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Interactions of Curcumin and Its Derivatives with Nucleic Acids and their Implications

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Abstract: Curcumin (diferuloylmethane) is a yellow polyphenol found in the rhizome of the annual herb turmeric (Curcuma longa) belonging to the family Zingiberaceae. Its interaction with a huge number of molecular targets like cytokines, growth factors, transcription factors, receptors, pro-inflammatory enzymes, protein kinases and adhesion molecules has been studied extensively. Interaction of curcumin with nucleic acids has been the focus of extensive research in recent years. Curcumin is observed to be genotoxic and antigenotoxic agent in time and concentration dependent manner. Curcumin and its derivatives either alone or as metal complexes have been reported to bind directly to DNA. The interactions are mainly as DNA minor groove binding or as DNA intercalating agents. The similarity in the shape of curcumin to DNA minor groove binding drugs is the motivation for exploring its binding to DNA minor grooves. Thus curcumin is a "double edged sword": having therapeutic potential as a minor groove binder but at the same time it may cause DNA damage in the cell at high concentration. The purpose of this review is to summarize the current information related to interaction of curcumin metal complexes and its derivatives with nucleic acids and the implication such interaction can have on therapeutics.

Keywords: Curcumin metal complex, Genotoxic and antigenotoxic agent, Reactive oxygen species (ROS), DNA damage, DNA minor groove binding, DNA intercalation.

1. INTRODUCTION

Turmeric has been used for thousands of years as a traditional medicine, coloring agent and spice in Asian countries. The major curcuminoids found in turmeric are curcumin (77%), demethoxycurcumin (17%) and bisdemethoxycurcumin (3%) [1]. The first chemical characterization of curcumin was done in 1910 [2]. It exists in keto (**1**) and enol (**2**) forms (Fig. **1**) and regarded as the most active constituent of turmeric [3]. Curcumin has been described in hundreds of published papers over the past few decades, studying its antioxidant, anti-inflammatory, cancer chemo-preventive and chemotherapeutic properties [4]. It has been reported to bind a huge number of molecular targets like signalling molecules, growth factors, transcription factors, receptors, pro-inflammatory enzymes, protein kinases and adhesion molecules (Fig. **2**) [5]. In the pursuance of enhanced pharmacological properties, researchers have developed many synthetic curcumin derivatives by adding various functional groups in aromatic rings and linker region of the curcumin molecule to improve the binding of these derivatives to targets through polar interactions [6]. The purpose of this review is to summarize the available scientific knowledge on the interaction of curcumin with nucleic acids which is recently emerging as a field of interest.

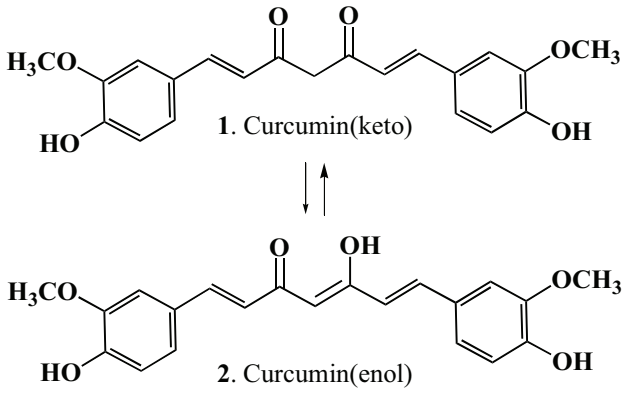

Fig. (1). Chemical structures of keto and enol forms of curcumin.

2. CURCUMIN AS GENOTOXIC AND ANTIGENO-TOXIC AGENT

Several studies have revealed that depending on dose, curcumin can act as an antigenotoxic or genotoxic agent. When curcumin acts as an antigenotoxic agent it scavenges reactive oxygen species (ROS) [7, 8], activates detoxifying enzymes (GPx, GR, G6PDH, catalase, GST and QR) [9] and

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induces the single stranded cleavage repair in DNA [10] while as a genotoxic agent it generates hydroxyl free radicals which attack the deoxyribose moiety of DNA to cause the strand breaks [11, 12]. Independent studies have shown that curcumin at low doses (upto 5µg/ml) is anti-genotoxic but at high doses (>8µg/ml) causes genotoxicity [13-18]. Pre-treatment with curcumin at a low dose (2µg/mL) significantly decreased cyclophosphamide (CPA)-induced micronucleus formation in human hepatoma G2 (HepG2) cells. However, curcumin alone at 8 µg/mL enhanced micronucleus formation. At doses higher than 8µg/mL, curcumin increased the frequency of chromosomal aberrations in HepG2 cells [14]. Curcumin at 10µg/mL induced mutagenic changes and potentiated doxorubicin and gamma radiation-mediated chromosomal aberrations in Chinese hamster ovary cells [13, 19]. Curcumin induces both mitochondrial and nuclear DNA damage with the former being more extensive than the latter [18].

