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A review on genotoxicity in aquatic organisms and environment

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Abstract
Genotoxicity studies used to explore the puissance of a compound to interact with the genetic constituents. Any alteration in the genetic code either due to gene mutations (point mutations) or DNA strand breaks may lead to fundamental changes. DNA damage in a somatic cell may results in a somatic mutation, which may lead to malignant transformation (cancer). Many chemicals having the genotoxic potential are being emitted to surface water through various discharges. Most engineered nanoparticles (ENPs) are capable of causing genotoxic responses such as DNA or/and chromosomal fragmentation, DNA strand breakage, but at unrealistic high concentrations. Genotoxicity tests are gaining importance through the development of several techniques to directly detect the DNA damage. These tests are relied on the fact that any change to DNA is having long-lasting and profound consequences.

Keywords: aquatic environment, aquatic fauna, asaays, genotoxins, genotoxicity

1. Introduction
Genotoxicity is a word in genetics defined as a destructive effect on a cell's genetic material (DNA, RNA) affecting its integrity. Genotoxic substances are known to be potentially mutagenic or carcinogenic when inhaled, ingested or penetrate the skin. As many mutations may ultimately result in cancer (or be part of the multistep process of carcinogenesis), mutagens are typically also carcinogens. Genotoxins can cause three primary effects on organisms by putting impact on their genetic information. Genotoxins can be carcinogens (cancer-causing agents), mutagens (mutation-causing agents) or teratogens (birth defect-causing agents). In most of the cases, genotoxicity leads to mutations in various cells and other body systems. DNA damage in a somatic cell may result in a somatic mutation, which may lead to malignant transformation (cancer). For genotoxicity assessment many *in-vitro* and *in-vivo* tests have been developed that, with a range of endpoints, detect DNA damage or its biological consequences in prokaryotic (e.g. bacterial) or eukaryotic (e.g. fishes, mammals, yeast or birds) cells.

During the past decade, toxicological studies have undergone a remarkable evolution by putting major emphasis on teratogenicity, chronic toxicity, carcinogenicity, and mutagenicity (Flora and Izzotti, 2007) [16]. Research is going on to find solution for reducing the effect of genotoxins. One of the best methods to depreciate the effect of mutagens and carcinogens is to identify and add the anticlastogens/ antimutagens (substances which suppress or inhibit the process of mutagenesis by acting directly on the mechanism of cell) and desmutagens (substances which somehow destroy or inactivate, partially or fully the mutagens, thereby affecting less cell population) in diets and also increase their use. Nature has bestowed us with medicinal plants. This is the need of the hour to investigate them for being used as anti-mutagenic and anti-carcinogenic agents or drug additives.

In order to assay for genotoxic molecules, researchers assay for DNA damage in the cells that have been exposed to the toxic substances. This DNA damage can be in various forms i.e., single and double strand breaks, cross-linking, loss of excision repair, alkalilabile sites, point mutations, and structural and numerical chromosomal aberrations. The compromised integrity of the genetic material has been known to cause cancer. Consequently, many high technological techniques including Ames Assay, *in vitro* and *in vivo* Toxicology Tests and Comet Assay, Micro-Nuclei count have been developed to assess the genotoxic potential of chemicals to cause DNA damage which may results in cancer (Nagarathna *et al*., 2013) [28].

2. Mechanisms

The genotoxic substances induce damage to the genetic material in the cells through interactions with the DNA structure and sequence. For example, the transition metal chromium interacts with DNA in its high-valent oxidation state so to occur DNA lesions leading to carcinogenesis. The metastable oxidation state Cr (V) is achieved through reductive activation. The researchers performed an experiment to study the interaction between DNA with the carcinogenic chromium by using a Cr (V) Salen complex at the specific state of oxidation. The interaction was specific to the guanine nucleotide in the genetic sequence.

In order to narrow the interaction between the Cr (V)-Salen complex with the guanine base, the researchers modified the bases to 8-oxo-G so to have site specific oxidation. The reaction between the two molecules caused DNA lesions; the two lesions observed at the modified base site were spiroiminodihydantoin and guanidinohydantoin. To further analysis of the site of lesion, it was observed that polymerase stopped at the site and adenine was inappropriately incorporated into the DNA sequence opposite of the 8-oxo-G base. Therefore, these lesions predominately have G >T transversions. High-valent chromium is seen to act as a carcinogen as researchers found that "the mechanism of damage and base oxidation products for the interaction between DNA and high-valent chromium are relevant to *in-vivo* formation of DNA damage leading to cancer in chromate-exposed human populations." Consequently, it shows how high-valent chromium can act as a carcinogen with 8-oxo-G forming xenobiotics.

