IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 11, Issue 6 Ver. III (Nov. - Dec.2016), PP 80-84
www.iosrjournals.org

Synthesis, characterization and pharmaceutical applications of Curcumin metal complex

Dr.A.Gubendran* Dr. M.Amutha[3,] P.Dhanasekaran[2,] A.Imayatharasi [2], M.Vijayalakshmi [2]

1Associate professor Department of chemistry Saraswathi Narayanan College, Madurai, Tamilnadu, India.
2 M.Phil Scholars, Department of chemistry Saraswathi Narayanan College, Madurai, Tamilnadu, India.
3Assistant professor, Department of chemistry V.V.Vanniaperumal college for women Virudhunagar, Tamilnadu, India

Abstract: *Nowadays People are often down with dengue, pneumonia, and viral infected fever because of unclean surrounding. This is the first attempt to use curcumin complex in a model anti-bacterial assay experiment on Staphylococcus aureus, E. coli, Klebsiella pneumonia and Pseudomonas fluorescence.Results show thatcurcumincomplex has significant higher activity compared to pure curcumin. Curcumin copper complex was synthesized by using DMSO and ethanol solvent mixture at 350^{o}C and characterised by FT- IR spectral analysis. The compound was used to assay the anti-bacterial activity on Staphylococcus aureus, E. coli, Klebsiella pneumonia and Pseudomonas fluorescence. Minimuminhibition zone for the four pathogens bacterial were compared. On the basis of MCI zone area the activity of the complex is as follows Klebsiella pneumonia>,E.coli,> Staphylococcus aureus> Pseudomonas fluorescence. Our results provide a promising role to use copper- curcumin complexes in diverse biological applications.*

Keywords:*copper- curcumin complex, FT-IR,Staphylococcus aureus, E. coli, Klebsiella pneumonia and Pseudomonas fluorescence*

I. Introduction

Scientific researchesspanning over more than four decades have confirmed the diverse pharmacological effects of curcumin and established its ability to act as a therapeutic agent for several diseases. Lot of research is being carried out in different medicinal aspects on curcuminowing to its unique structural activity and relationship in biological aspects[1-4]. Inorganic chemists have used its metal chelating abilities through beta di keto group to form new structural entities with modified bio chemical activities as shown in figure 1.

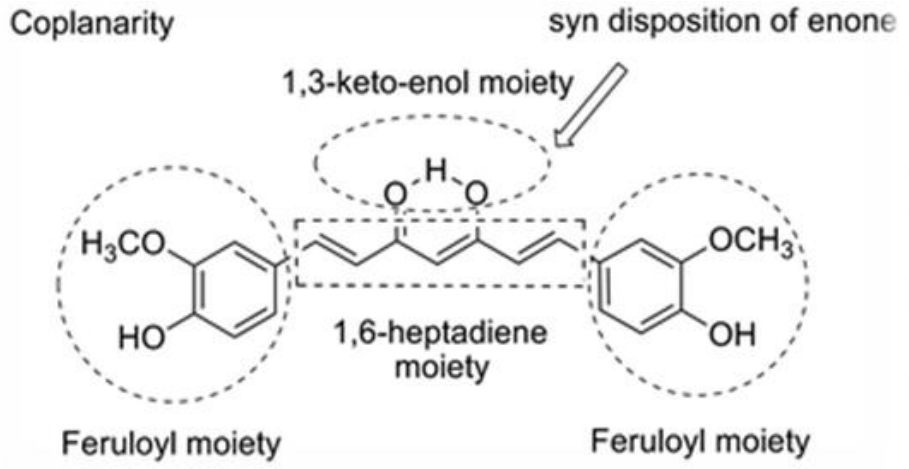

Figure1. Structure of curcumin

1.2 Metal curcumin complex on pathogens

People are mostly affected by pathogens due to contaminated water, uncleaned surroundings and mosquitoesand theysuffer from Dengue, Pneumonia and Urinary infections. ***Staphylococcus aureus, E. coli,Klebsiella pneumonia and Pseudomonas fluorescence*** are playing a vital role in causing the above diseases[5-7].

Signs and symptoms of infection

Staphylococcus aureus

Most of the symptoms caused by *Staphylococcus aureus*in skin and soft tissue infections such as cellulitis. The area affected by it is usually red; painful, swollen and can feel warm to touch.