Curcumin-induced DNA damage has been studied in various cell lines, such as mouse-rat hybrid retina ganglion cells, Jurkat T-lymphocytes, colorectal carcinoma HCT116 cells, gastric mucosa cells and human lung cancer cell lines PC-9 [16, 20-23]. These studies have concluded that curcumin has a major contribution in inducing DNA damage at high concentrations. However, the differential behavior of curcumin due to concentration variation is not understood currently and requires further investigations. Else this could turn out to be the Achilles heel of curcumin while finding wide acceptance as an anticancer agent in future inspite of its current promises.

3. CURCUMIN AS METAL CHELATING AGENT

Turmeric powder can be used to remove Cu(II) from aqueous solution as it contains compounds acting as sequestering agents for toxic metals [24]. It has been established that curcumin and its derivatives form complexes with a wide range of metals. These metal complexes have been reported to bind to DNA with high affinity. Based on structure-function relationship studies, three sites in curcumin have been ascertained to which metals bind (Fig. **3**). Two of these sites are contributed by the phenolic and methoxy groups on the two benzene rings and the third site is due to the presence of 1,3-diketone system between the rings [25]. Chena *et al.* confirmed this by resonance light scattering (RLS) technique where they observed enhancement in the intensity of Cu(II) with increase in curcumin concentration [26].

Curcumin helps in decreasing amyloid aggregation or oxidation induced neurotoxicity by chelating copper/iron ions which exist in high concentration in Alzheimer's disease. Spectroscopic studies using $CuCl_2$, $FeCl_2$ and $ZnCl_2$ found that curcumin has high affinity towards Cu^{2+} or Fe^{2+}, where each Cu^{2+} and Fe^{2+} ions appeared to bind at least two curcumin molecules whereas Zn^{2+} showed little binding. When curcumin was added to cultured liver cells, there was increase in the mRNA level of ferritin and α-GST but the protein level of ferritin was decreased due to inhibition of translation which normally happens when iron chelators are present [27]. A similar study has suggested the effect of curcumin on transferrin receptor1 and iron regulatory protein activation as an indicator of iron depletion due to iron chelation by curcumin [28]. Thus curcumin is an iron chelator and modulates the proteins of iron metabolism in cells and tissues.

Borsari *et al.* demonstrated that when curcumin and diacetylcurcumin react with Fe^{3+} in water/methanol 1:1 solution near neutral pH, these molecules form complexes like $FeH_2CU(OH)_2$ and $FeDCU(OH)_2$, {H_2CU=curcumin and DCU= diacetylcurcumin monoanion, respectively} which at basic pH gets ionized to $[FeH_2CU(OH)_3]^-$ and $[FeDCU(OH)_3]^-$. ^1H NMR data suggested that β-diketo

