Effect of exposure to cadmium on the hippocampus in adult albino rat and the possible role of L-carnitine

Faten Y. Mahmoud, Ashraf H. Abd El-Hakim, Ayman S. El Deen Amer, Mariam W. Fidal

Department of Human Anatomy and Embryology, Faculty of Medicine, Assiut University, Assiut, Egypt

Correspondence to Marian W. Fidal, MSC, Department of Human Anatomy and Embryology, Faculty of Medicine, Assiut University, Assiut, Egypt
Tel: +20 1066795671;
e-mail: mrmrmrmr466@yahoo.com

Received 30 July 2018
Accepted 10 September 2018

Journal of Current Medical Research and Practice
September-December 2019, 4:240–250

Background
The hippocampus is an important structure for formation of new memories. Cadmium is one of the most toxic agents that can affect hippocampal neurons. L-carnitine is an antioxidant.

Aim of work
To demonstrate the effects of cadmium on principal cells of hippocampus of adult rats and possible protective role of L-carnitine.

Materials and methods
A total of 42 adult rats aged 1 month were subdivided into four subgroups: group I was the control group, which received no treatment. Group II was administered cadmium given at a dose of 4 mg/kg/day for 1 month. Group III (sham control) was administered L-carnitine given at a dose of 200 mg/kg/day for 1 month. Group IV was administered cadmium and L-carnitine given to the rats at the same previous doses and duration. For each group, six rats were used for light microscopic study (gallocyanin chrom alum stain), and six rats were used for electron microscopy (group III studied only by light microscopy). Principal cell count and thickness were measured and statistically analyzed.

Results
Principal cells in group II showed degenerative changes. Morphometric data showed a significant decrease in measured parameters. In group III, the results were similar to those of the control group. In group IV, semithin sections and the ultrastructure of the principal cells showed obvious improvement of cells. Morphometric data also increased compared with those treated with cadmium.

Conclusion
Cadmium induces changes in the structure of the principal cells of the hippocampus in adult rats. L-carnitine plays an important in protection of the hippocampus.

Keywords:
cadmium, hippocampus, L-carnitine

J Curr Med Res Pract 4:240–250

2357-0121

Introduction

The hippocampus plays an important role in the formation of new memories about experienced events [1].

Cadmium is a toxic agent that has many health hazards [2]. Food is the largest source of cadmium exposure through application of phosphate fertilizers [3]. Inhalation is another source of cadmium exposure as it is released in the air during the manufacture of numerous industrial products [4]. Smoking is another important source of cadmium exposure [5]. Cadmium can cross an intact blood barrier [6].

L-carnitine is an antioxidant that can cross an intact blood–brain barrier [7].

Materials and methods

The experiments were performed at the Human Anatomy and Embryology Department of Assiut University, Faculty of Medicine.

Drugs used in this experiment were as follows: cadmium chloride was dissolved in water and was given orally (4 mg/kg) [8]. The dose is considered sublethal [9]. L-carnitine (200 mg/kg/day) was given orally [10]. A total of 42 adult male rats were subdivided into four subgroups: group I was the control group (12 rats), which received no treatment.

Group II was administered cadmium (12 rats). Cadmium was given to the rats from the age of 30 days and continued daily till the age of 60 days. Group III was administered L-carnitine (sham control) (six rats). L-carnitine was given to the rats from the age of 30 days and continued daily till the age of 60 rats.

Group IV was administered cadmium + L-carnitine (12 rats). Drugs were given as previously described.

Animals were anesthetized by halothane and killed by cervical decapitation. Six rats were used for light microscopic study in each group (gallocyanin chrom alum stain). Moreover, six rats were used in each group for electron microscopy (for group III, only light microscopy was used).

Morphometric studies

In this work, estimation of thickness of the granular cell layer of the dentate gyrus and pyramidal cell layer of CA1 and CA3 fields was done. The thickness was measured after drawing the actual limit of the layer using the following equation: magnification = length in the picture/actual length. Cell count was done by using the Image Analyzer 'soft imaging system-Olympus company' on an area of 12 360 μm^2 for the granule cells and for the pyramidal cells in the CA3 and CA1 fields. Data were presented as mean ± SD. Statistical analysis of data was tested for significance using one-way analysis of variance and post-hoc test 'Tukey' through the computerized statistical package (Social Package of Social Scientists, IBM Incorp., New York, USA) 'SPSS.' Finally, significance was considered according to the *P* value level of significance: *P* value more than 0.05 → no significance, *P* value less than 0.05 → significant, and *P* value less than 0.01 → highly significant.