Klebsiella pneumonia is a bacterium that normally lives in the intestine of human and is spread through person - to- person contact, occur through the use of contaminated medical equipment.

Similarly, the use of contaminated intravenous catheters can lead to bloodstream infections.

Pseudomonas fluorescence is a gram negative rod shaped bacterium commonly found in decaying organic material such as leaves, soil, plants and water surfaces. *Pseudomonasfluorescence* contain soluble green fluorescent pigments called pyoverdin that are produced when the iron concentration in the surrounding environment[8-11].

E. coli. Symptoms begin between one and five days after abdominal cramping, severe watery diarrhea that may change to bloody stools, gas, loss of appetite/nausea, vomiting fatigue, fever.

*E.coli*highly affects the urinary tract. The urinary tract comprises the kidneys, ureters, bladder, and urethra as shown in figure. UTIs are diagnosed usually by isolating and identifying the urinary pathogen*E.coli* from the patient[12-17].

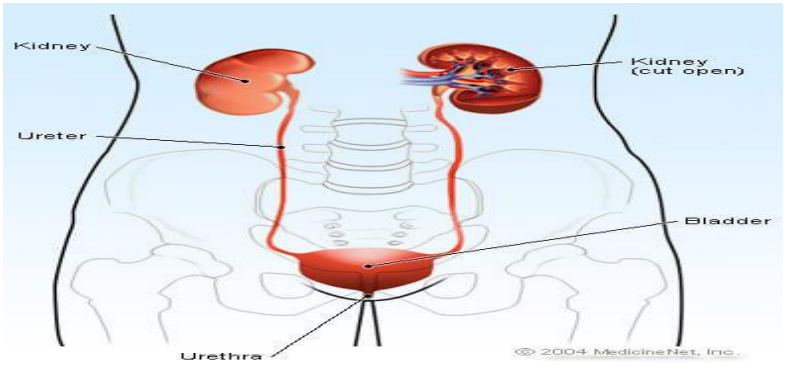

Figure.2 Urinary tract of human

People are affected by the above pathogens are in need of low cost medical therapy. Curcumin metal complex plays a vital role as a therapeutic agent and serves the society in many ways.

II. Methods

2.1 Synthesis of Curcumin

Fresh rhizomes were cleaned, washed with deionized water, sliced and dried in the sun for one week and again dried at 50 °C in a hot air oven for 6 hours. Dried rhizomes were cut in small pieces, powdered. Approximately 20g of sample were taken and set up with various solvent from nonpolar to polar. 150mL of solvent was added and extracted according to their boiling point for 6 hours. The solvents used were Hexane (b.pt = 69° C), Chloroform (B.P = 61°C), Ethyl acetate (b.pt=77°C), Methanol (b.pt=65°C), and Acetone (b.pt=56.53°C). And one sample was extracted with hexane for 2 hours and hexane extract was discarded and the powder was re-extracted with methanol for 6 hours. After completion of extraction the dark brown extract was then cooled, filtered, concentrated using rotary evaporator, and finally by vacuum suction to get a crude dried extract which was black orange in color. Each raw sample of turmeric was extracted by the same method and yield was calculated.*Curcuma longa* (Turmeric) rhizome were collected from Assam - Lakhadong variety. All solvents / Chemicals used were of AR / HPLC grade and obtained from E-Merck. The reference standard of Curcumin was purchased from Sigma Chemicals Co. U.S.A[19-23]

2.2 Synthesis of Curcumin- copper complex

The Cu(II)–curcumin complex was synthesized by mixing equi-molar amounts of Cu(II)nitrate (1.0 mmol) and curcumin (0.37 g, 10 mmol) in ethanol and the mixture was heated at 60°C for 1 h under a nitrogen atmosphere and the reaction was further continued for 2h under reflux. Then the complex solution formed was concentrated and the solid residue was separated by filtration and washed several times by water/ethanol to remove unreacted curcumin[19-23].