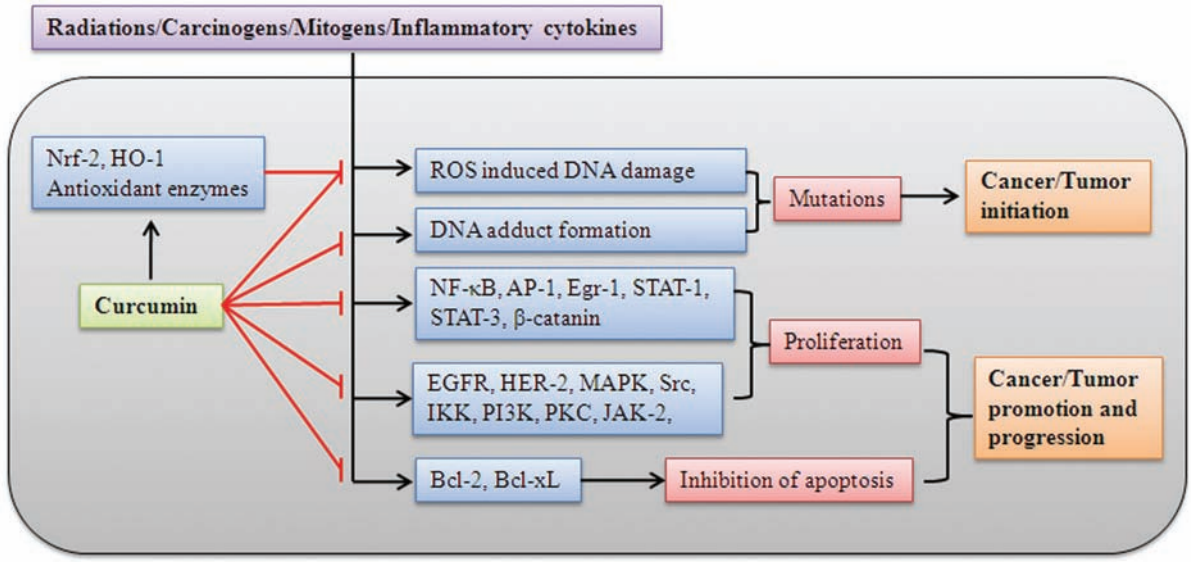


Fig. (2). Anticarcinogenic effects of Curcumin (Abbreviations: Nuclear factor-E2 p45-related factor-2 (**Nrf-2**), Heme Oxygenase-1 (**HO-1**), Nuclear factor kappa-light-chain-enhancer of activated B cells (**NF-κB**), Activator protein 1 (**AP-1**), Early growth response protein-1 (**EGR-1**), Signal Transducers and Activators of Transcription-1 (**STAT-1**), Epidermal growth factor receptor (**EGFR**), Human Epidermal Growth Factor Receptor-2 (**HER-2**), Mitogen-activated protein kinases (**MAPK**), IκB kinase (**IKK**), Phosphatidylinositol 3-kinase (**PI3K**), Protein kinase C (**PKC**), Janus kinase-2 (**JAK2**), B-cell lymphoma-2 (Bcl-2), B-cell lymphoma-extra large (**Bcl-xl**)).

moiety of the ligands is involved in metal chelation under both the pH conditions [29].

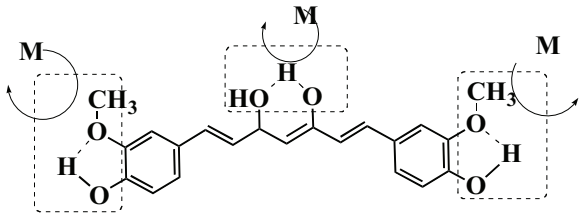


Fig. (3). Three metal binding sites (M) in curcumin: two of these sites are contributed by the phenolic and methoxy groups on the two benzene rings and the third site is due to the presence of 1,3-diketone system between the rings.

4. CURCUMIN METAL COMPLEXES EXIHIBIT ROS INDUCED DNA DAMAGE

Although a limited number of studies have suggested that curcumin produces ROS (O_2^-, H_2O_2) in the presence of metals such as Cu(II) and Fe(II) which cause DNA damage in supercoiled circular plasmid DNA (pUC18 and pBR322) as a result of that the molecules become open circular. It was proved that ROS are involved in cleavage by adding catalase which resulted in inhibition of DNA breakage [10, 30-35]. Similar results were reported when Balb-C mouse lymphocytes were treated with curcumin-Cu(II) complex. It was found that at high concentration (50 μM) although curcumin alone induces DNA strand breaks, the presence of copper increases the DNA damage [36]. Human prostate cancer cells (LnCaP, PC3 and DU145) treated with heteroleptic palladium(II) complex (**3**) (Fig. **4**) of curcumin also exhibit ROS-induced DNA damage [37].

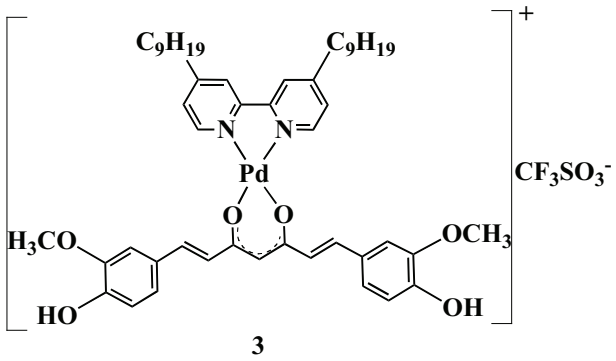


Fig. (4). Chemical structure of heteroleptic palladium(II) complex of curcumin which exhibits ROS-induced DNA damage.

In vitro studies have shown that Cu(II)-curcumin complex causes oxidation of guanine residues at C8 and increases DNA damage in proportion to Cu(II) concentration [38]. Curcumin treated with Cytochrome P450 (CYP 2D6, CYP1A1, or CYP1A2) induced DNA damage in the presence of Cu(II) especially at 5'-TG-3', 5'-GC-3', and 5'GG-3' sequences. The DNA damage inhibited by both catalase and bathocuproine, suggests that reactive species derived from the reaction of H_2O_2 with Cu(I) participate in DNA damage. Formation of 8-oxo-7,8-dihydro-2'-deoxyguanosine by oxidation of guanine was significantly increased by CYP2D6-treated curcumin in the presence of Cu(II) [39, 40]. It was seen that there is an induction of DNA damage by dietary curcumin upon copper accumulation in Long-Evans Cinnamon (LEC) rats through the formation of nuclear and mitochondrial etheno-DNA adducts [41].

