Abstract
Copper is one of the most prevalent biological transition metals, and plays a fundamental role in the biochemistry of the human nervous system. Without its catalytic presence, in trace or ultra trace amounts, many biochemical reactions would not take place. Copper becomes potentially toxic to cells when its concentration surpasses normal levels, because at higher concentrations, it generates free radicals (ROS). ROS damages DNA by breaking the DNA strands or modifying the bases and/or deoxyribose sugars, leading to conformational changes and stability of DNA. These conformational changes in DNA may lead to DNA stability in neurodegenerative disorders such as Alzheimer’s disease and Parkinson’s disease. In this review, we have focused on copper induced conformational change in DNA and DNA damage, and its implications on Alzheimer’s disease.

Keywords: Trace metals, Alzheimer’s disease, DNA polymorphism, oxidative stress, DNA damage, Parkinson’s disease

Introduction
Metals play an important role in the biological processes of living systems and also in most of the chemical reactions in the body. They play a critical role in many of the enzymatic and metabolic reactions. Small deviations from normal levels of metals are recognized as symptoms of malfunctions or diseases (1). Several metals such as Na, K, Mg, Ca, and P present fairly at large concentrations and are known as macro-elements in organisms and are essential to serve as structural components of tissues of the body, and essential for the development and function of the brain (2,3). A second set of metals that are present in relatively small quantities are known as trace elements or trace metals; they control essential biological processes of living cells and without their catalytic presence many biological reactions would not take place. Their presence in optimum levels is very important in health point of view. Some of the examples for the trace metals are Fe, Cu, Mn, Zn, Co, Mo, Cr and I. Trace elements are grouped into three main categories: 1) Essential metals like Fe, Cu, Zn and Mn, which participate in the control of various metabolic and signaling pathways. 2) Beneficial, but not essential elements like F, V, Br and Li. 3) Pb, Cd, Hg, Ag and Al, which are not essential but associated with toxic effects (4-6).

Trace metals are very essential to help in a variety of important cellular events, such as catalysts for chemical reactions or electron transport during energy production. However, their rich coordination chemistry and redox properties are such that they are capable of escaping out of the control mechanisms such as homeostasis. A growing amount of results provide evidence that these metals interact with nuclear proteins and
DNA, and cause oxidative deterioration of these biological macromolecules (7). Due to their redox properties and importance, cells have evolved complex machinery for strict control of metal-ion homeostasis for the survival of living organisms (8). Metal ion transporters participate in maintaining the required levels of various metal ions in the cellular compartments (9). However, disruption of these mechanisms, or absorption of detrimental metals, alters the ionic balance and their chemical reactivity, and become harmful to the body. Oxidative damage to DNA and proteins can result in a disease state, including several neurodegenerative disorders such as Alzheimer’s disease (10-12). Understanding the interactions of metal ions with various intracellular and extracellular components of the central nervous system is essential. The importance of copper for brain function and its role in human health is one of the most important current research areas. Hence, in the present review, the current trends on the role of copper on conformational and polymorphism of DNA with relevance to human health is discussed.