2.3 FTIR

IR spectra of curcumin and its complexes were recorded onspectrometer in KBr discs with resolution of4 cm^{-1} and scans of 32. The spectral range was from 4000 to400 $cm^{-1.}$

2.4 Antibacterial Activity of Compounds - on Pathogens -Well Diffusion Method

Antibacterial activity of the extract of compounds was determined using well diffusion method. It was performed by sterilizing Mueller Hinton agar media. After solidification, wells were cut on the Mueller Hinton agar using corn borer. The test bacterial pathogens were swabbed onto the surface of Mueller Hinton agar plates. Wells were impregnated with 25 µl of the test samples. The plates were incubated for 30 min to allow the extract to diffuse into the medium. The plates were incubated at 30^{o}C for 24 hours, and then the diameters of the zone of inhibition were measured in millimeters. Each antibacterial assay was performed in triplicate and mean values were reported [24-30].

III. Results and Discussion

It is reported that there exist several possible complex structures of Copper-curcumin [31-34].IR spectral studies reveals the structure of the newly synthesized compound as shown in figure 3.ACD -Chem sketch software tool exhibit the properties of the compound as shown in the table 1.

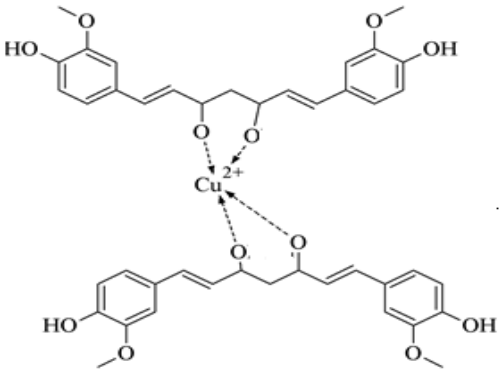

Figure 3.Molecular structure of Cu-Curcumin complex

Table-1 Molecular properties of Cu-Curcumin complex

Molecular Formula:	$C_{42}H_{40}CuO_{12}^{2+}$
Formula Weight:	800.3047028
Composition:	C(63.03%) H(5.04%) Cu(7.94%) O(23.99%)
Monoisotopic Mass:	799.180481 Da
Nominal Mass:	799 Da
Average Mass:	800.3047 Da
M+:	799.179932 Da
M-:	799.181029 Da
[M+H]+:	800.187757 Da
[M+H]-:	800.188854 Da
[M-H]+:	798.172107 Da
[M-H]-:	798.173204 Da

Characterization by FTIR

Characterizations of the metal complexes were done by FT-IR spectroscopy as shown in figure 4. IR Spectrum of curcumin showed a sharp peak at 1628 cm^{-1} corresponding to the mixtures of stretching vibrations of $\nu_{C=C}$, and $\nu_{C=O}$ in curcumin. The most prominent band obtained at 1512 cm^{-1} is attributed to highly mixed vibrations of $\nu_{C=O}$, ν_{CCC}, $\nu_{CC=O}$ and aromatic ν_{CC}, ν_{CCH}. Deformation vibrations of the two methyl groups are pure. These are observed at 1460-1430cm^{-1}.The FT-IR spectra of Curcumin and that of the metal complexes show that the C=O stretching band of Curcumin at 1628 cm^{-1} is shifted to a lower wavenumber, that is, 1621 cm^{-1} on complexation with Cu(II) implying that the conjugation of the metal ions takes place through the β-diketone moiety of Curcumin. However, the position of vibrational band around 3450 cm^{-1} of Curcumin remains unchanged on complexation with metal ions (Figure). Literature data suggest that the phenolic OH group of curcumin is not involved in complexation with other metal ions exhibiting unaltered vibrational band around 3500 cm^{-1} in the FT-IR spectra of Curcumin-metal complexes [14, 21]. Again, the enolic OH of Curcumin is primarily important for its antioxidant and free radical scavenging property [14–16, 22]. Consistent with the previous reports, our observations lead to the conclusion that the binding of Cu(II) does not involve the phenolic OH group of Curcumin causing no loss of antioxidant property of the ligand molecule.