Song *et al.* synthesized and characterized rare earth metal complexes with curcumin and 1,10-phenanthroline-5,6-dione (**4**) (Fig. **5**). The general formula of the complexes was REL_3L' (RE = samarium (Sm), europium (Eu), and dysprosium (Dy), L=curcumin, L'= 1,10-phenanthroline-5,6-dione) To study the interaction of complexes with DNA, they treated pBR322 plasmid DNA (0.37 μM) with the varied concentrations (0-0.08 μM) of complexes at physiological pH and temperature. The results suggested that SmL_3L' can cleave plasmid DNA at physiological pH and temperature through oxidation of bases. It was found that the cleavage process was sensitive to pH and optimum temperature for cleavage was 37 °C [42].

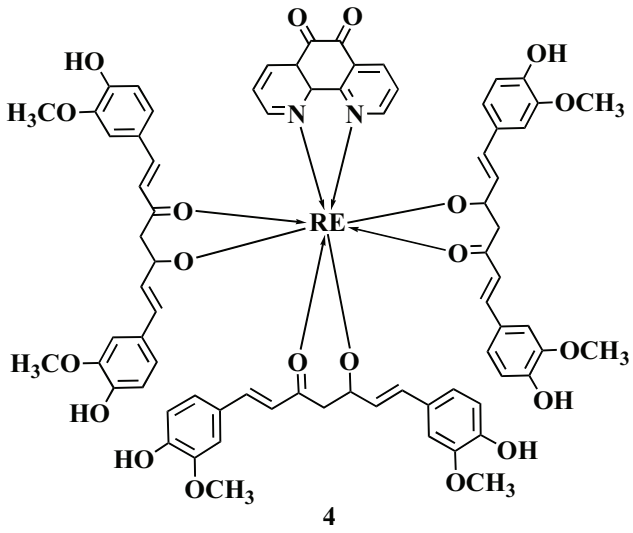
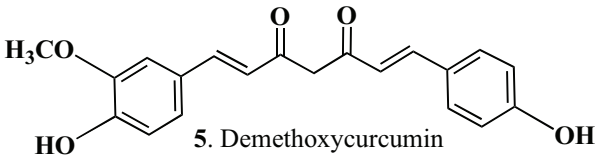


Fig. (5). Chemical structure of rare earth metal (RE) complexes of curcumin with 1,10-phenanthroline-5,6-dione which can cleave plasmid DNA at physiological pH and temperature.

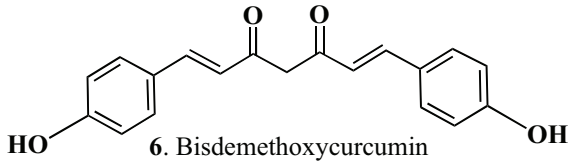
5. CURCUMIN DERIVATIVES AS MAJOR AND MINOR GROOVE BINDERS OF DNA

It is now evident from various studies that curcumin directly interacts with nucleic acids. In general, interactions of small molecules like curcumin with DNA have three common binding modes: (i) electrostatic interaction, which is due to the negatively charged sugar- phosphate backbone, (ii) hydrophobic binding against minor or major grooves of DNA, preferentially binding to AT-rich regions [43] and (iii) intercalation between the stacked base pairs of native DNA [44]. Thus small molecules interacting with double stranded DNA (dsDNA) can be classified according to their binding modes as groove binders (non-intercalators) and intercalators. The potential of curcumin and its natural derivatives

(demethoxycurcumin (**5**) and bisdemethoxycurcumin (**6**)) (Fig. **6**) for DNA binding were studied using restriction digestion of DNA sequences with enzymes such as *EcoRI* (G:AATTC), *HindIII* (A:AGCTT), *SmaI* (CCC:GGG) and *BamHI* (G:GATCC). Analysis showed that the curcuminoids prevent *EcoRI* and *HindIII* from digesting at the respective restriction sites by directly binding to AT-rich base pairs in the sequences whereas allow the restriction digestion by *SmaI* and *BamHI* both of whose sequence are GC-rich [25]. However it is not known if curcumin also inhibits the activity of *EcoRI* and *HindIII* directly.



