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Nuclear Abnormalities in the Blood Erythrocytes of African Cat Fish, *Clarias gariepinus* Exposed to Aluminium Chloride

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Abstract: Aluminum (Al) is the most abundant metal and the third-most common chemical element in the earth's crust. Industrialization, natural process like mining, increased usage of Al for domestic, construction, transportation facilities, etc lead to the wide dispersal of Al throughout the environment. Soil acidification increases the mobilisation of Aluminium to surface waters. When the concentration of Aluminium elevates in aquatic bodies, this metal becomes more soluble and becomes potentially toxic to fishes. Aluminium is recognized as the main toxicant causing mortality of fishes and hence it remains as a major environmental problem. Generally metal genotoxins produce erythrocytic nuclear abnormalities (ENAs), which were considered as indicators of genotoxic damage in fishes. In the present study, juveniles of African Cat fish, *Clarias gariepinus* were exposed to different sub lethal concentrations (50, 100, 150 & 200 ppm) of Aluminium Chloride ($AlCl_3$) for 96 hrs to investigate the effect of $AlCl_3$ on the nucleus of erythrocytes. The results showed cellular as well as nuclear abnormalities such as swollen cells, heamolyzed cells, Binucleated, notched nucleus, Micronucleus, lobed nucleus, blebbed nucleus. Previous studies on Aluminium toxicity in higher vertebrates reveal that Aluminium acts as a genotoxin by breaking the chromosomes or interfering with the formation of mitotic spindles, there by altering the balanced distribution of chromosomes during cellular division. The present investigation also proves the genotoxic effective of Aluminum Chloride, which acts as an aneugenic and the clastogenic chemical capable of inducing chromosomal aberrations in African Cat fish, *C. gariepinus*.

Key words: Aluminium · Clastogenic · Nuclear abnormalities · Genotoxic · Sub lethal

INTRODUCTION

Environmental genotoxins show a very aggressive mode of action and are able to induce DNA damage in organisms even at low levels of exposure [1]. Particularly, metals as genotoxins damage the genetic material of the aquatic organisms and thereby initiate a cascade of impairments at the molecular, cellular, organ level of an organism resulting in impaired metabolism, abnormal development, reduced survival, growth, reproduction potency [2].

Aluminium (Al) is the third most common and abundant metal on earth's crust [3, 4] with the increasing level of Aluminum production at the global level up to 57.6 Million MT in 2016 [5]. The Aluminum based industries liberate hazardous substances during their technological processes and the emission of the effluents result in severe environmental hazards [6]. In addition to industrialization, natural process like mining, increased usage of Al for domestic, construction, transportation facilities, etc lead to the wide dispersal of Al throughout the environment. Soil acidification increases the mobilisation of Aluminium to surface waters [7, 8]. When the concentration of Aluminium elevates in aquatic bodies, this metal becomes more soluble and potentially toxic to freshwater fishes as the pH decreases below 6.0. In acidified waters, Aluminium is recognized as the main toxicant causing mortality of fishes [9]. Hence, Al remains as a major environmental problem [10].

Generally metal genotoxins produce erythrocytic nuclear abnormalities (ENAs), which were considered as indicators of genotoxic damage in fishes [11, 12]. The

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formation of morphological nuclear abnormalities was described first in fish erythrocytes by Carrasco *et al*. [13]. Studies on the genotoxic effects of Aluminum on aquatic invertebrates [14] as well as on human [15, 16, 17] were already reported but research regarding the potential genotoxicity of Aluminium on Cat fish is still lacking. In the present study, an attempt has been made to detect genotoxicity with reference to nuclear abnormalities in the erythrocytes of African Cat fish, *C. garipinus* exposed to Aluminium Chloride.

MATERIALS AND METHODS

Juveniles of *C. gariepinus* measuring 1gx5cm mean weight and length respectively were purchased from AM fish farm, Madurai. They were acclimatized in de-chlorinated water (tap water exposed to air for greater than 24 hours) in 120L capacity plastic trough for 96 hrs [18]. A total number of 50 experimental fishes were randomly divided into five equal groups, each containing 10 fishes. The first group served as a control. The other four groups were subjected to sublethal concentration viz 50, 100, 150 and 200 ppm (mg/L) of $AlCl_3$. Each treatment had three replicates. Troughs were covered with mosquito nets to prevent fish from jumping out. At the end of 96 hrs exposure, fishes were randomly sampled from each group. Blood samples were collected by heart puncture using disposable sterile syringe fitted with an insulin needle.