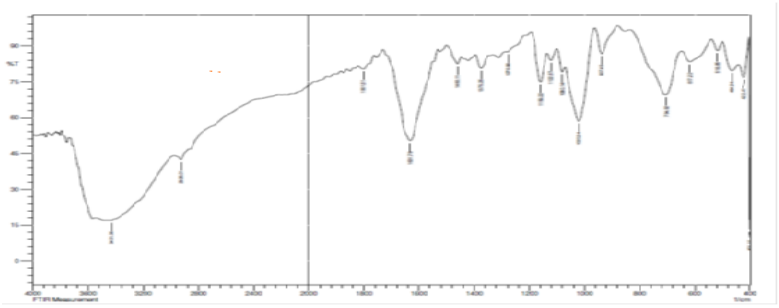

Figure 4.IR spectra for Cu-Curcumin complex

Pharmaceutical applications of Cu-Curcumin complex;The compound was used to assay the anti-bacterial activity on *Staphylococcus aureus, E. coli, Klebsiella pneumonia and Pseudomonas fluorescence.* Minimuminhibition zone for the four pathogens were compared**.***On the basis of MCI zone area the activity of the complex is as shown in the table-2.*The order of the MIC zone isas follows, *Klebsiella pneumonia> E. coli > Staphylococcus aureus> Pseudomonas fluorescence as shown in figures 5a - 5d***.** These results provide a promising role to use copper- curcumin complexes in diverse biological applications

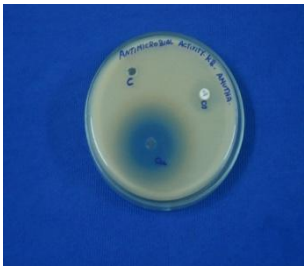

Figure.5a: Cu-Curcumin complex on*Klebsiella pneumonia*

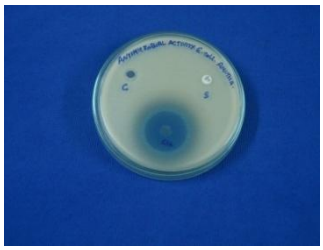

Figure.5b: Cu-Curcumin complex on *E. coli,*

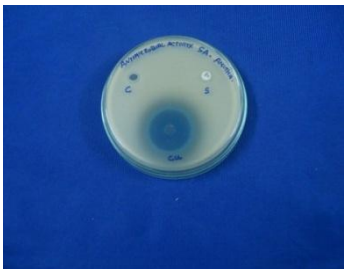

Figure 5c: Cu-Curcumin complex on *Staphylococcus aureus*

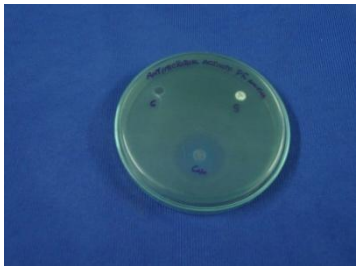

Figure5d: Cu-Curcumin complex on *Pseudomonas fluorescence*

Table: 2. Antimicrobial activity of the compounds against bacterial pathogens

Test organism	Cu-curcumin	solvent	standard
Staphylococcus aureus	40	NZ	16
E. coli	43	NZ	14
Klebsiella pneumonia	47	NZ	23
Pseudomonas fluorescence	32	NZ	19

Solvent used : DMSO (Dimethyl Sulphoxide)
Standard used: Ampicillin 10 µg.

IV. Conclusion

The novel Cu-Curcumin complex was synthesized and its structure was confirmed by FT-IR spectra.The interaction of curcumin and Cu(II)was the significant Cu(curcumin)$_2$. The diffuse reflectance IR spectra indicated that the complex was reasonably stable both in aqueous solution and in solid state.Pharmaceutical applications of Cu-Curcumin complex was studied for *Staphylococcus aureus, E. coli, Klebsiella pneumonia and Pseudomonas fluorescence.*On the basis of MCI zone area the activity of the complex is in the order, *Klebsiella pneumonia> E. coli > Staphylococcus aureus> Pseudomonas fluorescence.* Resultsobtained provide a promising role of copper- curcumin complexes in diverse biological applications especially for UTI patients. It is simple to prepare and cost-effective drug for patients.

