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SHORT COMMUNICATION

The Effects of Dichloroacetic Acid (DCA) On the Cerebellum of Male Albino Rats

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ABSTRACT
Histological effects of DCA exposure on cerebellum and on its various layers, little research is focused on DCA exposure on histological features with the well organized three cortical cell layers; the outer molecular layer containing stellate and basket cells, the middle purkinje layer with a single layer of large purkinje cells, the inner granular layer in the present study, we assessed the effects of long-term DCA exposure on various layer of cerebellum. DCA was administered for 30 days, 60 days and 90 days orally via cannula, using dose rate 125mg/kg-body weight to albino rats. Twenty Four adult male albino rats weighed between 150-170g were used for this study. They were devided into four groups A, B, C & D of six rats each. The results were compared to control adult rats, given vehicle in identical manner. After 30 days, 60 days and 90 days exposure, the cerebellum was carefully dissected out and quickly fixed in 10% formalin for routine histological study after H & E method. 30 days led to slight reduction in cellular size of the molecular layer (ML) than in granular cell layer (GCL) in cerebellum. The histological result showed cerebellum organization marked distortion at 60 days in granular cell layer (GCL) than in purkinje cell layer (PCL) followed cellular degenerative changes in the cerebellum and distortion of granular cell layer (GCL) (sparse cell distribution) than purkinje cell layer (PCL) in cerebellum at 90 days.
***Key Words**:- Dichloroacetic acid (DCA), Purkinje cell layer (PCL), Granular cell layer (GCL), Molecular cell layer (ML), Cerebellum.*

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INTRODUCTION

DCA is a major disinfection by-product (DBPs). It is used as a topical astringent, fungicide and medicinal disinfectants a test reagent for analytical measurements, to treat lactic acidosis and in the synthesis of organic materials, including pharmaceuticals [1]. It is a colourless to slightly yellow liquid with a pungent odour [2]. Chlorine as a disinfectant the use of chlorine in the treatment of drinking water has virtually eliminated water borne diseases, because chlorine can kill or inactivate most microorganisms commonly found in water. Disinfection is essential to safe guard drinking water; the health risks from disinfection by-products are much less than the risks from consuming water that has not been disinfected. DCA is formed from organic material during water chlorination. The health effects associated with exposure to haloacetic acids will vary with the specific compound. DCA is considered to be a probable carcinogen to humans, based on sufficient evidence in animals and inadequate evidence in humans. Animal's studies have shown links between exposure to DCA and liver tumours in both mice & rats. DCA was found to be more persistent in an aquatic environment.

DCA is neurotoxic in both laboratory animals and humans [3]. DCA produce peripheral neuropathy in rats and dogs reported hindlimb weakness, paralysis, neuropathology, and myelin vacuolization in the brain mostly associated with myelinated axons by DCA. Peripheral neuropathy has recently been shown to be particularly severe in adults receiving DCA as a treatment for the inherited syndrome of

mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes (MELAS); [4] it has been suggested that this may reflect differences in DCA metabolism between children and adults. Several studies have investigated [3] DCA-induced toxicity in animals, but observations have highlighted lesions in the CNS rather than peripheral nerves. In the present study, we characterized a rat model of DCA-induced peripheral neuropathy to investigate the impact of DCA on different cellular components of the PNS and to model the potential age-dependent peripheral neurotoxicity that has been inferred from recent clinical experience [5].

MATERIAL AND METHODS

Animals:- Twenty four adult albino rats were used in the study. They were fed with normal rat chow & water was provided *ad libitum* throughout the duration of the experiment. The rats were weighed using the beam balance and the weights were ascertained to be between 150-170g before the commencement of the experiment. The animals were devided into four groups (A, B, C & D). Group-D was control and groups – A, B & C were treated and six animals in each groups.

DCA administration:- The rats in the treatment groups-A, B & C were given 125mg/kg-body weight dose of DCA with orally. The control group-D was fed with normally rat chow and pellets without DCA for 30 days, 60 days and 90 days. The rats were sacrificed after 30 days, 60 days and 90 days of the experiment. The brain quickly dissected out and fixed in 10% formalin for routine histological techniques.