Immediately after sampling, blood was smeared on clean glass slides, dried overnight, fixed with methanol for 10 min and stained with Giemsa (5%) [19]. These prepared slides were examined under an Olympus CH20*i* optical microscope. Micronuclei and other nuclear abnormalities were identified using the criteria described by Fenech *et al*. [20].

RESULT

Blood cell morphologic study on African Cat fishes exposed to sub lethal concentrations of Aluminium Chloride reveals nuclear abnormalities such as swollen cells (Fig. 1b), heamolyzed cells (Fig. 1c), Binucleated (Fig. 1d), notched (Fig. 2a), Micronucleus (Fig. 2b), lobed (Fig. 2c), blebbed (Fig. 2d), Fragmented nucleus (Fig. 2 e) and Polar nuclei (Fig. 2f) respectively when compared to control (Fig. 1a). Thus the present study proves the role of $AlCl_3$ as a metal genotoxin, responsible for the occurrence of these nuclear abnormalities.

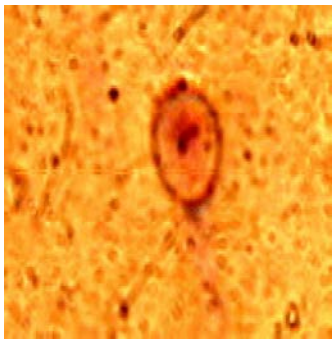

Fig. 1a: Control

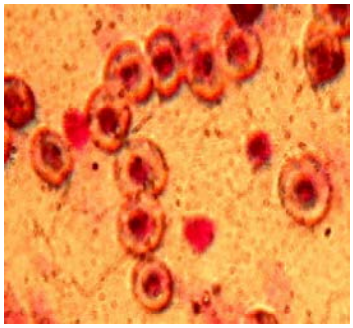

Fig. 1b: Swollen cells

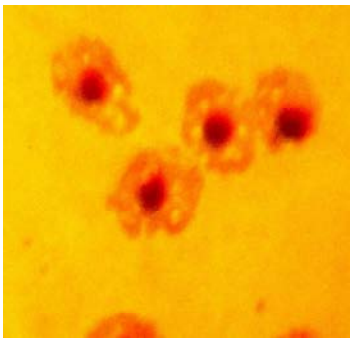

Fig. 1c: Heamolyzed cells

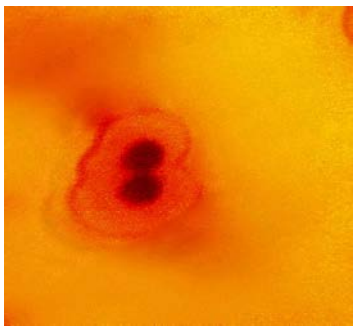

Fig. 1d: Binucleated

Fig. 1: Cell abnormalities in the erythrocytes of African Cat fish, *Clarias gariepinus* exposed to Aluminium Chloride