**Copper Metabolism:** Copper is the third most abundant transition metal in the body and the brain and second most important metal that may participate in oxygen-dependent physiological functions that serve to maintain normal cellular process (13). Copper exists physiologically in two oxidation states, as a divalent cupric [Cu(II)] extracellular circulating copper and as a monovalent cuprous [Cu(I)] intracellular. Changes in oxidation state make copper a paradoxical trace element. As a matter of fact, Cu(I) ↔ Cu(II), reversible transition can interchange between these forms by accepting or donating an electron. This allows the copper to participate in biochemical reactions as a reducing or oxidizing agent and can bind readily to many enzymes in both the oxidation states (14,15). Because of this dual role, copper can be essential or toxic depending on the oxidation states (16). Intracellular copper is not free but it is bound/chelated to either transport proteins such as ceruloplasmin and copper-albumin, storage proteins (metallothioneins), or copper containing enzymes (17,18). Some of the copper dependent enzymes for the normal function of the cells and tissues are cytochrome c oxidase, Cu/Zn superoxide dismutase (SOD1), ceruloplasmin (Cp), and dopamine β-hydroxylase (Table 1). Either a deficiency or an excess of Cu can result in serious consequences to the organism. When the Cu concentration is insufficient, cells do not have enough copper for production of active enzymes, since Cu is important functional catalytic center for some enzymes. The decreased production of active enzymes leads to a decline of metabolic activity. For example, cytochrome c oxidase, involved in energy metabolism, is negatively affected by unusually low Cu concentrations since it does not produce active enzyme under these conditions. Therefore, the cell is unable to carry out its essential metabolic activity (19). In addition to the enzymes involved in energy metabolism, other enzymes are responsible for the removal of cellular free radicals is greatly affected when the available Cu is decreased. The clearest case for this is that of superoxide dismutase (SOD), which has Cu and zinc at its catalytic center (20). On the other hand, an excess of Cu is associated with oxidative stress and can be toxic at both the cellular and tissue level. Cu is generally found in its bivalent state (Cu²⁺), but, in its monovalent form (Cu⁺), it is able to transfer one electron and generate reactive oxygen species (ROS) such as hydroxyl radicals (21,22). These radicals are responsible for cellular damage due to protein oxidation, lipid peroxidation in membranes and DNA damage (Fig. 1).

In biology, copper is vital for cells because it participates directly in the biological processes, but can become toxic on overexposure. The toxicity of this metal makes them dangerous for the body at certain levels of micromolar concentration. Hence, controlled metal homeostasis is essential. Public health point of view, importance of its deficiency or excess in the human body is the subject of current research. It is estimated that an healthy adult human body...
Table 1. Some enzymes in humans that use copper as a cofactor

<table>
<thead>
<tr>
<th>Cu containing enzymes</th>
<th>Functions</th>
<th>Consequences of loss or deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tyrosinase</td>
<td>Synthesis of dopamine, epinephrine, norepinephrine which are the important neurotransmitters. It also assists the synthesis of melanin.</td>
<td>Loss of pigmentation: albinism</td>
</tr>
<tr>
<td>Dopamine β-hydroxylase</td>
<td>Norepinephrine synthesis</td>
<td>Hypoglycemia, hypotension</td>
</tr>
<tr>
<td>Ceruloplasmin</td>
<td>A carrier protein required for normal Fe metabolism and antioxidant production</td>
<td>Anemia, Neurodegeneration, Diabetes.</td>
</tr>
<tr>
<td>Cytochrome c oxidase</td>
<td>Energy production through electron transport chain in the mitochondria. Reduces oxygen to water in muscle and other tissues.</td>
<td>Respiratory deficiency, Encephalopathy, Cardiac failure</td>
</tr>
<tr>
<td>Cu/Zn Superoxide dismutase</td>
<td>anti-oxidant property/ Antioxidant defense</td>
<td>Oxidative stress, Neurodegeneration, Hepatocellular carcinoma</td>
</tr>
<tr>
<td>Lysyl oxidase</td>
<td>Covalent cross-linking of collagen and elastin</td>
<td>Arterial aneurysms, Cardiovascular dysfunction</td>
</tr>
</tbody>
</table>

(70 kg) contains 110 mg of copper of which, 10 mg in the liver, 8.8 mg in the brain, 6 mg in the blood, 46 mg in the skeleton and bone marrow and 26 mg in the skeletal muscle (23). WHO recommended daily intake for adult body is around 1-1.6 mg which meets body needs. There is a continual turnover of copper with most of it being recycled. About 15% of the copper absorbed from the diet and the remaining 85% is excreted as bile; liver plays a central role in copper homeostasis. Copper is absorbed via the intestinal epithelium in to the blood circulation, where it is bound/chelated to the albumin, transcuprin or histidine and forms an exchangeable pool of Cu(II). Liver is a central organ in copper metabolism as it receives all dietary copper and regulates the whole body copper content by excretion in the bile. The balance between intracellular and extracellular content of copper is driven by cellular compartmentalization (24). The balance between copper necessity and toxicity is achieved both at the cellular and the tissue and organ levels. Cells regulate the traffic of copper ions and maintain the amount necessary.
for biological functions avoiding excess levels. Increase or decrease in the copper level in the cells due to failure of copper homeostasis may lead to many diseases including neurodegenerative disorders such as Alzheimer’s disease. Copper levels in normal and AD brain are shown in table-2.