3. Genotoxicity test techniques

The purpose of testing genotoxicity is to determine whether a substrate will influence genetic material or can cause cancer. These tests can be performed in both prokaryotic and eukaryotic cells. The following standard tests are recommended for genotoxicity assessment based upon the considerations mentioned above:-

1. A test for gene mutation in prokaryotes
2. An *in-vivo* test for chromosomal damage using eukaryotic hematopoietic cells
3. An *in-vitro* test with cytogenetic evaluation of chromosomal damage with eukaryotic cells (ICH, 1998) [21].

Bacterial Reverse Mutation Assay

The Bacterial Reverse Mutation Assay also known as the Ames Assay, is being used in laboratories for testing for gene mutation. The technique uses many different bacterial strains in order to compare the different changes in the genetic material. The result of the test detects the majority of genotoxic carcinogens and genetic changes; the types of mutations detected are frame shifts and base substitutions.

In vivo Testing

The main purpose for *in vivo* testing is to estimate the potential of DNA damage that can affect chromosomal structure or disturb the mitotic apparatus that changes chromosome number. The factors that could influence the genotoxicity are ADME and DNA repair. It can also detect the genotoxic agents which may miss in *in vitro* tests (Furman and Grace, 2013).

In vitro Toxicology Testing

The purpose of *in vitro* testing is to determine whether a substrate, product, or environmental factor induces genetic damage. One technique includes cytogenetic assays using different prokaryotic cells. The types of aberrations detected in cells affected by a genotoxic substance are chromatid and chromosome gaps, chromosome breaks, chromatid deletions, fragmentation, translocation, complex rearrangements and many more (Furman and Grace, 2013). This is similar to the micronucleus test and chromosome aberration assay, which detect structural and numerical chromosomal aberrations in prokaryotic cells (Kolle and Susanne, 2013) [25].

4. Genotoxicity assessment assays

4.1 Comet Assay

A more useful approach for assessing DNA damage is the single-cell gel (SCG) or comet assay. Comet Assay is one such state-of-the-art technique for quantitating DNA damage and repair in eukaryotic cells and some prokaryotic cells. This technique is more advantageous as it detects low levels of DNA damage, requires only a very small number of cells, is cheaper than many techniques, is easy to execute, and quickly displays results. However, it does not identify the mechanism underlying the genotoxic effect or the exact chemical or chemical component causing the breaks.

Ostling and Johanson (1984) [34] were the first to develop a micro-cell gel electrophoresis technique for detecting DNA damage at the level of the single cell. Subsequently, Singh *et al*. (1988) [44] introduced a micro-cell gel technique involving electrophoresis under alkaline (pH>13) conditions for detecting DNA damage in single cells. Alkaline comet assay is capable of detecting a wide variety of DNA damages such as DNA single-strand breaks, double-strand breaks, oxidatively induced base damages, alkali-labile sites, and sites undergoing DNA repair (Jarvis and Knowles, 2003) [22].

Schnurstein and Braunbeck (2001) [42] investigated the suitability of an *in vitro* version of the comet assay with primary hepatocytes and gill cells from zebrafish (*Danio rerio*). Within the scope of an 18-month biomonitoring study, primary cells were used to identify the genotoxic potential of native water samples from different sites along the major German rivers, Rhine and Elbe, and to evaluate the sensitivity and practicability of the chosen assay. Depending on the endpoint measured, considerable differences were detected with respect to the number of genotoxic surface water samples. Coughlan *et al*. (2002) [14] measured genotoxic damage, expressed as single-strand DNA breaks, in cells isolated from gills, haemolymph, and digestive gland from the clam *Tapes semidecussatus*, using the comet assay. Throughout the study of three weeks after exposing the clams to sediments, significant differences in DNA damage were recorded for each tissue type between clams exposed to the two sediment samples. Rajaguru *et al*. (2003) [36] determined the genotoxic properties of water and sediment collected from the Noyyal River, in common carp (*Cyprinus carpio*) using the alkaline comet assay. Upon electrophoresis, extensive DNA damage, measured as the DNA length: width ratio of the DNA mass, was observed in erythrocytes, kidney and liver cells of fish after exposure to the polluted water samples and the amount of damage is having direct relation with the duration of exposure. The highest levels of DNA damage were obtained with samples taken at downstream of urban centers. The results indicated that the Noyyal River system was contaminated with the genotoxic substances and that the comet assay has sufficient sensitivity to detect the genotoxicity.