Review of Literature

[1]. B. Marchetti, M.P. Abbracchio, Trends Pharmacol. Sci. 26 (2005) 517.
[2]. S. Mandel, O. Weinreb, T. Amit, M.B.H. Youdim, J. Neurochem. 88 (2004) 1555.
[3]. Z.Z. Chong, F.Q. Li, K. Maiese, Prog. Neurobiol.75 (2005) 207.
[4]. O. Weinreb, S. Mandel, T. Amit, M.B.H. Youdim, J. Nutr. Biochem.15 (2004) 506.
[5]. M.T. Carri, A. Ferri, M. Cozzolino, L. Calabrese, G. Rotilio, Brain Res. Bull. 61(2003) 365.
[6]. G.L. Millhauser, Acc. Chem. Res. 37 (2004) 79.
[7]. R. Riek, Nature 444 (2006) 429.
[8]. H.Y. Hu, Chin. Sci. Bull. 46 (2001) 1.
[9]. M.L. DeMarco, V. Daggett, C. R. Biol. 328 (2005) 847.
[10]. A.I. Bush, Trends Neurosci. 26 (2003) 207.
[11]. P. Zatta, G. Tognon, P. Carampin, J. Pineal Res. 35 (2003) 98.
[12]. S.A. Frautschy, W. Hu, P. Kim, S.A. Miller, T. Chu, M.E. Harris-White, G.M. Cole,Neurobiol. Aging 22 (2001) 993.
[13]. A. Barik, B. Mishra, L. Shen, H. Mohan, R.M. Kadam, S. Dutta, H.Y. Zhang, K.I.Priyadarsini, Free Radical Bio. Med. 39 (2005) 811.
[14]. X.D. Huang, C.S. Atwood, M.A. Hartshorn, G. Multhaup, L.E. Goldstein, R.C.Scarpa, M.P. Cuajungco, D.N. Gray, J. Lim, R.D. Moir, R.E. Tanzi, A.I. Bush,Biochemistry 38 (1999) 7609.
[15]. V.D. John, K. Krishnankutty, Appl. Organomet. Chem. 20 (2006) 477.
[16]. V. Rajakrishnan, P. Viswanathan, K.N. Rajasekharan, V.P. Menon, Phytother.Res. 13 (1999) 571.
[17]. T.M. Kolev, E.A. Velcheva, B.A. Stamboliyska, M. Spiteller, Int. J. QuantumChem. 102 (2005) 1069.
[18]. K. Krishnankutty, V.D. John, Synth. React. Inorg.Met.-Org. Chem. 33 (2003)343.
[19]. L. Baum, A. Ng, J. Alzheimers Dis. 6 (2004) 367.
[20]. K. Krishnankutty, P. Venugopalan, Synth. React. Inorg.Met.-Org. Chem. 28(1998) 1313.
[21]. S. Daniel, J.L. Limson, A. Dairam, G.M. Watkins, S. Daya, J. Inorg. Biochem.98(2004) 266.
[22]. M. Borsari, E. Ferrari, R. Grandi, M. Saladini, Inorg. Chim.Acta 328 (2002) 61.
[23]. O. Vajragupta, P. Boonchoong, H. Watanabe, M. Tohda, N. Kummasud, Y.Sumanont, Free Radical Bio. Med. 35 (2003) 1632.
[24]. K.I. Priyadarsini, D.K. Maity, G.H. Naik, M.S. Kumar, M.K. Unnikrishnan, J.G.Satav, H. Mohan, Free Radical Bio. Med. 35 (2003) 475.
[25]. S. Awasthi, U. Pandya, S.S. Singhal, J.T. Lin, V. Thiviyanathan, W.E. Seifert, Y.C.Awasthi, G.A.S. Ansari, Chem. Biol. Interact. 128 (2000) 19.
[26]. B. Marchetti, M.P. Abbracchio, Trends Pharmacol. Sci. 26 (2005) 517.
[27]. S. Mandel, O. Weinreb, T. Amit, M.B.H. Youdim, J. Neurochem. 88 (2004) 1555.
[28]. Z.Z. Chong, F.Q. Li, K. Maiese, Prog. Neurobiol.75 (2005) 207.
[29]. O. Weinreb, S. Mandel, T. Amit, M.B.H. Youdim, J. Nutr. Biochem.15 (2004) 506.
[30]. M.T. Carri, A. Ferri, M. Cozzolino, L. Calabrese, G. Rotilio, Brain Res. Bull. 61(2003) 365.
[31]. G.L. Millhauser, Acc. Chem. Res. 37 (2004) 79.
[32]. R. Riek, Nature 444 (2006) 429.
[33]. H.Y. Hu, Chin. Sci. Bull. 46 (2001) 1.
[34]. M.L. DeMarco, V. Daggett, C. R. Biol. 328 (2005) 847.