**Copper and oxidative stress**

Copper is a redox-active metal that participates in diverse metabolic processes in living organisms. Copper is known to have a definite role in the nucleus. It is an essential component of chromatin and is involved in chromatin scaffold proteins. Physiologically, it exists both as oxidized Cu (II) and as reduced Cu (I), and can bind readily to many enzymes in both oxidation states, preferentially via thiol groups (25). The cupric ion [Cu(II)] in the presence of superoxide anion radical can be reduced to cuprous ion [Cu(I)] and it is the most toxic ion, which can induce the production of more reactive ROS such as highly reactive hydroxyl radicals through the decomposition of hydrogen peroxide via the Fenton or Harber–Weiss reactions (26). Biomolecular damage may occur from the reaction of \( \cdot \text{O}_2^- \) with copper (II) as follows.

\[
\text{Cu(II)} + \text{O}_2^- \rightarrow \text{Cu(I)} + \text{O}_2
\]

\[
\text{Cu(I)} + \text{H}_2\text{O}_2 \rightarrow \text{Cu(II)} + \text{OH}^- + \text{OH}^-
\]

The hydroxyl radical is highly reactive with a half-life in aqueous solution of less than 1 nanosecond (27), hence, it instantaneously reacts with DNA, proteins, membrane lipids, resulting in extensive impairment of cellular functions. Interaction of \( ^\cdot \text{OH} \) with DNA causes severe damage to DNA, which ultimately leads

![Fig. 2. Mechanism of oxidative stress induced cell death](image-url)

**Table 2. Evidence for the metal Dyshomeostasis in Alzheimer’s Disease (AD)**

<table>
<thead>
<tr>
<th></th>
<th>Copper</th>
<th>Iron</th>
<th>Zinc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control neuropil</td>
<td>4 µg/g</td>
<td>19 µg/g</td>
<td>23 µg/g</td>
</tr>
<tr>
<td>Total amyloid plaque</td>
<td>25 µg/g</td>
<td>53 µg/g</td>
<td>69 µg/g</td>
</tr>
<tr>
<td>AD neuropil</td>
<td>19 µg/g</td>
<td>39 µg/g</td>
<td>51 µg/g</td>
</tr>
</tbody>
</table>

to mutations, such as strand breaks and oxidation of bases (28). It has been proposed that the extent of DNA strand breaking by $\cdot$OH is governed by the accessible surface areas of the hydrogen atoms of the DNA backbone. In intact cells, the damage to DNA may come from endogenous copper ions exposed to oxidants (Fig-2), which will affect adversely the biological processes, such as signal transduction and transcription.

Brain is vulnerable to oxidative stress, since it utilizes about 7.3% of total body copper, which is comparable to that of the liver (about 9%) (29,30). The brain comprises 2% of the total body mass, but it exhibits the highest rate of oxidative metabolism, consuming about 20% of total body oxygen inspired and carries out the ATP turnover at a high rate (31). Since approximately 5% of the oxygen consumed by cells is estimated to be reduced to ROS, relatively higher amounts of ROS may be generated in the brain as compared to other tissues that use less oxygen. Moreover, the brain is rich in poly-unsaturated fatty acids, amino acids and neurotransmitters, which are particularly susceptible to ROS damage (32-34). Paradoxically, the brain is endowed with disproportionately low levels of antioxidant activity, which makes it particularly susceptible to oxidative stress (35). Over exposure to oxidative radicals can adversely affect gene expression and basic metabolic processes (36). Increasing evidence suggests that oxidative stress is associated with normal aging, and neurodegenerative diseases such as AD, PD, Huntington’s disease (HD) and ALS (37-40). Various studies report the action of copper-containing compounds in the induction of DNA damage. Becker et al (43) reported that the DNA strand breaks in PM2 phage DNA were induced by aliphatic and aromatic aldehydes in combination with CuCl$_2$. Therefore, the increased oxidative DNA damage may lead to DNA instability in neuronal cells. The decrease in anti-oxidant defenses and a reduction in base excision repair may contribute to reduced gene expression in the human brain. DNA damage may contribute to reduced gene expression (44), which may influence the rate of subsequent functional decline and the vulnerability of the brain to age-related neurodegenerative diseases.