5. Demethoxycurcumin



6. Bisdemethoxycurcumin

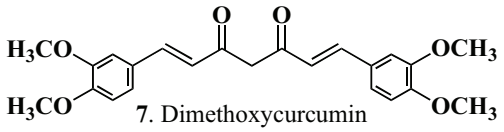
Fig. (6). Chemical structures of demethoxy and bisdemethoxycurcumin which prevent *EcoRI* and *HindIII* from digesting AT-rich restriction sites.

Circular dichroism and absorption spectroscopy techniques along with molecular modeling studies have proven beyond doubt that curcumin binds to the minor groove of the DNA double helix and is proposed to be a promising molecular probe to study biologically important pH and cation-induced conformational changes of nucleic acids [45]. Independent studies investigating the interaction between curcumin and DNA employing various electrochemical methods such as cyclic voltammetry, differential pulse voltammetry and hanging mercury drop electrode (HMDE) using carbon paste electrodes or modified glassy carbon electrode, have suggested that higher curcumin concentration causes conformational changes in DNA double helix [46-48].

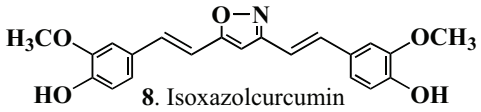
Studies on the interaction between yeast RNA and curcumin- cetyltrimethylammonium bromide (CU-CTAB) complex by absorption spectroscopy and ^{1}H NMR spectroscopy suggested that CTAB first forms complex with yeast RNA by its positive charge, which in turn interacts with two carbon atoms of the carbonyls of curcumin through hydrogen bonds and hydrophobic forces and form CU-CTAB–nucleic acid ternary complex [49].

Apart from curcumin binding to the major and minor grooves of the DNA duplex, it binds to RNA bases and to the backbone phosphate group. This was found in a study using FT-IR and UV-visible spectroscopic analysis where no conformational changes were observed upon the interaction of curcumin with the nucleic acids (both DNA & RNA). Instead, it was found that curcumin binds to DNA through thymine O_2 group in the minor groove and through guanine and adenine N7 in the major groove as well as to the backbone PO_2 group. RNA binding occurs via uracil O_2 and guanine and adenine N7 atoms as well as the backbone phosphate group. Interestingly, the interaction of curcumin was stronger with DNA than RNA [50].

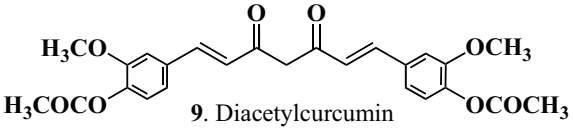
Fourier Transform Raman Spectroscopic study at physiological pH on curcumin-dGMP interaction at varying concentrations showed that at low concentration, curcumin/ dGMP (1/50) interaction is mainly through backbone PO_2 group. At higher concentration, curcumin (1/10) interact with guanine (N7) [51]. Furthermore, the UV-absorbance, gel-electrophoresis, fluorescence, CD spectroscopic and docking studies of binding of curcumin derivatives such as dimethoxycurcumin (**7**), isoxazolcurcumin (IOC) (**8**), diacetylcurcumin (DAC) (**9**) and a triglycyl curcumin derivative (**10**) (Fig. **7**) with calf thymus DNA showed that these derivatives do not intercalate but bind to the minor groove preferentially at AT-rich region [43, 52-54]. Others have also confirmed that curcumin and its derivatives are not intercalators but minor groove binders by performing ethidium bromide, 4'-6-Diamidino-2-phenylindole (DAPI) and Hoechst 33258 displacement assays [43, 52, 53].



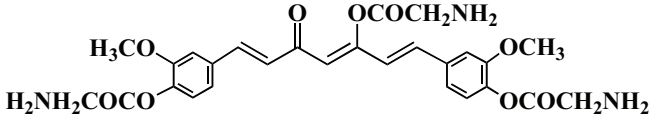
7. Dimethoxycurcumin



8. Isoxazolcurcumin



9. Diacetylcurcumin



10. Triglycylcurcumin

Fig. (7). Chemical structures of dimethoxycurcumin, isoxazolcurcumin (IOC), diacetylcurcumin (DAC) and triglycylcurcumin which preferentially bind to the AT rich minor groove.