Histological study:- The tissue were dehydrated in an ascending grade of alcohol (ethanol), cleared in xylene and embedded in paraffin wax. Serial sections of 8 micron thick were obtained using a rotatory microtome. The deparaffinized sections were stained routinely with H & E. Photomicrographs of the designed sections were made for further observations [6].

RESULTS

The control sections of the cerebellum showed normal histological features with the well organized three cortical cell layers; photomicrograph of cerebellum of Albino rats of control group showing normal histological features with the molecular layer (ML), large purkinje cells (PCL), and the dense layer of granular cell layer (GCL) (Fig-1 & 2). The treated sections of the cerebellum showed some histological changes that were at variance with those obtained in the control. 30 days led to slight reduction in cellular size of the molecular layer (ML) than in granular cell layer (GCL) in cerebellum (Fig-3 & 4). The expose DCA (125mg/kg b.w.) cerebellum organization marked distortion at 60 days in granular cell layer (GCL) than in purkinje cell layer (PCL) followed cellular degenerative changes in the cerebellum (Fig-5 & 6). The DCA (125mg/kg b.w.) treated rat histology registered distortion of granular cell layer (GCL) (sparse cell disribution) than purkinje cell layer (PCL) in cerebellum at 90 days (Fig-7 & 8).

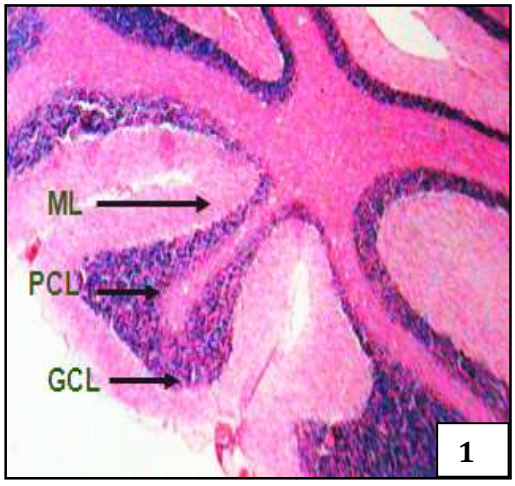

Fig-1 40X H & E CONTROL CEREBELLUM

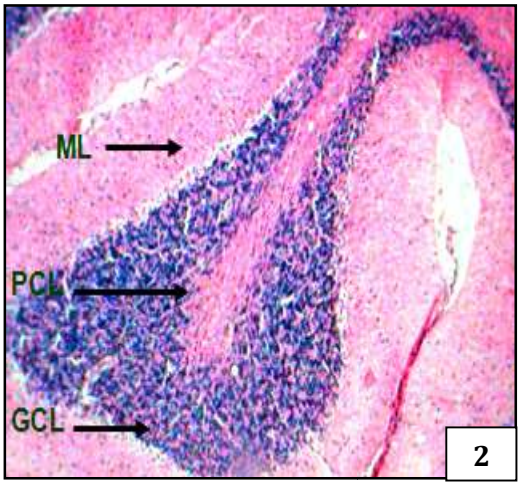

Fig-2 100X H & E CONTROL CEREBELLUM

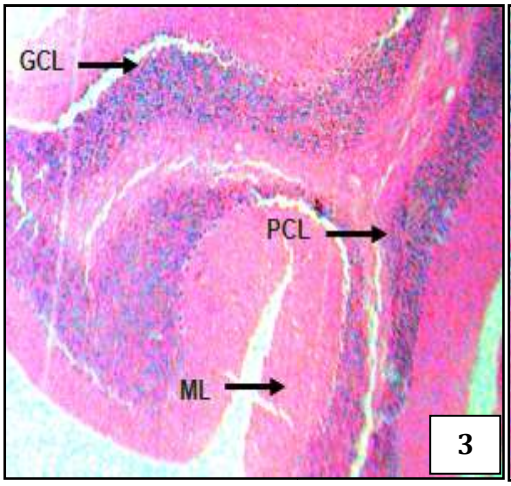

Fig-3 40X H & E 30-DAYS CEREBELLUM

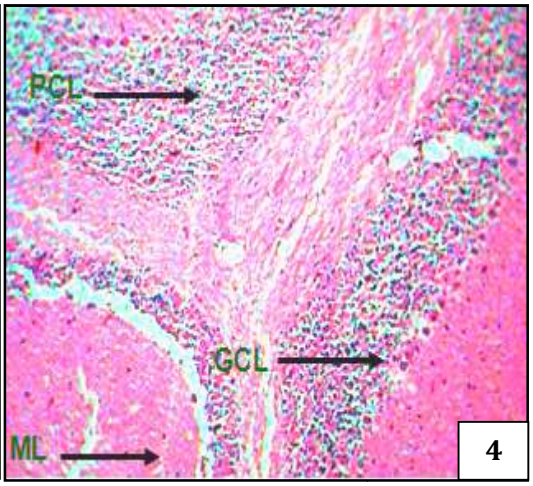

Fig-4 100X H & E 30-DAYS CEREBELLUM

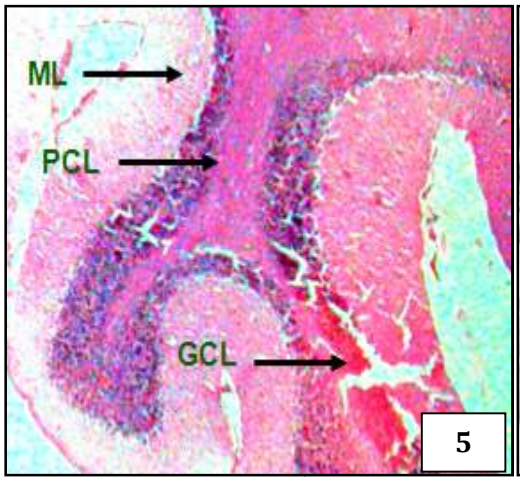

Fig-5 40X H & E 60-DAYS CEREBELLUM

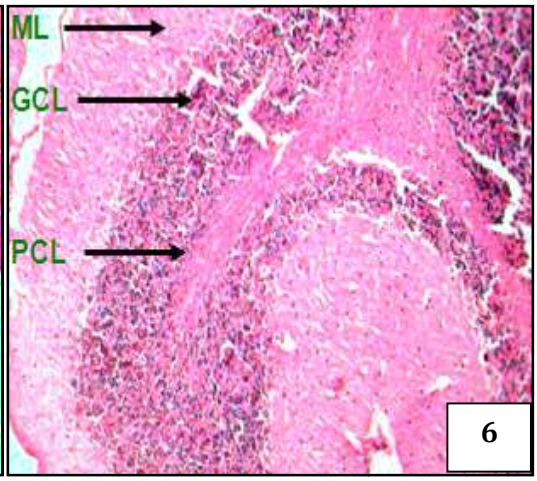

Fig-6 100X H & E 60-DAYS CEREBELLUM

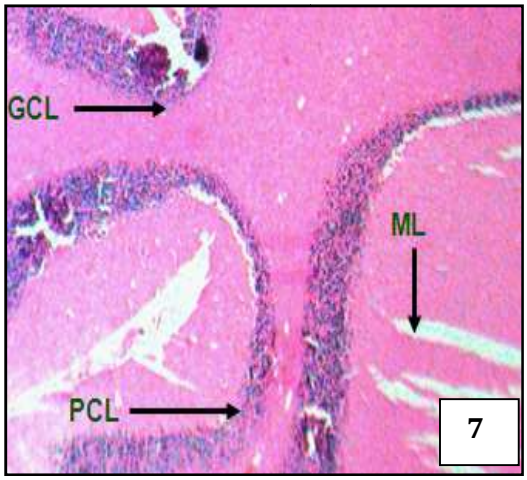

Fig-7 40X H & E 90-DAYS CEREBELLUM

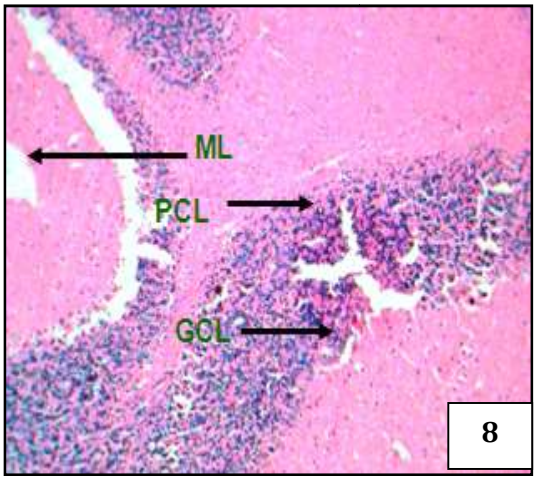

Fig-8 100X H & E 90-DAYS CEREBELLUM

Fig- (1 & 2) Photograph representing the transverse sections of cerebellum of albino rat **(control group). (H & E 40X & 100X)**

