexes of bis(3-acetylcoumarin) thiocarbohydrazone. They synthesized, studied structure, physico-chemical properties and biological activities of above mentioned metal ions complexes of thiocarbohydrazone ligands. The ligand was obtained by condensation of N,N'-thiocarbohydrazide with 3-acetylcoumarin. The metal complexes of Co(II), Ni(II) and Cu(II) with bis(3-acetylcoumarin)thiocarbohydrazone were synthesized and isolated as solid products and characterized by analytical means as well as by spectral techniques such as FT-IR, 1H NMR and EPR and UV spectrometry. The ligand acts as bidentate, through NO or NN, neutral in coordinating the M (II) ions. The bonding sites are the azomethine nitrogen, lactone carbonyl oxygen and respective anion counterparts. The metal complexes exhibit either octahedral or distorted octahedral structures. The complexes are found to be soluble in dimethyl formamide and dimethylsulphoxide. Molar conductance values of the complexes prepared in dimethyl sulphoxide indicate the non-electrolytic nature of the complexes.

M.V. Hathi et al.[8] in 2009 investigated the formation constants of binary chelates of chalcones of 4-hydroxy coumarin derivatives as a ligand with Cu (II), Ni (II), Co (II) and Mn (II) pH metrically. Co(II), Ni(II) and Cu(II) metal ions were selected for equilibrium study in water with ligand, which co-ordinates through O and O of –OH and > C=O respectively. They found that Cu (II) has greater lattice and solution energies, hence higher formation constant for complexes of Cu (II) ions was observed amongst three, Cu (II) shows higher stability as expected. Co (II) complexes with ligand were more stable than corresponding Ni (II) complexes. This was attributed to the size of the metal ions. The order of stability constants of the metal chelates under investigation was Mn(II) < Co(II) < Ni(II) < Cu(II) which is in conformity with the Irving Williams natural order of stabilities.

Mustafa Bulut et al. [15] in 2011, synthesized 7-oxy-3-(4-methoxyphenyl) coumarin-substituted peripherally and non-peripherally tetrakis- and peripherally octakis-tetrachloro zinc (II) phthalocyanine complexes were described for the first time in their study. The new compounds were characterized by elemental analysis, IR, 1H NMR, UV–vis spectroscopy and mass spectra. The photophysical and photochemical properties are important for photodynamic therapy applications and these properties of studied phthalocyanine complexes were investigated in N, N-dimethyl formamide (DMF). The effects of the number of the substitution and the position (peripheral or non-peripheral) on the photophysical and photochemical parameters of the zinc (II) phthalocyanine complexes were reported. The fluorescence quenching behaviour of the studied zinc (II) phthalocyanine complexes by the addition of 1, 4-benzoquinone was also described.

Elham S. Aazam[16,17] in 2010, synthesized mononuclear and binuclear metal complexes of coumarin derivatives with Cu(II) & Zn(II) metal ions. They synthesized divalent Cu and Zn complexes using the new bidentate Schiff base ligand formed by the condensation of 2-hydroxy-1-naphthaldehyde and 7-amino-4-methylcoumarin. The emission spectral studies for the ligand revealed its fluorescent nature. The coordination ability of HL towards M(II) complexes were examined by different spectroscopic methods that unequivocally determine the two coordination sites of L, naphthanolic oxygen and azomethine nitrogen. Emphasis had been given to the examination of the structural geometry of the M(II) chelated complexes. On the basis of spectral data it was confirmed that the metal to ligand stoichiometry for [{Cu(L)2}2], [Zn(L) (HL)(OAc)] and [Cu(L)(acac)] were 1:2, 1:2 and 1:1 respectively. The existence of dimeric copper complex [{Cu(L)2}2] was investigated by ESR studies.

Metal Complexes formed by some Schiff base Coumarin Derivatives and Their Importance:

Metal complexes of coumarin derivatives have antimicrobial activity. It is due to the chelation property of these compounds. The complexes of metallic salts are more potent than the parent drug. These complexes have many other applications such as antifungal, antibacterial, and anti-tumor. It is already mentioned in introduction. So it is necessary to

prepare new metal complexes of coumarin derivatives and study of their physicochemical properties is important for better biological activities [18] and stability.

Synthesis of Schiff base coumarin derivatives will be achieved by condensation of substituted acetyl coumarins with different aliphatic and aromatic amines. The transition metal (II) ions such as Co(II), Ni(II), Cu(II), Zn(II), Pd(II) and Cd(II) complexes will be prepared by refluxing metal salt solution and the alcoholic solution of these ligands [1].

Acetyl coumarin is expected to condense with amino group of different aliphatic or aromatic compounds, giving Schiff bases containing coumarin moiety [3, 16,19]. This will gives organic compound with solubility in variety of solvents. The product formed will have O, N-donor functional groups; will behave as a good chelating ligand.

It would form stable metal chelates with bivalent transition metal ions. The complexes so formed will have square planar, tetrahedral or octahedral geometries [2,3]. The coumarin moiety may or may not take part in coordination bond formation, which will be confirmed by structural analysis. The physicochemical studies will predict the stability of the complexes along with their analytical applications.

CONCLUSION

A coumarin based Schiff base ligand can be synthesized by suitable method given in literature. It would possess O, N-donor functional groups. So a bidentate or multidentate ligand obtained by this method. It would forms stable chelates with transition metal ions. The physicochemical studies will reveal the stability and spectral properties of the metal complexes so formed. Moreover these complexes may have some medicinal properties and analytical application in quality control laboratory.

Disclosure: The authors report no conflicts of interest in this work.

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