6. METAL COMPLEXATION ENHANCES THE GROOVE BINDING AFFINITY OF CURCUMINOIDS

Binding studies of Al-curcumin complex (ACC) ([Al(curcumin) $(EtOH)_2$]$(NO_3)_2$) (**11**) (Fig. **8**) with DNA performed using multi-spectroscopic and voltametric techniques showed that ACC binds to DNA in non-intercalating mode to the AT base pairs rich minor groove. FT-IR analysis showed that there was a major decrease in the intensity of AT bases and minor decrease in the intensities of GC bases and phosphates. This together indicated a strong and direct binding of ACC to thymine (O_2) and adenine (N7) of DNA

bases located in the minor groove and weak electrostatic interaction of ACC with the phosphate backbone [55]. In a study examining the interaction between DNA and mononuclear transition metal (Cu(II), Co(II), Ni(II), Mn(II)) complexes of macrocyclic tetraaza diacetyl curcumin (**12-15**) (Fig. **9**), it was found that these complexes bind through the minor groove. Amongst these, Cu(II) complex was found to have the highest degree of interaction [56].

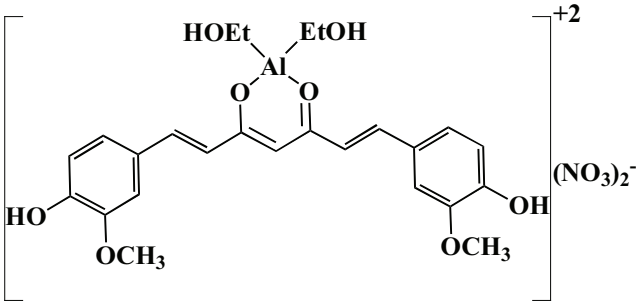


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Fig. (8). Chemical structure of Al-curcumin complex (ACC) ([Al(curcumin) $(EtOH)_2$]$(NO_3)_2$) which directly binds to thymine (O2) and adenine (N7) of DNA bases located in the minor groove.

7. IN-SILICO STUDIES OF CURCUMIN DNA INTERACTIONS

In-silico studies looking into the interaction of DNA with curcumin as well as its derivatives either in pure form or their metal complexes are providing a plethora of supporting evidences complementing the experimental findings. Comparative docking studies of curcumin and nicotine on consensus sequence ["GGGCATGCCTAGGCATGCC"] of human p53 gene showed that they bind to thymidine 6 of the p53 gene with free energy changes of -272.75 and -163.74 kcal/mol respectively suggesting that binding of curcumin on DNA is more stable than nicotine. Curcumin also interacts with nicotine with free energy change of -129 kcal/mol and reduces the availability of nicotine for DNA binding suggesting that curcumin has potential to protect DNA by not only competitively binding to it directly but also by binding to nicotine [57].

Docking studies of curcumin with two DNA duplexes [$d(GTATATAC)_2$ and $d(CGCGATATCGCG)_2$] followed by molecular simulations and free energy analysis of the complexes using molecular mechanic-poisson-boltzmann surface area (MM-PBSA) to assess binding affinity, predicted that curcumin binds in the minor grooves of AT-rich DNA sequences of DNA. However, unlike the known minor groove binders (netropsin and distamycin) where the binding is mainly by electrostatic interaction, it was found that binding of curcumin is mainly favored by van der Waals and hydrophobic interactions [58].

Caruso *et al.* synthesized and characterized ruthenium–arene complex of curcumin (p-cymene)-Ru-(demethoxy-curcuminato)-chloro (**16**) (Fig. **10**). Docking studies of this complex with a guanine rich B-DNA decamer predicted dipolar interaction of Ru with N7(guanine) and was confirmed with electrospray ionization mass spectrometry. This complex was also tested against several tumor cell lines (MCF7, HCT116, A2780, CP8, A549, U87) and showed excellent activity on the colorectal tumor cell line HCT116 (IC50 = 13.98 ± 1.503 μM) [59].