Results

Dentate gyrus

In group I: light microscopic study demonstrated that the dentate gyrus appears to be distinguished into three layers: outer molecular layer, intermediate granular cell layer, and inner polymorphic layer (Fig. 1). The granule cells have oval to round nuclei with scanty cytoplasm (Fig. 2). The ultrastructural study shows that it contains a round euchromatic nucleus with prominent nucleolus. The nucleus is surrounded by a thin rim of cytoplasm that contains numerous mitochondria, free ribosomes, and rough endoplasmic reticulum (Fig. 3).

In group II: light microscopic examination of granule cells shows that most of the cells appeared swollen with faint cytoplasm. Some cells have darkly stained nuclei and vacuolated cytoplasm (Fig. 4). Electron microscopic (EM) examination revealed that the nucleus has peripheral chromatin condensation. The cytoplasm appeared to be rarified with the presence of damaged mitochondria and lysosomes. Marked loss of free ribosomes could be revealed (Fig. 5).

In group III: light microscopic examination of the granule cells showed that they appeared nearly similar to those of the control (Fig. 6).

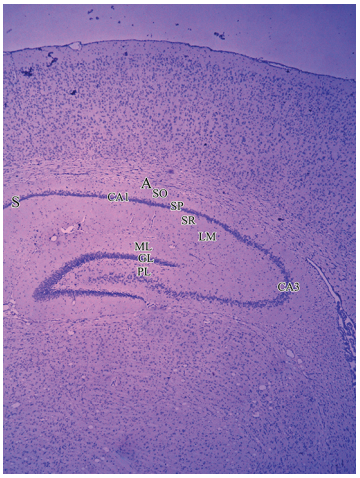
In group IV: light microscopic examination showed the granule cells similar to those of the control, with a few cells having darkly stained nuclei and vacuolated cytoplasm (Fig. 7). EM examination showed that they have round euchromatic nuclei with prominent nucleoli. The cytoplasm had many free ribosomes, mitochondria, some vacuoles, and dilated rough endoplasmic reticulum (Fig. 8).

Morphometric results

Dentate gyrus

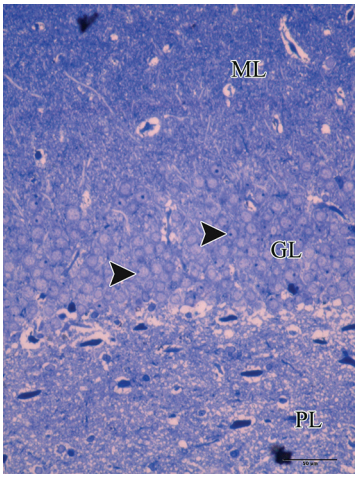
Thickness: there is decrease in the thickness of the granular cell layer of the dentate gyrus in the adult rats treated with cadmium. This decrease in the thickness is statistically highly significant ($P < 0.01$)

Figure 1



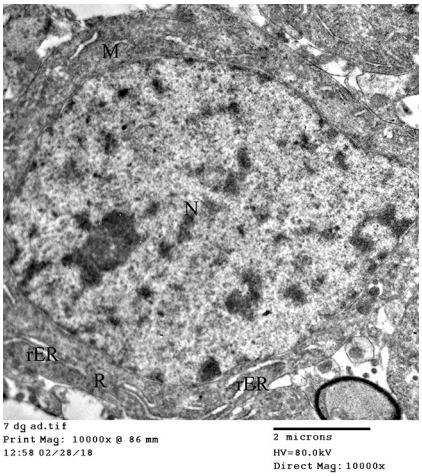
A coronal section of hippocampus of an adult control rat. Molecular layer (ML), granular cell layer (GL), polymorphic layer (PL), alveus (A), stratum oriens (SO), stratum pyramidale (SP), stratum radiatum (SR), stratum lacunosum moleculare (LM), and subiculum (S). Gallocyanin, ×40.

Figure 2



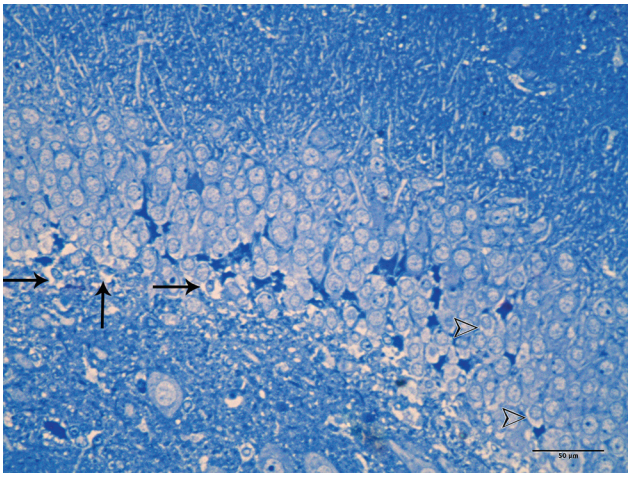
A semithin section of the dentate gyrus of a control adult rat showing the granular cell layer (GL). The granule cells contain large round nuclei (arrow heads). Molecular layer (ML) and polymorphic layer (PL). Toluidine blue, ×400.