De Andrade *et al*. (2004) [15] assessed the genotoxicity due to

multiple sources of pollution in the peripheral blood of two native estuarine fish (mullet and sea catfish) and evaluated possible interactive genotoxic effects from multiple contaminants and the seasonal variation of the genotoxicity. The increase in DNA damage appears to be related to the density of people residing nearby area. Whitehead *et al*. (2004) [51] tested whether agricultural chemical runoff was associated with instream genotoxicity in native fish and selected DNA strand breakage as a genotoxicity biomarker for conducting the study. The results indicated that DNA strand breaks were significantly elevated in fish exposed to San Joaquin River compared to a nearby reference site. Time-course measurements in field experiments supported a linkage between induction of DNA strand breakage and the timing of agricultural runoff. A possible genotoxic effect of surface water treated with disinfectants for potabilization was detected by Buschini *et al*. (2004) [11]. The comet assay was applied in circulating erythrocytes of *Cyprinus carpio*. Genotoxic damage was shown in fish exposed to water disinfected with sodium hypochlorite and chloride dioxide. The comet assay showed an immediate response, *i.e*. DNA damage that was induced directly in circulating erythrocytes, when genotoxic damage in stem cells of the cephalic kidney is expressed in circulating erythrocytes. The quality of the untreated surface water seems to be the most important parameter for the long-term DNA damage in circulating erythrocytes. Siu *et al*. (2004) [45] exposed Green-lipped mussels (*Perna viridis*) to water-borne benzo[a] pyrene (B[a]P) for 12 days and monitored the relative levels of DNA strand breakage in mussel haemocytes. The increase in the proportion of strand breakage occurred with the increase in B[a]P concentration.

The sensitivity of the widely distributed freshwater bivalve mollusk *Corbicula fluminea* to the DNA-damaging alkylating-agent methylmethanesulfonate (MMS) was studied using comet assay (Rigonato *et al*., 2005) [37]. The results showed that *C. fluminea* is an optimal bioindicator for the determination genotoxic contaminants in aquatic environments. Ateeq *et al*. (2005) [2] evaluated the genotoxic potential of two widely used herbicides; 2,4-dichlorophenoxyacetic acid (2,4-D) and 2-chloro-2,6-diethyl-N-(butoxymethyl) acetanilide (butachlor) in erythrocytes of freshwater catfish, *Clariasbatra chus*. The results of comet assay showed a significant increase in comet tail length indicating DNA damage was observed at all concentrations of both the herbicides compared to the control. The mean comet tail length showed a concentration-related and time-dependent increase as the maximum tail length recorded at highest concentration and longer duration of 2,4-D (9.59 mm) and butachlor (9.28 mm). This study confirmed that the comet assay applied on the fish erythrocyte is a useful tool in determining potential genotoxicity of water pollutants and might be appropriate as a part of a monitoring program.

Kopjar *et al*. (2008) [26] assessed the DNA integrity in erythrocytes using the alkaline comet assay to study the impacts of water pollution on Balkan loaches (*Cobitis elongata*) inhabiting the Sava and Kupa rivers. The results suggested a genotoxicity of the aquatic environment in the Sava River and demonstrated significantly lower levels of DNA damage in fish captured from the Kupa River. The African catfish *Clarias gariepinus* on exposure to different concentrations of lead nitrate showed DNA strand breakage using comet assay (Osman *et al.*, 2008) [31]. A strong correlation between lead concentration, time of exposure, and DNA strand breakage was observed. Simoniello *et al*. (2009) [43] evaluated DNA damage using alkaline comet assay applied on erythrocytes after *in vivo* exposure of *Prochiloduslineatus* to different concentrations of Cypermethrin as a probable chemical mutagen. The results revealed a significantly higher level of DNA damage at all concentrations of Cypermethrin in comparison with the control. They have standardized the technique for one of the most common native fish species that will be useful for biomonitoring genotoxicity in polluted waters of the region.

