IJPSR (2020), Volume 11, Issue 12 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 09 December 2019; received in revised form, 08 April 2020; accepted, 11 April 2020; published 01 December 2020

DNA INTERACTION STUDIES BY UV OF COPPER COMPLEX BASED ON HETEROCYCLIC CHALCONES

M. M. Maste *, V. Hegde, S. Mutalik Desai, A. Saxena, P. Inamdar and P. Debnath

Department of Pharmaceutical Chemistry, KLE College of Pharmacy, KLE Academy of Higher Education and Research, Belagavi - 590010, Karnataka, India.

Keywords:

Heterocyclic chalcones, Copper complex, UV titration, DNA interaction

Correspondence to Author:
Dr. Meenaxi M. Maste

Associate Professor, Department of Pharmaceutical Chemistry, KLE College of Pharmacy, KLE Academy of Higher Education and Research, Belagavi - 590010, Karnataka, India.

E-mail: menaimm@gmail.com

ABSTRACT: Privileged structures have been widely used as an effective template in medicinal chemistry for drug discovery. Chalcone is a common simple scaffold found in many naturally occurring compounds. Chalcones, considered as the precursors of flavonoids and isoflavonoids, are abundant in edible plants. Chalcone metal complexes and their derivatives have been known over the past fifty years. Copper is an essential element, and hence it is used to synthesize metal complexes. Copper possesses a broad spectrum of activity and a higher DNA binding ability when compared to platinum drugs. The metal-based drugs may range from natural products to artificial organic molecules. Their exceptional magnetic optical radioactive are used in many non-invasive methods like magnetic resonance imaging (MRI), position emission tomography (PET), optical imaging. Copper-based metal complexes have been studied extensively towards DNA interaction aspects. The binding ability of the complexes has been explored based on the results of DNA binding studies assessed by different spectroscopic techniques like UV absorption titration. Thus, we are reporting DNA interaction studies using UV spectroscopic titrations of the copper complex based on heterocyclic chalcones to signify it as an efficient interacting agent.

INTRODUCTION: Natural sources always led to the discovery and invention of new chemical entities as potent drugs. Chalcones are one of the major classes of naturally occurring compounds found as petal pigments and also in hearth wood, leaf, bark, roots, fruits of various trees and plants [1]. They are among the most suitable plant pigments which produce yellow, red or blue pigmentation in petals [2]. Chalcones, have a common chemical moiety of 1,3-diaryl-2-propen-1-one which is also called as chalconoid belonging to flavonoid family.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.11(12).6232-36

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.11(12).6232-36

Chemically, chalcones consist of two aromatic ring systems linked with a three-carbon α,β- unsaturated carbonyl system, *i.e.*, ketone [3]. A huge number of synthetic routes have been set forth for the synthesis of chalcones, the most prototypical and accepted being the Claisen–Schmidt condensation in an acidic or a basic media under homogeneous conditions [4]. Chalcones and their derivatives have a huge importance in medicinal chemistry, displaying a wide range of important pharmacological activities such as antiviral [5], antimicrobial [6], antihyperglycemic [7], antiulcer [8], analgesic [9], antimalarial [10] activities.

Metals have an acclaimed a vital place in medicinal chemistry [11]. Therapeutic properties and applications of metals can be traced back to almost 500 years. Group 3-12 of the periodic table are known as transition metals because they fill the d subshell

(ultimate region), leaving 4s subshell incompletely filled (penultimate region). This property of transition metals resulted in the foundation of coordination complexes. Metal complex or coordination compound is a structure consisting of a central metal ion or atom, which is known as coordination center, which is bonded or surrounded by ions or molecules known as ligands. Chalcones are effective metal ion chelators and hence can easily form metal-coordinated compounds. The chalcones act as bidentate ligand and coordinating through deprotonated oxygen and ketonic oxygen atoms.