Figure 3



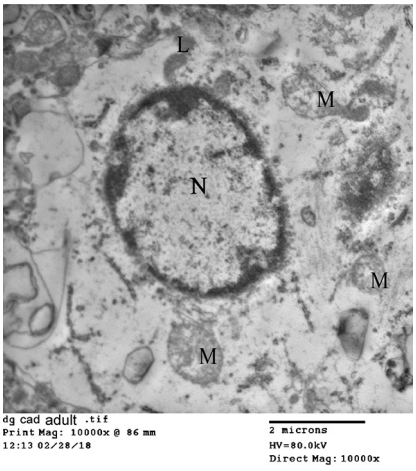
An electron photomicrograph of granule cell of an adult control rat. The cell has a round euchromatic nucleus (N). The nucleus is surrounded with thin rim of cytoplasm containing mitochondria (M), rough endoplasmic reticulum (rER) and free ribosomes (R). ×10 000.

Figure 4



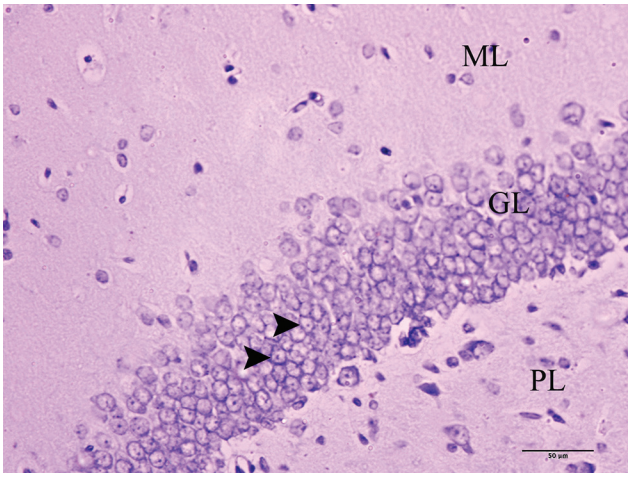
A semithin section of the dentate gyrus of an adult rat treated with cadmium. Many of the granule cells appeared to be swollen with faint cytoplasm (open arrow heads). Some cells have darkly stained nuclei and vacuolated cytoplasm (arrows). Toluidine blue, ×400.

Figure 5



An electron micrograph of granule cell in an adult rat treated with cadmium. The nucleus (N) shows peripheral chromatin condensation. The cytoplasm appears to be rarified with damaged mitochondria (M) and lysosomes (L). ×10 000.

Figure 6



A coronal section of the dentate gyrus of an adult rat treated only with L-carnitine showing the granule in the granular cell layer (GL) contain large round vesicular nuclei (arrow heads). Molecular layer (ML) and polymorphic layer (PL). Gallocyanin, ×400.

(Table 1 and Histogram 1).

There is increase in the thickness of the granular cell layer of the dentate gyrus in the adult rats treated with L-carnitine. This increase in the thickness is statistically insignificant ($P > 0.05$) (Table 1 and Histogram 1).

There is decrease in the thickness of the granular cell layer of the dentate gyrus in the adult rats treated with both cadmium and L-carnitine in comparison with those of the control group. This decrease in the thickness is statistically insignificant ($P > 0.05$). However, the thickness of the granular cell layer of the dentate gyrus of this group in comparison with those treated with cadmium is increased. This increase in thickness is highly significant ($P < 0.01$) (Table 1 and Histogram 1).

Cell count

There is decrease in mean number of the granular cells of the dentate gyrus in adult rats treated with cadmium. This decrease in the mean number is statistically highly significant ($P < 0.01$) (Table 2 and Histogram 2).

There is slight increase in the mean number of the granular cells of the dentate gyrus in the adult rats treated with L-carnitine. This increase in the mean number is statistically insignificant ($P > 0.05$) (Table 2 and Histogram 2).