Klobucar *et al*. (2010) [24] assessed the genotoxicity of freshwaters using caged carp (*Cyprinus carpio*). The comet assay was used to detect genotoxicity due to multiple sources of pollution in the peripheral blood of a native fish species (*Hyphessobrycon luetkenii*) (Scalon *et al.,* 2010) [40]. Water samples were collected seasonally from three sampling sites and the fish were assessed under laboratory conditions. The results indicated that the Sinos River was contaminated with substances that are genotoxic to fish, including the waters near the river spring. Boettcher *et al*. (2010) [8] exposed rainbow-trout liver (RTL-W1) cells *in vitro* to acetone extracts of sediments collected at 10 selected sites along the upper Danube River and analyzed in the comet assay in order to correlate the genotoxic potential of sediments with genetic damage in fish. This *in vitro* bioassay showed excellent correlation, indicating comparability of genotoxic potentials *in vitro*. With respect to the ecological status of the Danube river, the results overall indicate a moderate to severe genotoxic potential with a highly differential localization. Fedato *et al*. (2010) [17] performed the comet assay on hemocytes and gill cells of *Corbicula fluminea* on its exposure to gasoline. The results revealed DNA damage in hemocytes and gill cells.

Osman *et al*. (2012) [32] monitored in detail the genotoxic potential of the river Nile by performing comet assay to the blood of fish collected from both downstream and upstream sites. The damage was significantly higher in peripheral blood erythrocytes of Nile tilapia and African catfish collected from heavily polluted areas. DNA damage in erythrocytes from Nile tilapia (*Oreochromis niloticus niloticus*) and African catfish (*Clarias gariepinus*) was shown to be related to contaminant levels in downstream areas. From all the studies mentioned above, the comet assay has proven to be a useful tool for investigating the genotoxic effects of *in vitro* and *in vivo* chemical exposure to aquatic invertebrate and fishes.

4.2 Micronuclei and Nuclear Lesions Tests

Micronucleus test was proposed independently by Heddle (1973) [20] and Schmid (1975) [41] as an alternative and simpler approach to assess chromosome damage *in vivo*. The micronuclei (MN) test is one of the most widely applied methods since it allows a convenient and easy application, in particular in genotoxicological studies with aquatic organisms. Micronuclei arise from chromosome fragments or whole chromosomes that lag at cell division due to lack of centromere, damage in centromere region, or defect in cytokinesis. These fragments left behind are incorporated in the secondary nuclei, called micronuclei (MN). Micronuclei formation can occur in any of the dividing cells of any species. The count of micronuclei has served as an index of chromosome breaks and mitotic spindle apparatus dysfunction (Ayllon and Garcia, 2000) [3].

The MN test presents several advantages over other cytogenetic studies such as sister chromatid exchanges or

chromosome aberrations, which are time-consuming and not very effective due to the relatively large number of small chromosomes of many aquatic animal species. Nuclear lesions (NL) are genotoxic analogues of MN that may also be the result of the action of a genotoxic agent. The micronucleus (MN) test, one of most frequently used in environmental genotoxicity studies, has served as an index of cytogenetic damage for over 30 years (Fenech *et al*., 2003) [18]. The micronucleus test is a simple and sensitive assay for "*in situ*, *in vivo* and *in vitro*" evaluation of genotoxic properties in aquatic environment as a part of the biomonitoring programs. The use of Brown trout, *Salmotrutta*, European eel, *Anguilla anguilla*, and European minnow, *Phoxinus phoxinus*, as *in situ* pollution bioindicators were evaluated by Rodriguez-Cea *et al*. (2003) [38] using the micronucleus test in renal erythrocytes. *In situ* surveys of wild freshwater ecosystems with different levels of pollution showed that micronuclei are induced in brown trout inhabiting polluted sites.

The micronucleus test is considered to be one of the most efficient approaches for the assessment of exposure to contaminants (Fenech *et al.,* 2003) [18]. Çavas and Ergene-Gozukara (2005) [12] evaluated the genotoxic effects of effluents from a petroleum refinery and a chromium processing plant in *Oreochromis niloticus* using the micronucleus test. The results showed that both effluents had genotoxic potential. On the other hand, the level of genetic damage induced by petroleum refinery effluent was considerably higher than that of chromium processing plant effluent. The results further indicated that nuclear abnormalities other than micronuclei may also be used as indicators of genotoxic damage.