Copper and Apoptosis: Copper is a redox active metal. Exposure of excessive copper to cells and tissues can result in acute damage to the cell membranes. This leads to loss of cell integrity and thereby cell death. Chronic excessive copper accumulation in brain and other organs lead to the production of reactive oxygen species (ROS). ROS are products of normal cellular metabolism and plays a dual role as both deleterious and beneficial species (45). Beneficial effects of ROS occur at moderate concentrations and involve physiological roles in cellular responses to noxia, in defense against infectious agents and in the function of a number of cellular signaling systems (46). The harmful effects of free radicals include oxidative stress and this occurs in biological systems when there is an overproduction of ROS on one side and a deficiency of enzymatic and non-enzymatic antioxidants on the other (47-49). Disturbances in the normal redox-state of cells can cause toxic effects through the production of highly reactive free radicals that damage to biological molecules inhibiting their normal function, which may be implicated in a number of human diseases as well as in the ageing process (50-52). Further, some reactive oxidative species act as cellular messengers in redox signaling. Thus, oxidative stress can cause disruptions in normal mechanisms of cellular signaling.

Over accumulation of copper in brain and other organs will increase in the rate of radical formation leading to several undesirable effects of proteins, lipids and DNA damage leading to cell death. This oxidative damage/stress is believed to be involved not only in the toxicity in the brain but also in the impairment in neuronal and endocrine function, which can lead to cell death (53). It is reported that the DNA damage in
AD brain occurs due to oxidative stress (54). Literature data and our unpublished data suggests that copper at the micromolar concentrations may lead to structural alterations in DNA that may cause the DNA damage and impairment in neurons, and ultimately neuronal cell death (apoptosis).

**Copper induced DNA damage**: ROS formed due to excess amount of copper in cells can damage cellular macromolecules, such as nucleic acids, lipids, and proteins (55). Hydroxyl radical is known to react with all components of DNA molecule in nucleus and mitochondria. It slots into DNA double bonds of DNA bases as well as deoxyribonucleotide backbone, interacts with purine and pyrimidine bases and also with the deoxyribose backbone, and causes permanent damage to DNA (56). Exposure of DNA to copper ions has been reported to result in single strand and double-strand breaks, affecting DNA-DNA and DNA-protein interaction and DNA base modification that could lead to alterations in transcription, incorporation of replication errors, genomic instability (57-59) and induction of signal transduction pathways (60). Several reports indicate that guanine is the most vulnerable to oxidative damage (61-62). It is well established that OH radical adds to position 8 in the ring structure of guanine in DNA, and forms an initial product called 8-hydroxy-2-deoxyguanosine radical (8OHdG) (63), which is a good biomarker of oxidative stress of an organism and a potential biomarker in the pathogenesis in Alzheimer’s disease (64, 65). Oxidative genomic DNA modifications, oxidative damage and the induction of mutation in DNA may participate at multiple stages of neurological disorders. Because of the critical role of DNA in cellular function, oxidative damage to DNA may be one of the important factors in neuron degeneration in AD as reported by Nunomura et al (66). Copper ion induces significantly more DNA base damage, showing a propensity for guanine-containing regions (67). Copper is an important structural metal ion in chromatin, being present at about one copper ion per kilo base (68,69). For these reasons, there is increased interest in the ability of copper ion to participate in DNA damaging reactions *in vivo*. Mutation or disrupted expression of genes that increase DNA damage often result in premature aging. Oxidative DNA damage has effects on cells and is intermediate biomarkers of a disease, which plays a role in the etiology of neurological disorders.