Table 1 Dentate gyrus thickness at the site of the crest in the albino rats (in μm)

Adult	Control	Cadmium	L-carnitine	Cadmium+L-carnitine
Mean±SD	75.17±6.58	60.61±6.12	76.33±7.64	74.85±5.57
P^1		0.000*	0.873	0.997
P^2			0.000*	0.000*

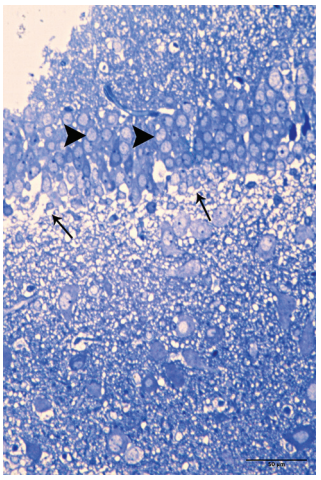
*Significant. Using one-way analysis of variance. *P* value 1 compares the three experimental groups with the control group. *P* value 2 compares L-carnitine group and cadmium+L-carnitine group with cadmium alone group.

Table 2 Dentate gyrus cell count (per an area 12 360 μm²)

Adult	Control	Cadmium	L-carnitine	Cadmium+L-carnitine
Mean±SD	97.36±3.35	78.39±5.37	98.75±2.58	92.33±3.67
P^1		0.000*	0.429	0.000*
P^2			0.000*	0.000*

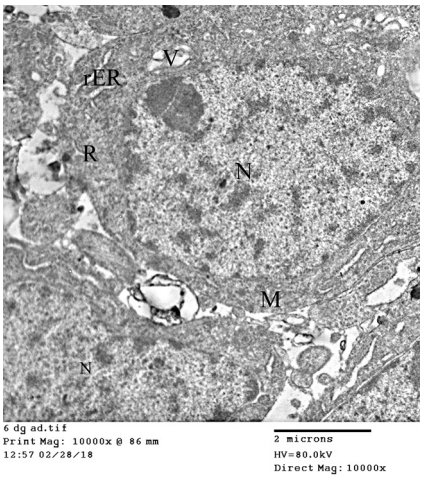
*Significant.

Figure 7



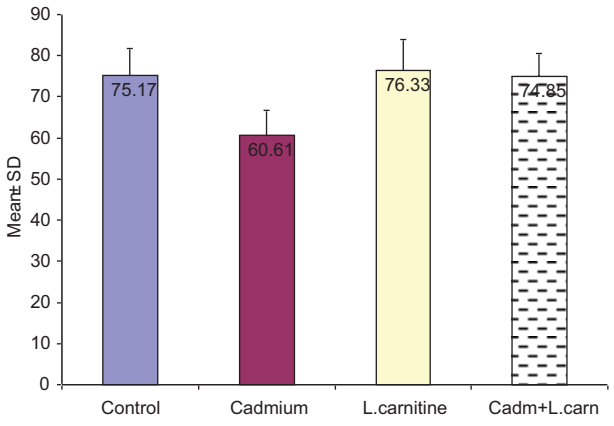
A semithin section of the dentate gyrus of an adult rat treated with both cadmium and L-carnitine showing most of the granule cells similar to those of the control (arrow heads). Some cells have darkly stained nuclei (arrows). Toluidine blue, ×400.

Figure 8



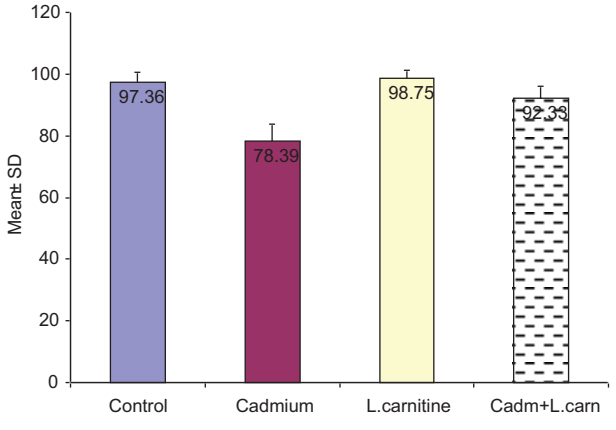
An electron photomicrograph of granule cell of an adult rat treated with both cadmium and L-carnitine. The cell has a round achromatic nucleus. The cytoplasm contains free ribosomes (R), mitochondria (M), some vacuoles (V), and dilated rough endoplasmic reticulum (rER). ×10 000.

Histogram 1



Showing the variation of the granular cell layer thickness in the dentate gyrus (in μm) at the site of the crest of adult albino rat.

Histogram 2



Showing the variation of the granular cell count in the dentate gyrus per an area 12 360 μm² of the studied groups in adult albino rats.

There is decrease in the mean number of the granular cells of the dentate gyrus in the adult rats treated with both cadmium and L-carnitine in comparison with those of the control mothers. This decrease in the mean number is statistically highly significant ($P < 0.01$). However, the mean number of the granular cells of the dentate gyrus of this group in comparison with those of the cadmium-treated adult

rats is increased. This increase in the mean number is statistically highly significant ($P < 0.01$) (Table 2 and Histogram 2).