Copper is an essential trace element in chemistry. Several metal complexes are in clinical use (cisplatin being most successful) for the treatment of several diseases, and many are being currently tested in preclinical and clinical studies. Copper is an essential trace element in redox chemistry, development, and growth. The major function of copper molecules involves oxidation-reduction reactions in which they react directly with molecular oxygen to form free radicals. More recently, mixtures of copper chelators with copper salts have been reported as efficient apoptosis inducers and proteasome inhibitors as a potential antitumor agent.

DNA is the prime target for the development of novel drugs, and hence, DNA binding studies using spectroscopic techniques have been in the limelight in recent years. Studies indicate that transition metal complexes bind covalently with DNA by intercalation, groove binding, and external electrostatic binding. Among several types of transition metal complexes, copper has a better property for the hydrolysis of DNA because of its Lewis acid properties [12].

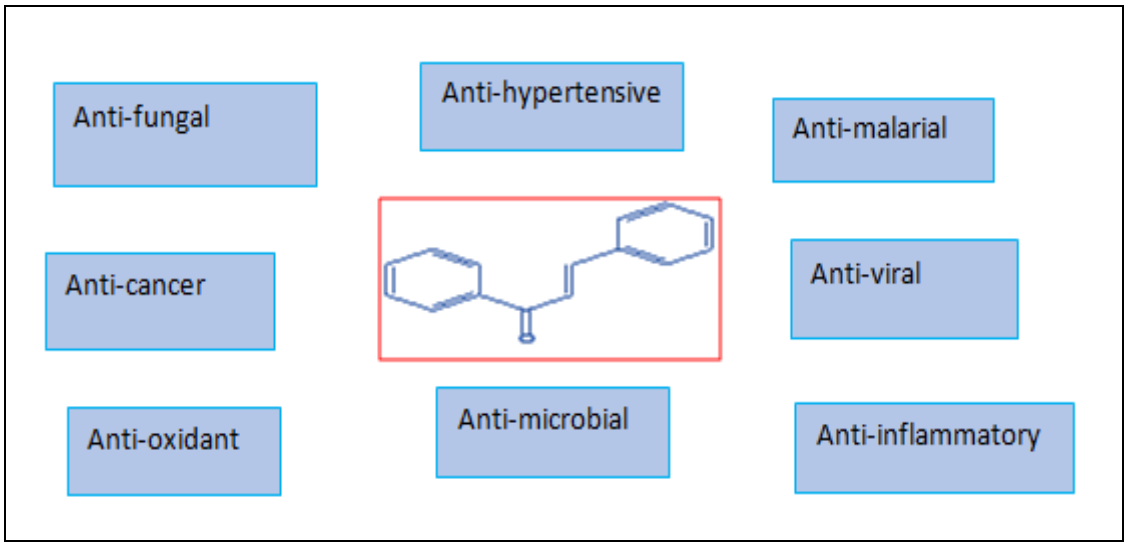
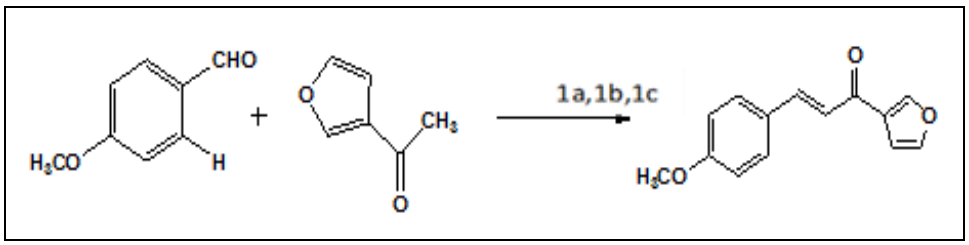


FIG. 1: BIOLOGICAL ACTIVITIES OF CHALCONES

MATERIALS AND METHODS:

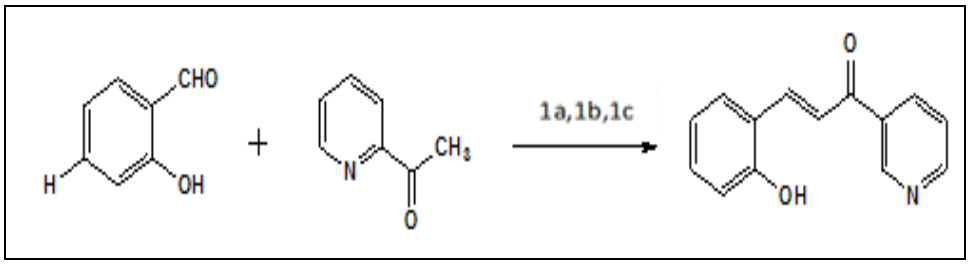
Synthesis of Parent Ligand {L}:

(E)-1-(furan-3-yl)-3-(4-methoxyphenyl)prop-2-en-1-one: Anisaldehyde and 2-acetylfuran dissolved in methanol was stirred at room temperature till mixture gets dissolved. The solution of KOH was added to the above mixture and refluxed at 0-5 °C for 82 h. The residue obtained is washed with cold water. The brown colored crystals were obtained and recrystallized using chilled ethanol.



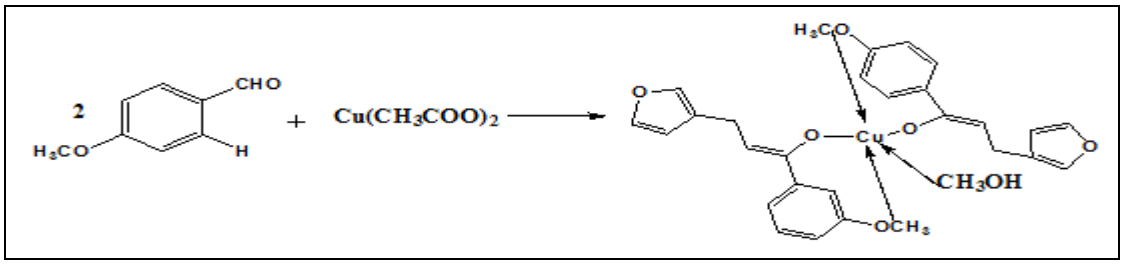
SCHEME 1: SYNTHESIS OF LIGAND L. 1a: NaOH, EtOH, 100-140°C; 1b: KOH, MeOH, 0-5°C ; 1c: KOH, MeOH , rt.

Synthesis of Parent Ligand {L-1}: (E)-3-(2-hydroxyphenyl)-1-(pyridine-3-yl)prop-2-en-1-one: The mixture of salicyaldehyde (0.1M) in ethanolic solution and 2-acetylpyridine (0.1M) in KOH was refluxed for 96 h. The brownish colored precipitate obtained was filtered and washed with cold water.



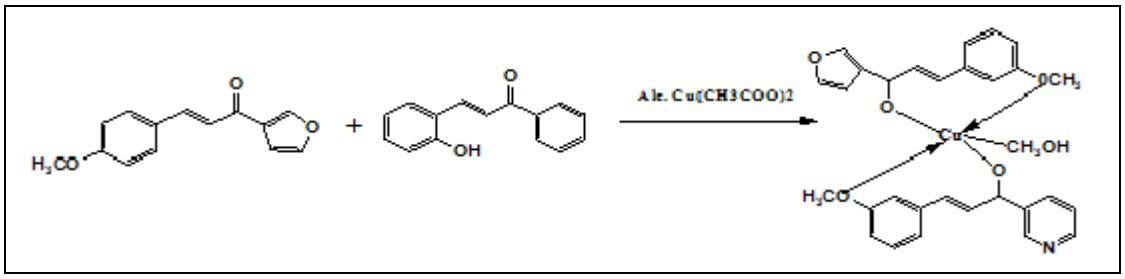
SCHEME 2: SYNTHESIS OF LIGAND L-1. 1a: NaOH, EtOH, 100-140°C; 1b: KOH, MeOH, 0-5°C; 1c: KOH, MeOH, rt

Synthesis of Metal Complex MEC-I: Molecular formula: $[C_{29}H_{29}CuO_7]$, Molecular mass: 553.08g/mol. 2 mmol of ligand solution in methanol was stirred with 1mmol of methanolic solution of copper acetate for 72 h at room temperature. The pale yellow colored crystals were obtained and washed with chilled ethanol.