**Copper-induced conformational changes in DNA**: DNA is a supercoiled negatively charged polymer of nucleotide units and found in cells usually as right handed double helix, B-DNA. The two strands have complementary sequences of nucleic acid bases, with the sugar-phosphate groups on the outside and the base pairs linked with the hydrogen bonding in the interior is intertwined in a helix. The positively charged copper ions interact directly or indirectly with the sites of negatively charged residues of DNA and it will result in conformational changes of the DNA structure. The binding sites on DNA could be the negatively charged phosphates of the backbone of both the strands and the electron donor atoms of the bases arranged in the helix. The predominant mode of copper binding takes place at the N7 and O6 of guanine and N1 of adenine bases and the N3 of cytosine bases, but copper will not bind to thymine. Binding of copper (II) ions to A-T base pairs is much less effective than binding to G-C base pairs. Copper is a redox trace metal essential for many biochemical processes. Because of the partially filled d-orbitals, they readily lose their water molecule and give inner sphere coordinated complexes (70). Reports of many authors show that copper binds directly to the bases and indirectly to the phosphate groups. Copper reacts chemically with the N7 of guanine and N3 of cytosine (71) and perturbs the double helix, which leads to the change of conformation and damage to the DNA. This change in conformation leads increased vulnerability to oxidation induced by ROS. It also damages the DNA through radical generation. It was theoretically postulated that the guanine base present in DNA would be more susceptible to OH radical induced conformational variations due to
overexposure to copper (72). When copper binds to stacked G-C base pairs, the DNA backbone conformation distorted and therefore, a change in conformation of B-DNA to an altered B-conformation takes place due to unwinding of the helix, which affects the DNA-protein interaction. The conformations of DNA and associated proteins are critical to the replication and transcription.

The conformational changes induced in native DNA by binding with copper (II) ions were of special interest, because it has been suggested that copper ions are able to regulate local DNA secondary structures. The B-form DNA are characterized by a positive long wavelength band at about 260–280 nm and a negative band around 245 nm. However, the position and amplitude of the CD bands show marked differences in terms of sequence diversity (73). Pertz et al (74) reported changes in DNA conformation in the presence of copper. Woisard et al (75) reported right handed B-DNA to Z-DNA (left handed helix) conformation conversions induced by copper and copper complexes. Poly d(GC).d(GC) oligonucleotide with alternating G-C sequence can exist in a left handed as well as a right handed conformation (76). Our study (77) and other studies (78,79) show that Al-maltolate induces the left handed Z-form of DNA with a characteristic negative band at 290 nm and a positive band at 270 nm and extremely deep negative band at 205 nm. Z-DNA has characteristic zig-zag phosphate backbone and the uniform alternating Watson-Crick base pair is achieved by purines adopting syn conformation and C3'-endo sugar-pucker. Z-DNA forms excellent crystals. These features of major DNA conformations are summarized in Table-3 and CD spectral data is summarized in Table-4. CD changes of Z-DNA were also noticed in (CCG)\textsubscript{12} sequence (80) and scDNA (81). These findings may be applicable to DNA in the presence of copper. Thus, the interactions of Al and Cu with DNA at different sites can lead to a variety of changes in DNA structure.

The stability of the DNA double helix is very important for DNA structure; slight variations in the DNA sequence can have profound implications on the stability of the DNA. In addition to hydrogen bonding, base stacking, interaction with copper(II) ions with DNA plays an important role in DNA duplex stability (82). At higher concentrations of Cu(II) ions and increased temperatures, an increase in T_m was observed due to DNA damage, which was resulted due to perturbation of DNA base stacking (83).