CA3 region

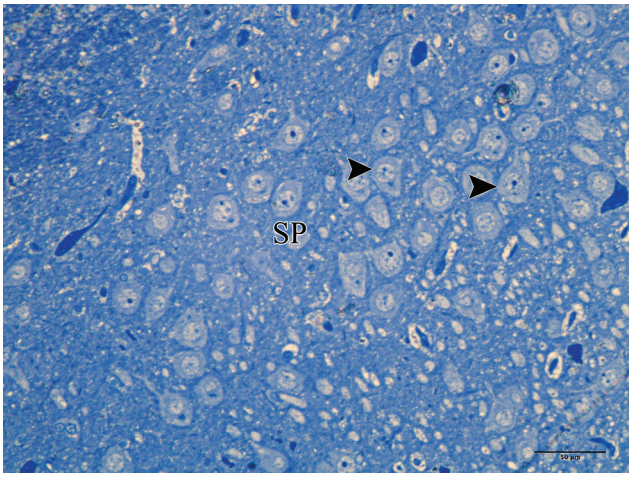
In group I: nissl-stained sections show that the pyramidal cells of the CA3 field have large round nuclei and prominent nucleoli (Fig. 9). The ultrastructural study shows that it has large round nucleus with fine granular chromatin. The surrounding cytoplasm is rich in the rough endoplasmic reticulum, free ribosomes, and mitochondria (Fig. 10).

In group II: examination of the pyramidal cells in CA3 field of the hippocampus showed the presence of many cells with darkly stained nuclei and vacuolated cytoplasm (Fig. 11). EM study revealed that the nucleus had fine dispersed chromatin. The cytoplasm showed marked loss of free ribosomes, presence of dilated rough endoplasmic reticulum, and many lysosomes (Fig. 12).

In group III: light microscopic examination of the pyramidal cells of CA3 field showed that they appeared nearly similar to those of the control (Fig. 13).

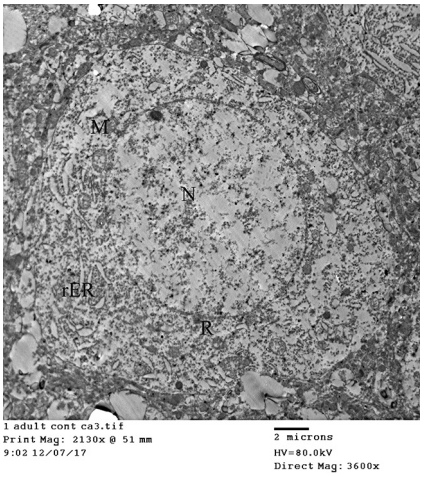
In group IV: examination of the pyramidal cells of CA3 field of the hippocampus showed normal appearance of most cells. A few cells had darkly stained nuclei (Fig. 14). EM study showed that the cells had normal appearance (Fig. 15).

Figure 9



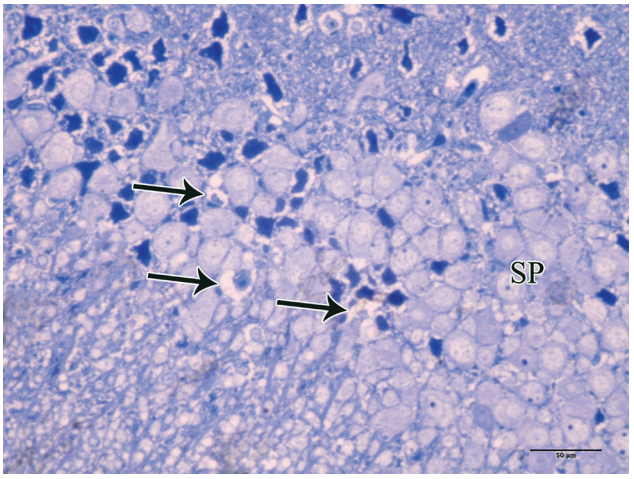
A semithin section of CA3 field of a control adult rat showing the stratum pyramidale (SP). The pyramidal cells are triangular in shape with large round nuclei (arrow heads). Toluidine blue, ×400.

Figure 10



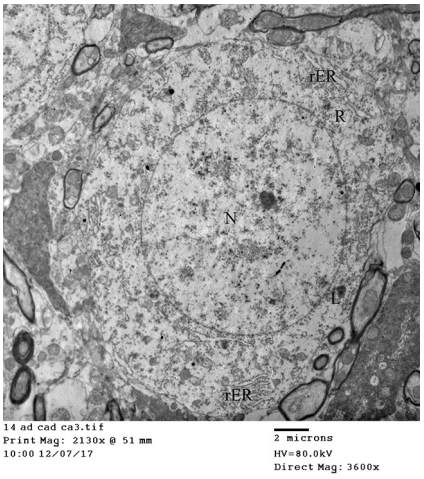
An electron photomicrograph of the CA3 pyramidal cells of an adult control rat showing a large pyramidal cell containing large round nucleus (N) with fine granular chromatin. The cytoplasm contains mitochondria (M), rough endoplasmic reticulum (rER) and ribosomes (R). ×3600.