SCHEME 3: SYNTHESIS OF METAL COMPLEX MEC-I

Synthesis of Metal Complex MEC-II: Molecular formula $[C_{30}H_{30}CuNO_6]$, Molecular mass 564.11g/mol, Mixture of methanolic solution of 1mmol ligand and 1mmol of L-1 is added to a methanolic solution of copper acetate solution and stirred on a magnetic stirrer and refluxed for 18 hours at room temperature.



SCHEME 4: SYNTHESIS OF METAL COMPLEX MEC-II

Preparation of Complex Solution MEC I: Metal complex MEC I is very soluble in ethanol. Hence the stock solution of 1mM (100ml) was prepared in ethanol by dissolving 0.55g of MEC I in 100ml of ethanol.

Preparation of Complex Solution MEC II: Metal complex MEC II is very soluble in ethanol. Hence the stock solution of 1mM (100ml) was prepared in ethanol by dissolving 0.56g of MEC II in 100ml of ethanol.

Preparation of DNA Solution: The DNA solution was prepared in distilled water (pH=7) of concentration 1mg/ml. The sodium salt of DNA was extracted from Salmon milt. (HIMEDIA® RM511-5G).

DNA Binding Studies by UV Spectroscopy: UV absorption titration was carried out by keeping the complex concentration at 40µM. complex solution was prepared in ethanol. Titration was carried out

by monitoring ligand-based transition of the complex along with 10µM increments of DNA.

RESULTS AND DISCUSSION:

DNA Interaction Studies of MEC I:

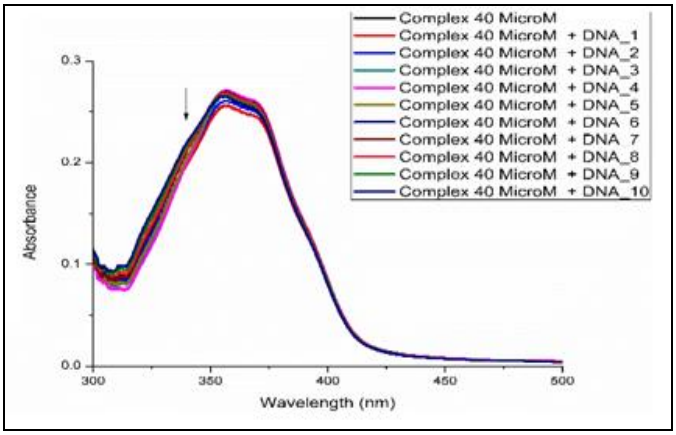


FIG. 2: DNA INTERACTION STUDIES OF MEC I

DNA Interaction Studies of MEC II:

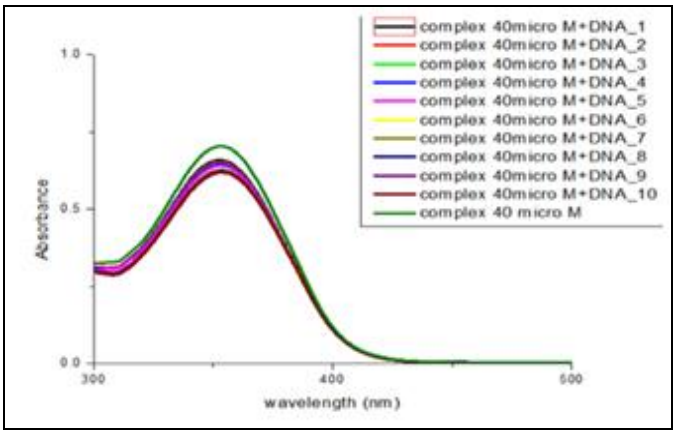


FIG. 3: DNA INTERACTION STUDIES OF MEC II

The complex synthesized from the ligand was assessed for the DNA interaction studies. Change in the π-π* transition of the complex was focused on finding out the interaction of the compound with DNA. The absorbance and λ_{max} of complex **Fig. 2, 3** was observed after successive increments of DNA. The hypochromic effect was observed, stating the effective interaction between complexity and DNA.