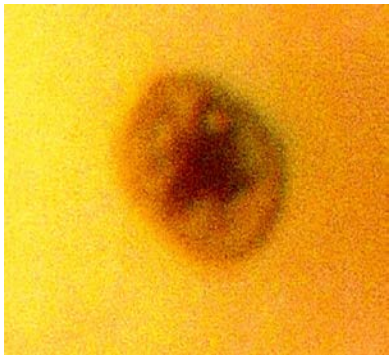

Fig. 2a: Notched Nucleus

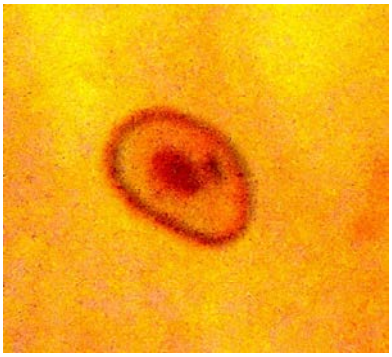

Fig. 2b: Micronucleus

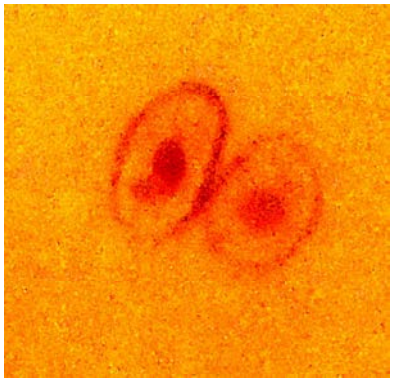

Fig. 2c: Lobed Nucleus

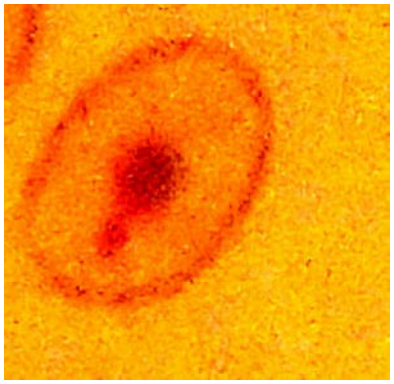

Fig. 2d: Blebbed Nucleus

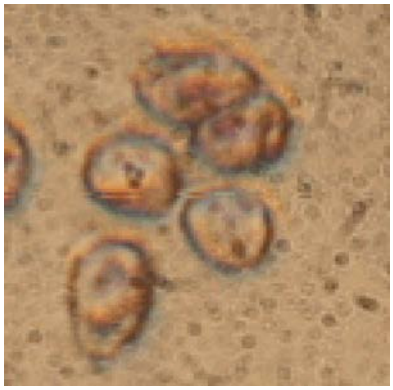

Fig. 2e: Fragmented nucleus

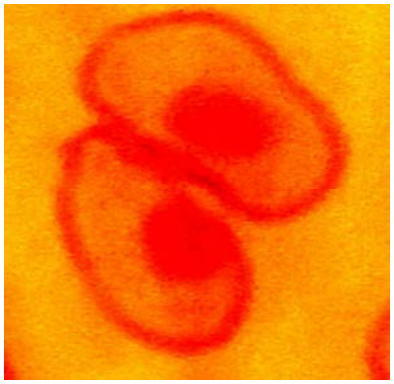

Fig. 2f: Polar nuclei

Fig. 2: Nuclear abnormalities in the erythrocytes of African Cat fish, *Clarias gariepinus* exposed to Aluminium Chloride

DISCUSSION

In the present study, sub lethal concentrations of Aluminium Chloride induces nuclear abnormalities such as swollen cells, heamolyzed cells , notched nucleus, binucleated cell, micronucleus, lobed and blebbed nucleus. According to Larsson *et al*. [21], the swelling of the RBC is as a result of hypoxic condition or osmotic stress or macrocytic anaemia in fishes exposed to metal pollution. Tort and Torres, [22] also observed erythrocyte swelling in the dog fish, *Scyliorhinus canicula* exposed to copper and suggested that swelling of erythrocyte may be a response of the fish against heavy metal pollution. Bhagwant and Bhikajee [23] reported

exposure of *Oreochromis* hybrid to sublethal concentration of Aluminium results in swelling of RBC, which is considered as an obvious sign of macrocytic anaemia. They also observed a significant decrease in the total RBC count, which could be due to the destruction of the erythrocytes. These deformed erythrocytes are considered as obvious signs of anemia [24].

A notched nucleus presents an appreciable depth into a nucleus that does not contain nuclear material [25]. Cavas and Ergene-Gozukara [26] suggested that notch formation in erythrocytes causes nuclear abnormality that leads to genotoxic damage. Notch nucleated and binucleated cells are indicators of abnormal cell divisions [27]. The formation of binucleated cells after exposure to higher concentrations of contaminants could be suspected as a result of alterations in chromosome segregation and cytokinesis. Fernandes *et al*. [28] reported that nuclear abnormalities such as notched or binucleated cells, which may be associated with aneuploidy, might have originated as a result of a failure of tubiline and the abnormal cells originate due to the difficulty of forming mitotic fuses caused by aneugenic actions of chemical. Binucleation affects the process of cell division which results in genetic imbalance that leads to carcinogenesis [29]. As the concentration of the genotoxin increases, there will be more damage to the DNA and more quantity of micronuclei will be formed in a binucleated cell [30, 31]. Micronuclei are very small fragments of chromatin material which are developed from broken section of chromosome or from the chromosomes that could not be incorporated into daughter nuclei [32]. MN is formed by the condensation of whole chromosomes or fragmented chromosomes that are not incorporated into the main nucleus during mitosis, due to aneugenic or clastogenic effects [33]. According to Ayllon and Garcia-Vazquez [25], blebbed nuclei present a relatively small evagination of the nuclear envelope, which seemed to contain euchromatin and lobed nuclei are those presenting evagination larger than the blebbed nuclei.