Figure 11



A semithin section of CA3 field of an adult rat treated with cadmium. Many of the pyramidal cells in the stratum pyramidale (SP) appear to have darkly stained nuclei and vacuolated cytoplasm (arrows). Toluidine blue, ×400.

Figure 12



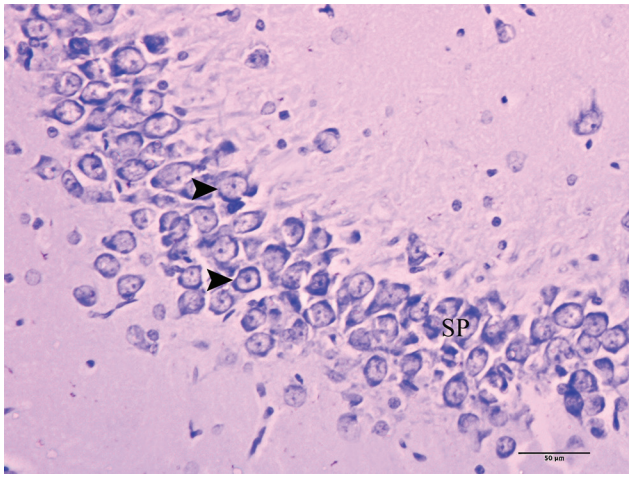
An electron micrograph of CA3 pyramidal cell of adult rat treated with cadmium showing the cytoplasm surrounding the nucleus (N) with marked loss of free ribosomes (R), dilated rough endoplasmic reticulum (rER), and lysosomes (L). ×3600.

Table 3 CA3 thickness in the albino rats (in μm)

Adults	Control	Cadmium	L-carnitine	Cadmium+L-carnitine
Mean±SD	65.08±6.47	51.69±4.18	66.39±2.75	62.56±3.18
P^1		0.000*	0.588	0.073
P^2			0.000*	0.000*

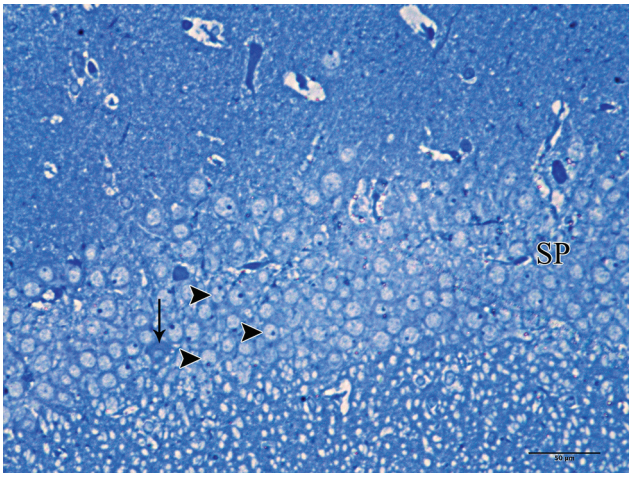
*Significant.

Figure 13



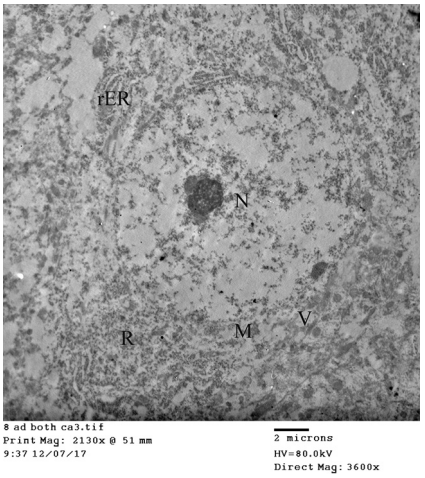
A coronal section of CA3 field of an adult rat treated with L-carnitine showing the stratum pyramidale (SP) with its pyramidal cells contain round vesicular nuclei (arrow heads). Gallocyanin, ×400.