Barsiene *et al*. (2006) [7] studied the genotoxicity of crude oil processed from the Statfjord B platform in the North Sea in gills of blue mussels (*Mytilus edulis*). The elevation of micronuclei increased progressively with increase in the duration of exposure. Barsiene and co-workers (2006) [7] assessed the genotoxicity, cytotoxicity and immunotoxicity potential of treated wastewater effluents (TWE) discharged from the Vilnius Wastewater Treatment Plant. The results revealed a significant increase of micronuclei in exposed specimens of *O. mykiss*. The frequency of micronuclei (MN) in gill cells of blue mussels (*Mytilus edulis*), peripheral blood of flounder (*Platychthys flesus*) and wrasse (*Symphodus melops*) which were collected from the Goteborg area of the North Sea (Barsiene *et al*., 2006) [7]. Ten times higher frequencies of micronuclei were found in flounder collected from the contaminated zone at Jordhammarvik and eight times higher micronuclei levels were recorded in fish from Nya Alvsborg, the inner part of the Göteborgharbour. In mussels, the highest response was established in specimens inhabiting the Ringhals zone.

Pavlica *et al*. (2008) [35] determined the frequency of micronuclei (MN) in haemocytes of native mussels, *Mytilus galloprovincialis*, collected along the Eastern Adriatic coast in Croatia. The highest frequency of MN was observed in summer and the results pointed out that seasonal changes were observed only at polluted sites, most probably caused by seasonality of pollution as well as by interaction between contaminants and higher metabolic and filtration rates in mussels, resulting in higher values of cytogenetic damage. Rybakovas *et al*. (2009) [39] analyzed Micronuclei (MN), nuclear buds (NB) and fragmented-apoptotic cells (FA) in mature peripheral blood and immature cephalic kidney erythrocytes of flounder (*Platichthys flesus*), dab (*Limanda limanda*) and cod (*Gadus morhua*) collected from the Baltic Sea and the North Sea. The highest levels of environmental genotoxicity were observed in flatfishes from areas close to oil and gas platforms in the North Sea and in zones related to the extensive shipping and potentially influenced by contamination from large European Rivers (Elbe, Vistula, Oder).

In vivo and *in vitro* exposures were used to assess the genotoxicity of lead (Pb) in *Prochilodus lineatus*. The comet assay using blood, liver and gill cells, occurrence of micronuclei (MN) and other erythrocytic nuclear abnormalities (ENA) were used to assess the genotoxic potential of lead in vivo. The results of the comet assay after in vivo toxicity proved lead to be genotoxic. MN frequency did not increase after Pb exposures but the frequency of the other ENA, such as kidney-shaped nuclei, segmented nuclei and lobed nuclei showed a significant increase indicating that ENA is a better biomarker for Pb exposure than MN alone after short-term exposures. The results of the comet assay performed with erythrocytes *in vitro* exposed to lead confirmed its genotoxic effect and showed that DNA damage increased with increasing exposure time. Moreover, the NRRA clearly indicated that Pb induces a destabilization of the lysosomal membrane. These results demonstrate the potential genotoxicity and cytotoxicity of lead after acute exposures (Monteiro *et al.,* 2011).

Obiakor *et al*. (2012) [29] explored the biomonitoring potentials of micronucleus test on waterborne pollutants. It then considers the interplay between such micronucleus formations and certain widespread environmental pollutants. In the biomonitoring studies, Osman *et al*. (2011) [33] detected six nuclear lesions NL beside micronuclei (MN) in the blood of Nile tilapia *Oreochromis niloticus niloticus* and African catfish *Clarias gariepinus* collected from the whole course of the rive Nile. Higher incidences of MN and NL were found in the blood of fish collected from the heavily polluted areas. The simple progressive increase of MN and NL frequencies along a water course found for the River Nile is a good example that MN counts are associated, in the wild, with pollution levels expected when a gradient of pollution exists along the water course. The results confirmed the usefulness of the erythrocyte MN and NL as powerful monitoring tools for detecting genotoxic agents in fresh water environment. Omar *et al.* (2012) [49] evaluated the genotoxic effects of toxic metals in cultured and wild Nile tilapia, *Oreochromis niloticus* and mullet, *Mugil cephalus* collected from polluted and non-polluted reference site. Heavy-metal concentrations (Cu2+, Zn2+, Pb2+, Fe2+ and Mn2+) in water and sediment samples were recorded. Genotoxicity assays such as the micronucleus (MN) test, DNA-fragmentation assay and other nuclear abnormalities (NA) were assessed. A significant decrease in CF values associated with a significant elevation in MN and NA frequencies was observed in fish collected from the polluted areas. Moreover, mixed smearing and laddering of DNA fragments in gills and liver samples of both fish species collected from the polluted areas indicate an intricate pollution condition. Similar results were observed on conducting a study by Yazici and Sisiman (2014) [52] in chub, *Leuciscus cephalus*, and transcaucasian barb, *Capoeta capoeta*, collected from contaminated site of the Karasu River.