This kind of nuclear abnormalities (notched, blebbed, lobed, micro nucleus and binucleated cells) were also reported in other fish species. Studies in killifish, *Fundulus heteroclitus* showed methyl mercury chloride was found to induce chromosomal aberrations and micronuclei formation [34] and inorganic mercury acts as a teratogen [35]. Jiraungkoorskul *et al*. [36] studied the sub lethal effects of lead, copper and cadmium in inducing nuclear abnormalities in the erythrocytes of *Oreochromis niloticus*, *Poronotus triacanthus* and *Puntius altus* and reported significant increase in the frequency of nuclear abnormalities. Such kind of nuclear abnormalities were also reported by Zhu *et al.* [37] in the erythrocytes of *C. carpio* exposed to copper. Similarly, Safina Kousar and Javed [38] reported that exposure to copper caused for the formation of nuclear abnormalities in the peripheral erythrocytes of *Labeo rohita*, *Cirrhina mrigala*, *Catla catla* and *Ctenopharyngodon idella*. Guner *et al*. [39] reported significantly increased frequency of nuclear abnormalities in the erythrocytes of *G. affinis* due to copper and cadmium toxicity.

Only a few studies were carried out to assess the genotoxic potential of Al on aquatic organisms. Al had been shown to induce chromosomal aberrations in Chromosome G and Balbiani rings of the dipteran *Chironomus riparius* larvae [40]. Studies on erythrocytes of the mosquito fish *Gambusia holbrooki* [41] and lymphocytes of the common carp Cyprinus carpio [42] revealed that Aluminium induces DNA damage. Roy *et al.* [43] found that Al induces chromosomal aberrations in human leucocytes. Migliore *et al*. [44] reported that Al induces micronuclei in human lymphocytes. Thus, mostly the genotoxic and cytotoxic potentials of aluminium have been studied only in vitro on cultured human lymphocytic cell lines [45, 17].

As reported by Banasik *et al*. [45], Al could induce DNA damage via three mechanisms: modification of chromatin structure, induction of reactive oxygen species and liberation of DNase from the lysosomes. The first mechanism was supported by the finding of Bharathi *et al*. [46] that Al can localize in the chromatin region of the nucleus of the exposed cells and bring out a conformation change in the DNA. Oxidative stress during aluminum exposure was attributed to electron leakage, enhanced mitochondrial activity and rapid electron chain activity; consequently, there is increase in ROS production [47, 48]. ROS subsequently disrupts the membrane potential, enhances the permeability of lysosomal membranes [49] and leads release of DNase into the cytoplasm and to its passage into the nucleus, where it could cut DNA. Thus, Aluminium, induces DNA damage, modifies the genes and disturbs cell cycle, which in turn may elicit cytotoxic, mutagenic and carcinogenic alterations. This was supported by the findings of Griffitt *et al.* [50] where they depicted that exposure to $AlCl_3$ resulted in down regulation of genes involved in cell cycle regulation and inhibition of apoptosis.

According to Sivaguru *et al*. [51] Aluminium can modify the structure of tubulin, thereby damage mitotic spindles and induce aneuploidy [52]. Letícia *et al*. [53] found that $AlCl_3$ acts as a genotoxic substance by breaking the chromosomes or interfering with the formation of mitotic spindles, there by altering the balanced distribution of chromosomes during cellular division. Hartwig [54] and Garcia medina *et al*. (2013) reported that Al toxicity also reduces the repair capacity of DNA, which leads to DNA damage, fragmentation of the genetic material and spontaneous occurrence of micronuclei.

CONCLUSION

In the light of the present investigation, it can be concluded that the African Cat fish, *Clarias gariepinus* exposed to sub lethal exposure of Al Cl_3 exhibits nuclear abnormalities such as swollen cells, heamolyzed cells, Binucleated cells, notched nucleus, Micronucleus, lobed nucleus, blebbed nucleus, which proves the effective role of Aluminum Chloride as an aneugenic and the clastogenic chemical capable of inducing chromosomal aberrations in fishes.

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