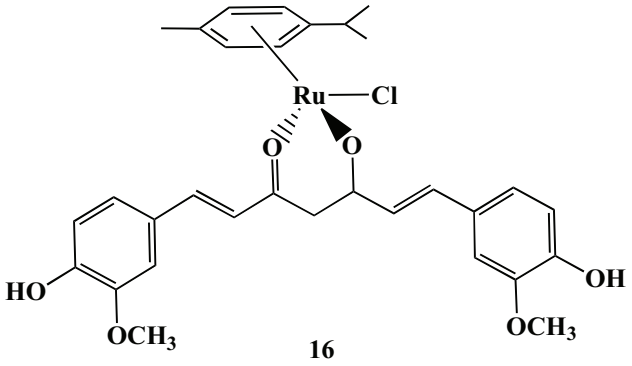

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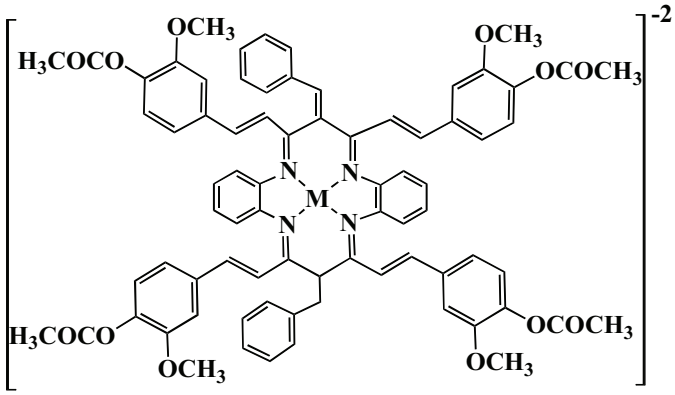
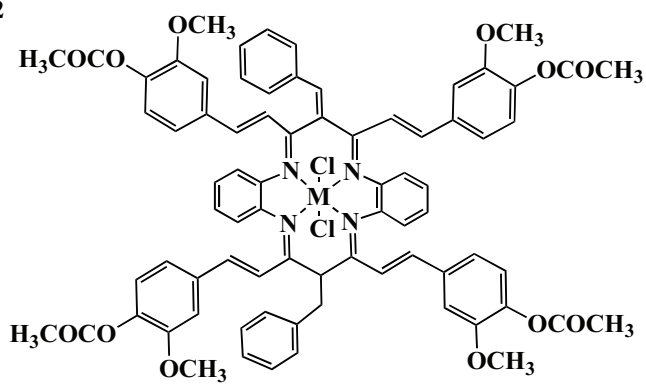
Fig. (10). Chemical structure of ruthenium-arene complex of curcumin found highly active against the colorectal tumor cell line HCT116.



12. M = Cu, **13**. M = Co, **14**. M = Ni



15. M = Mn

Fig. (9). Chemical structures of transition metal complexes of macrocyclic tetraaza diacetyl curcumin which bind to the DNA minor groove.

Table 1. Interaction of Curcumin and Its Derivatives with Nucleic Acids.

S. No	Mode of Action	Biomolecule/Cell Line Used for Study	References
1.	**Curcumin**		
	Prevents DNA damage (2-5μg/ml)	Chinese hamster ovary (CHO) cells, human hepatoma G2 (HepG2) cells & PC12 cells	[12,13,14]
	Prevents micronucleus formation in HepG2 Cells (2μg/ml)	HepG2 cells	[13]
	Causes DNA damage, chromosomal aberration and micronucleus formation (>=8 μg/ml)	Gastric mucosa cells, lymphocytes, CHO cells, HepG2 cells, human colon cancer cell line HT-29, PC12 cells, mouse-rat hybrid retina ganglion cell line, jurkat T-lymphocytes, colorectal carcinoma HCT116 cells & human lung cancer cell line PC-9	[12,13,14,15,16,17, 18,19,20,21,22]
	Acts as topoisomerase II poison (50 μM)	TK-10, MCF-7 & UACC-62 cell lines	[60]
	Binds preferentially to AT-rich region in minor grooves of DNA	Plasmid pBR322, bacteriophage lambda- DNA & calf thymus DNA	[24,44,45,46,47,56, 57]
2.	**Dimethoxycurcumin, bisdimethoxycurcumin, isoxazolcurcumin, diacetylcurcumin & triglycylcurcumin**		
	Bind preferentially to AT-rich minor grooves of DNA	Supercoiled plasmid pBR322, bacteriophage lambda-DNA & calf thymus DNA	[24,42,51,52,53]
3.	**Curcumin in the presence of Cu(II)**		
	ROS dependent DNA damage (50 μM of Curcumin in presence of 10–200 μM Cu(II))	Calf thymus DNA, pBR322 DNA plasmid	[30,33,38,40]
4.	**Curcumin Cu(II) complex**		
	ROS dependent DNA damage (8.14 μM)	CCRF-CEM leukemia cells & pBR322 DNA plasmid	[32,37]
5.	**Curcumin-Al(III) complex**		
	Binds to AT-rich region of minor groove	Calf thymus DNA	[54]
6.	**Curcumin-transition metal complexes [Cu(II), Co(II), Ni(II) & Mn(II)]**		
	Bind to AT-rich region of minor groove (120 μM curcumin Cu(II)complex)	pUC18 DNA	[55]
7.	**Curcumin-Ru-arene complex**		
	Binds to Guanine (N7) residue	Rich guanine B-DNAdecamer (containing only GC alternates)	[58]
8.	**Curcumin-earth metal complexes (Sm, Eu & Dy)**		
	Cause DNA damage (0.08 mM)	Plasmid pBR322 DNA	[41]
9.	**Curcumin-iron complex (Fe(II) & Fe(III))**		
	DNA intercalation	Salmon sperm DNA	[61, 62]
10.	**Curcumin-Zn(II) complex**		
	Partial inter-base intercalation	Synthetic DNA oligomers of sequence (5'-CGCGAATTCGCG-3' and 5'-AGCGACGTCGCT-3')	[63]