Figure 14



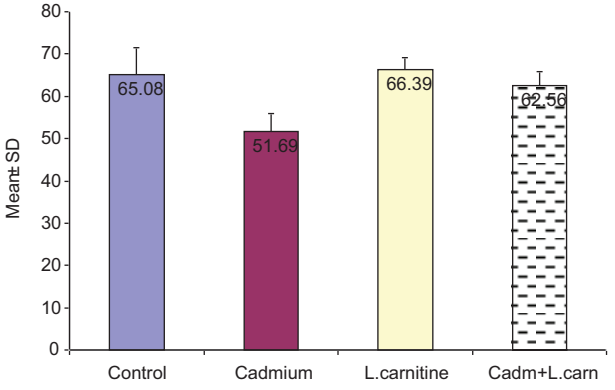
A semithin section of CA3 field of adult rat treated with both cadmium and L-carnitine. It shows normal appearance of most of the pyramidal cells (arrow heads) in the stratum pyramidale (SP). Few cells have darkly stained nuclei (arrow). Toluidine blue, ×400.

Figure 15



An electron photomicrograph of CA3 pyramidal cell of an adult rat treated with cadmium and L-carnitine. It has a rounded nucleus (N) with fine chromatin. The cytoplasm contains mitochondria (M), dilated rough endoplasmic reticulum (rER), ribosomes (R), and vacuoles (V). ×3600.

Histogram 3



Showing the variation of stratum pyramidale thickness in CA3 field (in μm) of the studied groups in adult albino rats.

CA3 field

Thickness: there is decrease in the thickness of the stratum pyramidale of CA3 field in the adult rats treated with cadmium. This decrease in the thickness is statistically highly significant ($P < 0.01$) (Table 3 and Histogram 3).

There is increase in the thickness of the stratum pyramidale of CA3 field in the adult rats treated with L-carnitine. This increase in the thickness is statistically insignificant ($P > 0.05$) (Table 3 and Histogram 3).

There is decrease in the thickness of the stratum pyramidale of CA3 field in the adult rats treated with both cadmium and L-carnitine in comparison with those of the control group. This decrease in the thickness is statistically insignificant ($P > 0.05$). However, the thickness of the stratum pyramidale of CA3 field of this group in comparison with those treated with cadmium is increased. This increase in thickness is highly significant ($P < 0.01$) (Table 3 and Histogram 3).

Cell count

There is decrease in mean number of the pyramidal

cells of CA3 in adult rats treated with cadmium. This decrease in the mean number is statistically highly significant ($P < 0.01$) (Table 4 and Histogram 4).

There is increase in the mean number of the pyramidal cells of CA3 in the adult rats treated with L-carnitine. This increase in the mean number is statistically highly significant ($P < 0.01$) (Table 4 and Histogram 4).

This decrease in the mean number is statistically highly significant ($P < 0.01$). However, the mean number of the pyramidal cells of CA3 of this group in comparison with those of the cadmium-treated adult rats is increased. This increase in the mean number is statistically highly significant ($P < 0.01$) (Table 4 and Histogram 4).

CA1 region

In group I: examination of the pyramidal cells of CA1 field shows that they are less sized than those of CA3 field and are characterized by their elongated cell bodies and oval nuclei (Fig. 16). The ultrastructural study shows that it has an oval nucleus with fine granular chromatin and prominent nucleolus. The surrounding cytoplasm contains rough endoplasmic reticulum, many free ribosomes, and mitochondria (Fig. 17).

In group II: nissl-stained sections showed that many of pyramidal cells in CA1 field had darkly stained nuclei. It also showed the presence of some cells with pyknotic nuclei and vacuolated cytoplasm (Fig. 18). EM examination showed peripheral chromatin condensation in the nucleus. The cytoplasm had many vacuoles and damaged mitochondria. Marked loss of the free ribosomes could be revealed (Fig. 19).

In group III: light microscopic examination of the pyramidal cells of CA3 field showed that they appeared nearly similar to those of the control (Fig. 20).

In group IV: light microscopic examination of the CA1 pyramidal neurons revealed that most cells had normal appearance. Few cells with darkly stained nuclei and vacuolated cytoplasm were found to be present (Fig. 21). EM examination revealed that the cell had an oval nucleus with fine granular chromatin. The cytoplasm contained a lot of free ribosomes, mitochondria, and rough endoplasmic reticulum (Fig. 22).

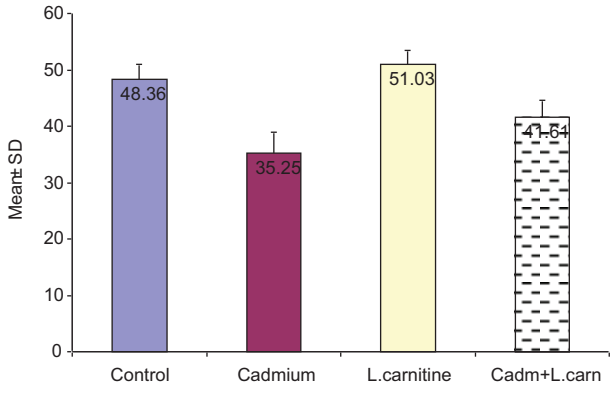
EM study of synaptic terminals

In group I: EM examination of the presynaptic terminals making contact with pyramidal neurons revealed that it is filled with synaptic vesicles and mitochondria (Fig. 23).