Supercoiling is an important aspect of DNA physiology in both prokaryotes and eukaryotic cells. Supercoiling-induced alterations in DNA structure and dynamics could affect the interaction with Copper. Copper preferentially binds to N_7 atom of guanine and at least is capable of forming chelation complexes with the O_6 in the same guanine and with other nearby bases resulting the 8-oxoG and strand breaks. Copper bind to G-C bases and breaks the hydrogen bonds between bases, thus tilts the bases leading to conformational change from B-DNA to C-DNA (84). The binding of copper to DNA leads to DNA damage through radical generation from oxidation by H_2O_2 (85). Double strand breaks, cross-linking and mispairing of DNA as a result of oxidative DNA damage have shown the positive role of aberrant copper. These changes in DNA conformational effects have important implications for genetic information transfer and activity of RNA polymerase. Conformation of the DNA is important for the normal activities of the cellular processes (86). Any change caused by Cu or Al in the conformation of DNA, alters the ability of the DNA to act as a template for RNA synthesis that also affects the function of neurons and the neurotoxic effects (87).

Dopamine is one of the neurotransmitters and plays an important role in neuronal function. In PD, dopaminergic neuronal cell loss is observed, which alters the levels of dopamine contributing to movement disorders. Even though it is an essential neurotransmitter required for the neuronal function, at high concentrations it...
becomes cytotoxic in the presence of copper and induces oxidative stress leading to DNA damage (88, 89). Several groups showed a possible link between copper-mediated oxidative DNA damage and dopaminergic neuronal cell death (90, 91). It is reported that dopamine content in CSF is 30±6 pg/ml in AD, compare to that of the normal 10±6 pg/ml. Dopamine induced DNA damage in the presence of Cu(II) ions normally takes place in the brain leading to dopaminergic neuronal cell death (92). Copper induced conformational changes in DNA are more progressive in the presence of dopamine, and can significantly disturb neurotransmission in a more systematic manner in the brain of AD patients and thus play an important role in neuropathology of AD and PD.

**Effect of copper on gene expression and health:** DNA conformations play a vital role in gene expression (93). B-DNA a predominant conformation participates in the gene expression. Any conformational change in the region of the gene is likely to have a profound effect on the transcription (94). Among the altered conformations, altered B-DNA and Z-DNA are observed in the promoter region of specific genes and correlated to their expression patterns (95). Copper dependent transcription factors regulate transcription of specific genes (96, 97). Genes regulated by copper-dependent transcription factors include genes for copper/Zinc superoxide dismutase (Cu/Zn SOD), catalase and proteins related to the cellular storage of copper. In yeast, copper promotes expression of enzymes protecting against oxidative stress, while it suppresses expression of genes that transport copper in to cells (Ctr1 and Ctr3) as well as reductases. Cleavage of the DNA strand by copper induced oxidative damage has the ability to cause the conformational change and become toxic to cells (98, 99). DNA damage in the brain has been implicated in a number of neurodegenerative diseases, such as Alzheimer's disease (AD).

SOD-1 has a major role in the defense against oxidative stress by catalyzing the dismutation of \(O_2^-\) to molecular oxygen (\(O_2\)) and \(H_2O_2\) using copper as cofactor, which can be converted by catalase and glutathione peroxidase (GPX) to water. Imbalance in the ratio of the reaction, results in the accumulation of \(H_2O_2\). A recent observation reveals that SOD-1 forms proteinaceous aggregates that are related with senile plaques in AD brain and these are implicated the involvement of oxidative damage to SOD-1 in the AD pathogenesis (100). Enhanced antioxidant enzyme activity may affect

![Fig. 3. Copper interaction with scDNA involved in copper mediated genotoxicity as well as oxidative damage via different mechanisms in brain cells](image-url)
the gene expression by altering the binding and/or availability of transcription factors such as nuclear factor kappaB (NFκB) (101) and the activator protein AP-1 (102) to DNA.