8. CURCUMIN AS DNA INTERCALATOR

In contrast to studies reported in section 6 above, curcumin was found to act as intercalating agent through the unknown clastogenic mechanism that may cause topoisomerase II poisoning. It was found that curcumin at higher concentration (50 μM) acts similar to anticancer agent etoposide and forms a ternary complex with DNA and topoisomerase II enzyme preventing re-ligation of DNA strand. This causes error in DNA synthesis and promotes apoptosis of cancer cells [60, 61]. In another study with immobilized dsDNA, curcumin was found to bind DNA

electrostatically at low ionic strength and intercalated at high ionic strength [48]. In UV-visible spectroscopic study, curcumin-Fe(II)/curcumin-Fe(III) complex interacted with salmon sperm DNA in an intercalating mode [62, 63].

Using two newly synthesized heteroleptic pentacoordinated Zn(II) complexes (**17**) (Fig. **11**) containing 4,4'-disubstituted-2,2'-bipyridines as main ligand and curcumin as ancillary ligand Pucci *et al*. demonstrated that the interaction modes of curcumin and curcumin-Zn(II) complexes with dsDNA favor their alignment perpendicular to the DNA axis through base stacking pi-pi interactions between aromatic rings suggesting a partial inter-base intercalation. *In vitro* studies of curcumin and curcumin-Zn(II) complexes against human prostate cancer (DU145, PC3, LNCaP) and neuroblastoma (SHSY-5Y, LAN-5) cell lines were carried out in which curcumin showed strongest growth inhibition in all the prostate cancer cell lines and selectively in the SHSY-5Y neuroblastoma cell line. However curcumin-Zn(II) complexes showed the strongest growth inhibition in LAN-5 neuroblastoma cell line [64].

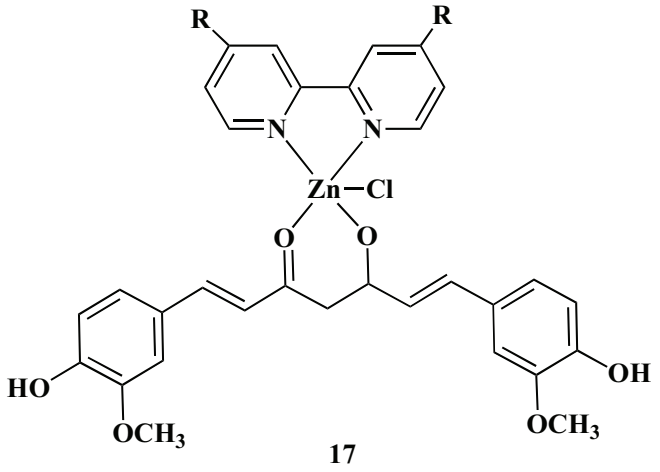


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Fig. (11). Chemical structures of heteroleptic pentacoordinated Zn(II) complexes of curcumin containing 4,4'-disubstituted-2,2'-bipyridines (R= C_9H_{19} and OH) which interact with DNA in an intercalating mode.

9. CONCLUSIONS AND FUTURE PROSPECTIVES

Current evidences suggest that curcumin behaves both as a genotoxic and antigenotoxic agent in a time and concentration dependent manner. Several curcumin and/or its derivatives and their metal complexes interact directly with DNA either by binding to the minor groove or as an intercalating agent (see Table **1**). The similarity in the shape of curcumin to DNA minor groove binding drugs such as netropsin and distamycin, is the motivation for exploring its binding to minor grooves of DNA [58, 65]. Curcumin is thus a "double edged sword" having potential for the development of minor groove binding drug for cancer therapeutics but at the same time it may cause DNA damage in the cell at high concentrations [66, 67]. It is already known that cancer cells are more susceptible than normal cells. On the other hand, genomic instability is evolving as a hallmark of cancer [68-70]. Together this provides an opportunity for developing curcumin based novel therapy in which DNA is the target as equally as proteins which are frequently reported in literature. It would be interesting to investigate the DNA binding potential of curcumin derivatives as a lead molecule for therapeutic implications.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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ABBREVIATIONS

GPx = Glutathione peroxidase

GR = Glutathione reductase

G6PDH = Glucose-6-phosphate dehydrogenase

α-GST = α-glutathione s-transferase

QR = Quinone reductase

dGMP = Deoxyguanosine monophosphate

FT-IR = Fourier transform-infrared spectroscopy

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