CONCLUSION: The heterocyclic metal complexes were subjected to DNA interaction studies using UV spectroscopic titration. In the UV titration, both the complexes showed decreased absorbance with each consecutive addition of DNA solution and thus stating an effective interaction with DNA.

ACKNOWLEDGEMENT: This author likes to acknowledge KLE College of Pharmacy, Belagavi for providing all the necessary facilities to carry out the research work successfully.

CONFLICTS OF INTEREST: The authors confirm that the contents of this review article bear no conflict of interest.

REFERENCES:

1. Iwashina T: The Structure and Distribution of the Flavonoids in Plants, Journal of Plant Research 2000; 113: 287-99.
2. Drewes SE and Hudson NA: Medicinal Plants of Southern Africa. Part 1. Dimeric Chalcone-based Pigments from *Brackenridge azanguebarica*. Journal of Chemical Society, Perkin Transactions 1987; 1: 2809-13.
3. Nowakowska Z: Synthesis, physicochemical properties and antimicrobial evaluation of new (E)- chalcones. European J of Medicinal Chemistry 2008; 43(4): 707-13.
4. Matos MJ, Vazquez-Rodriguez S, Uriarte E and Santana L: Potential pharmacological uses of chalcones: a patent review (from June 2011 - 2014). Expert Opinion on Therapeutic Patents. 2015; 25(3): 351-66.
5. Onyilagna JC, Malhotra B, Elder M and Towers GN: Comparative studies of inhibitory activities of chalcones on tomato ringspot virus (ToRSV). Canadian Journal of Plant Pathology 1997; 19(2): 133-7.
6. Mokle SS, Sayeed MA, Kothawar and Chopde: Synthesis and antimicrobial activity of some chalcone derivatives. International Jou of Chemical Science 2004; 2(1): 96-100.
7. Satyanarayana M, Tiwari P, Tripathi K, Shrivastava AK and Pratap R: Synthesis and antihyperglycemic activity of chalcone based aryloxypropanolamines. Bioorganic and Medicinal Chemistry 2004; 12(5): 883-89.
8. Mukarami S, Muramatsu M, Aihara H and Otomo S: Inhibition of gastric H+, K+-ATPase by chalcone derivatives, xanthoangelol and 4-hydroxyderricin, from Angelica keiskei Koidzumi. Journal of Biochemical Pharmacology 1991; 42(7): 1447-51.
9. Viana GS, Bandeira MA and Matos F: Analgesic and anti-inflammatory effecys of chalcones isolated from Myracrod ruonurundeuva Allemão. Journal of Phytomedicine 2003; 10(2-3): 189-95.
10. Go ML, Wu X and Liu XL: Chalcones: an update on cytotoxic and chemoprotective properties. Journal of Current Medicinal Chemistry 2005; 12: 483-99.
11. Inamdar PR, Hazarika J, Sridharan TB and Sheela A: Synthesis and DNA Binding Study of Zinc (II) Co-ordination complexes. Advanced Materials Research 2012; 584: 401-05.
12. Gielen M, Tiekink ER: Metallotherapeutic drugs and metal-based diagnostic agents: the use of metals in medicine. John Wiley & Sons; 2005 Sep 1.
13. Srinivasan S, Annaraj J and Athappan PR: Spectral and redox studies on mixed ligand complexes of Cobalt(III) phenanthroline/bipyridyl and benzoylhydrazones, their DNA binding and antimicrobial activity, Journal of Inorganic Biochemistry 2005; 99(3): 876-82.
14. Barve AC, Ghosh S, Kumbhar AA, Kumbhar AS and Puranik VG: DNA binding studies of mixed ligand cobalt(III) complexes. Transitional Metal Chemistry 2005; 30(3): 312-16.

How to cite this article:
Maste MM, Hegde V, Desai SM, Saxena A, Inamdar P and Debnath P: DNA interaction studies by UV of copper complex based on heterocyclic chalcones. Int J Pharm Sci & Res 2020; 11(12): 6232-36. doi: 10.13040/IJPSR.0975-8232.11(12).6232-36.