In humans, two Cu(I)-ATPases, ATP7A and ATP7B are expressed in all the tissues, particularly in the brain and the heart. ATP7B is predominant in liver and expressed in small amounts in brain and in both the genes mutations were discovered. The importance of ATP7A and ATP7B in copper homeostasis is illustrated by two genetic diseases, arising from these mutations, which promote the dysfunction of the ATPases and are sources of severe diseases, the Menkes syndrome for ATP7A and the Wilson disease for ATP7B (103,104). Menkes disease occurs due to copper accumulation in intestinal cells and copper deficiency in blood. As a result, essential cuproenzymes lack their cofactor and death occurs during early childhood (105). The Wilson disease results in copper overload in the liver and brain with risk of cirrhosis and neurological problems, and this disease is fatal in the absence of treatment. Both deficiency and overload of copper in human body has a consequence on health. B-DNA is a highly variable structural form of the DNA double-helix, and the sequence dependent structural variations play a critical role in protein recognition and binding. Changes in DNA conformation (altered B-DNA, A-DNA, CDNA and Z-DNA) can potentially affect various

Table 3. Structural parameters of DNA helices

<table>
<thead>
<tr>
<th>Structural parameters</th>
<th>A-DNA</th>
<th>B-DNA</th>
<th>Z-DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direction of helix rotation</td>
<td>Right handed</td>
<td>Right handed</td>
<td>Left handed</td>
</tr>
<tr>
<td>Residue per helical turn</td>
<td>11</td>
<td>10.5</td>
<td>12</td>
</tr>
<tr>
<td>Axial rise per residue</td>
<td>2.55Å°</td>
<td>3.4Å°</td>
<td>3.7Å°</td>
</tr>
<tr>
<td>Pitch (length) of the helix</td>
<td>2.82Å°</td>
<td>3.4Å°</td>
<td>44.4Å°</td>
</tr>
<tr>
<td>Base pair tilt</td>
<td>20°</td>
<td>-6°</td>
<td>7°</td>
</tr>
<tr>
<td>Rotation per residue</td>
<td>32.7°</td>
<td>34.3°</td>
<td>-30°</td>
</tr>
<tr>
<td>Diameter of helix</td>
<td>32Å°</td>
<td>20Å°</td>
<td>18Å°</td>
</tr>
<tr>
<td>Backbone</td>
<td>Altered smooth path</td>
<td>Smooth path</td>
<td>Zigzag path</td>
</tr>
<tr>
<td>Configuration</td>
<td>Anti</td>
<td>Anti</td>
<td>Anti</td>
</tr>
<tr>
<td>Glycosidic bond</td>
<td>Anti</td>
<td>Anti</td>
<td>Syn</td>
</tr>
<tr>
<td>Sugar puckering</td>
<td>C3' endo</td>
<td>C2' endo</td>
<td>C2' endo</td>
</tr>
</tbody>
</table>


Table 4. Copper-induced conformational changes in DNA

<table>
<thead>
<tr>
<th>Conformation</th>
<th>CD at Wavelength</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>~240-250 nm</td>
</tr>
<tr>
<td>A-DNA</td>
<td>Weakly negative</td>
</tr>
<tr>
<td>B-DNA</td>
<td>Negative</td>
</tr>
<tr>
<td>C-DNA</td>
<td>Negative</td>
</tr>
<tr>
<td>Z-DNA</td>
<td>Positive</td>
</tr>
<tr>
<td>Ø-DNA</td>
<td>______</td>
</tr>
</tbody>
</table>

Role of Copper on DNA Conformational Polymorphism
DNA reactions, including replication, transcription and epigenetic modifications (106), which may cause diseases in humans.

Conclusions

Copper exists in the cell nucleus at a relatively high concentration and closely associated with chromosomes and bases. Copper ions bind to the DNA, leading to DNA damage in two mechanisms. The “direct” damage may involve conformational changes of DNA. On the other hand, “indirect” damage is a consequence of copper induced formation of reactive oxygen species involving superoxide is shown in Fig. 3. B-DNA conformation is essential for the normal activities of the cell. Any variations in the conformation leads to changes in DNA conformation (altered B-DNA, A-DNA, C-DNA and Z-DNA), which can potentially affect various DNA reactions, including replication, transcription and epigenetic modifications. These conformational variations will have a biological importance in relevance to the brain disorders. Copper and its impact on the conformations of nucleic acids and production of ROS emphasizes the role of copper in the brain disorders, including Alzheimer’s disease and Parkinson’s disease. The histone and non-histone proteins present in chromatin protect the bases in DNA from oxidative DNA damage.

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