Jesus *et al*., 2016 [23] evaluated the incidence of nuclear abnormalities (NA) in four fish species from an impacted

river in Northeastern Brazil, characterized by accumulation of heavy metals and organic sewage. Two carnivores (*Serrasalmus brandtii* and *Hoplias malabaricus*) and two omnivore species (*Oreochromis niloticus* and *Geophagus brasiliensis*), used as food sources by local populations, were collected during the dry and the rainy season along Contas River basin. Nuclear abnormalities (bulbs, binuclei, lobes, micronuclei, notches, and vacuoles) were reported in all fish samples, with high occurrence in *S. brandtii* and *H. malabaricus*, species commonly found in local fish markets.

4.3 Oxidative stress

Lushchak *et al*. (2009) [30] conducted a study to evaluate the effects of Cr3+ exposure on goldfish by analyzing parameters of oxidative stress and antioxidant defense in liver and kidney of fish. Cr3+ exposure did not alter two parameters of oxidative stress—protein carbonyl content and lipid peroxide concentrations in either organ. However, Cr3+ exposure did decrease total glutathione concentration in liver by 34–69% and in kidney to 36–49% of the respective control values. Catalase activity was not significantly affected by 1–5 mg/l Cr3+ but was reduced by 57 and 42% in liver and kidney, respectively. Chromium exposure also reduced the activity of glutathione-S-transferase in both organs by 17–50% but did not affect glutathione reductase or glucose-6-phosphate dehydrogenase activities. A comparison of Cr3+ effects on liver and kidney metabolism indicated that the trivalent ion induces stronger oxidative stress than Cr6+ at the same concentrations.

Velma and Tchounwou (2011) hypothesized that OS plays a key role in chromium induced toxicity in goldfish leading to the production of reactive oxygen species (ROS) such as O_2, H_2O_2, OH and subsequent modulation of the activities of antioxidant enzymes such as glutathione proxidase (GPx), catalase (CAT), metallothioneins (MT), superoxide dismutase (SOD), genotoxicity and histopathology. The result clearly showed that the fish experienced OS as characterized by significant modulation of enzyme activities, induction of DNA damage and microscopic morphological changes in the liver and kidney. In both kidney and liver tissues, CAT activity was decreased whereas SOD activity and hydroperoxide levels were increased. In addition, GPx activity also increased significantly in higher test concentrations, especially in the kidney. MT induction and DNA damage were observed in both tissues in a concentration dependent manner.

Ameur *et al.* (2012) [1] evaluated the impact of environmental contaminants on oxidative stress, genotoxic and histopathologic biomarkers in liver of mullet (*Mugil cephalus*) and sea bass (*Dicentrarchus labrax*) collected from a polluted coastal lagoon (Bizerte Lagoon) in comparison to a reference site (the Mediterranean Sea). Antioxidant enzyme activities were lower in fish from the polluted site compared with fish from the reference site, suggesting deficiency of the antioxidant system to compensate for oxidative stress. DNA damage was higher in both fish species from the contaminated site indicating genotoxic effects.

5. Conclusion

Genotoxicity describes the property of chemical agents that damages the genetic information within a cell causing mutations in genetics. Genotoxins changes the chromosomal structures, forming rings, breaks, joins etc. These can be identified by the chromosomal aberration tests. Any drug which prevents the genotoxic effect of clastogenic agents are said to be anti-clastogenic or antimutagenic agent. DNA repair mechanisms, metabolism of harmful chemical clastogens and use of anticancer drugs are the major treatments for genotoxicity. The drugs which are used for treatment of genotoxicity and also act as anti cancer agents are alkylating agents, intercalating agents and enzyme inhibitors.

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