Fig- (3 & 4) The photomicrograph is representing the transverse section of cerebellum of albino rat after dosing 125mg/kg-bw DCA treated for **30 days**. **(H & E 40X & 100X)**

Fig- (5 & 6) Photograph representing the transverse sections of cerebellum of albino rat after dosing 125mg/kg-bw DCA for **60 days**. **(H & E 40X & 100X)**

Fig- (7 & 8) Photograph representing the transverse sections of cerebellum of albino rat after dosing 125mg/kg-bw DCA for **90 days**. **(H & E 40X & 100X)**

DISCUSSION

The result (H & E) reactions showed some cellular disruption & degenerative changes in purkinje & granular cell layer of the cerebellum in the treatment group compared to the control sections. The toxic effects of DCA on the cerebellum observed in this experiment may underline the possible effects already reported [7].

Eweka and Om'Iniabohs [8] explore that monosodium glutamate (MSG) was administered to adult Wister rats at the doses of 3g & 6g for 14 days. They observed that disruption of the purkinje and granular layers, sparse granular cell distribution, cellular degenerative changes in the granular layer at 6g of MSG.

Ghimire et al. [9] pragmatic that 20.0% (v/v) alcohol was given orally to female albino rats for two week. They found that diameter of purkinje cells, width of molecular and granular layers decreased in the cerebellum.

Tewari et al. [10] investigated orally administered nicotine impact on male rats at the doses of 5mg/day, 10mg/day for 60 days. They reported significant loss of white matter of cerebellum and odema and cytoplasmic vacuolation in white matter in treated group.

Eluwa et al. [11] studied the aqueous extract *Rauwolfia vomitoria* root bark was on male Wister rats at the doses of 600mg/kg and 500mg/kg b.w. for 7 days. After seven days they observed that slight reduction in cellular sizes in the molecular and purkinje layers, distortions in purkinje layer and granular layer at 600mg/kg treated group and the molecular and purkinje layer appeared normal, slight reduction in purkinje cell size and distortions in the granular cell layer at 500mg/kg treated group.

Dare et al. [12] studied the grapefruit extract (Citrus paradisi) on male Wistar rat for 15 days. The grapefruit juice 0.6ml/g bw/day, 0.8ml/g bw/day and 1.0ml/g bw/day was administered for 15 days to male wistar rat. After treatment they reported that the doses 0.8 and 1.0ml/g bw/day showed cellular degeneration and atrophy thus leading to a decrease in number of cells in the granular and purkinje layers respectively. The dose 0.6ml/g bw/day showed a normal cytoarchitecture of the cerebellum with a slight increase in number of granule cells in the granular layer.

Ramezani et al. [13] administered ethanol to rat at a dose of 6g/kg for 4 to 5 days. After treatment they observed sparse, shrunken and irregularly shaped in the purkinje cells. The purkinje cell layers showed a disconnected pattern, with a wide gap between the cells. Trivedi et al. [14] administered sodium fluoride (NaF) (6mg and 12mg NaF/kg bw/day, respectively) to albino mice for 30 days. After 30 days they reported that NaF treatment induced degenerative changes pycnotic nuclei, fatty infiltration and chromatolysis in cereberal hemisphere (CH), cerebellum (CB) and medulla oblongata (MO) at low and high doses. Rawi et al. [15] Orally administered acrylamide (15mg/kg/b.w.) to male rat for 28 days and reported vacuolization in cerebrum & cerebellum of male rat.

Finally, in summary the result of this study demonstrated that DCA caused neurotoxicity as indicated by histological changes in the cerebellum of brain.

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