In group II: ultrastructural study of the presynaptic terminal making contact with pyramidal cells showed marked loss of synaptic vesicles and the presence of damaged mitochondria (Fig. 24).

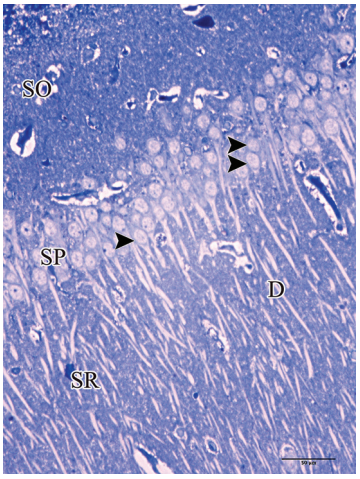
In group IV: ultrastructural study of the presynaptic terminal making synaptic contact with the pyramidal

Histogram 4



Showing the variation of pyramidal cell count in CA3 field per an area 12 360 μm² of the studied groups in adult albino rats.

Figure 16



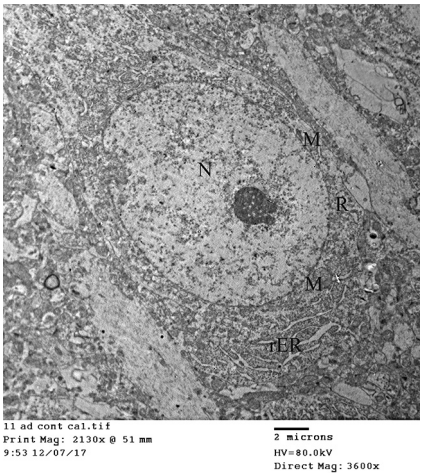
A semithin section of CA1 field of a control adult rat. The pyramidal cells of the stratum pyramidale (SP) are rounded with oval nuclei (arrow heads). Apical dendrites (D) pass toward stratum radiatum (SR). Stratum oriens (SO). Toluidine blue, ×400.

Table 4 CA3 cell count (per an area 12 360 μm²)

Adult	Control	Cadmium	L-carnitine	Cadmium+L-carnitine
Mean±SD	48.36±2.66	35.25±3.70	51.03±2.47	41.61±2.99
P^1		0.000*	0.001*	0.000*
P^2			0.000*	0.000*

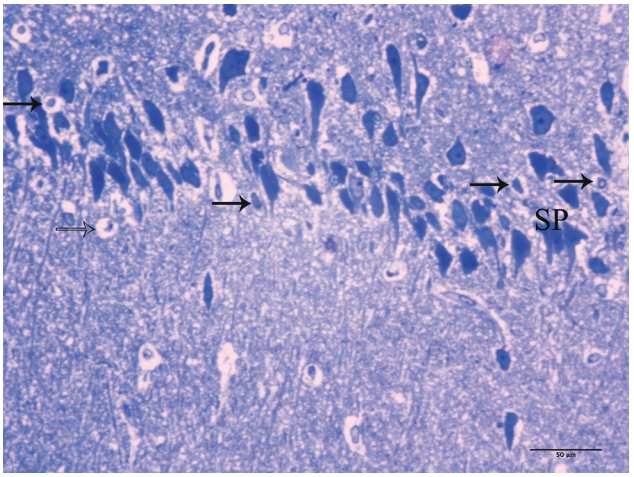
*Significant.

Figure 17



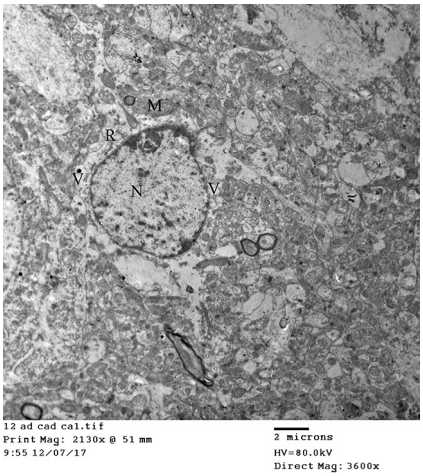
An electron photomicrograph of CA1 pyramidal cells of an adult control rat having oval nuclei (N) with fine granular chromatin. The cytoplasm contains mitochondria (M), rough endoplasmic reticulum (rER), and free ribosomes (R). ×3600.

Figure 18



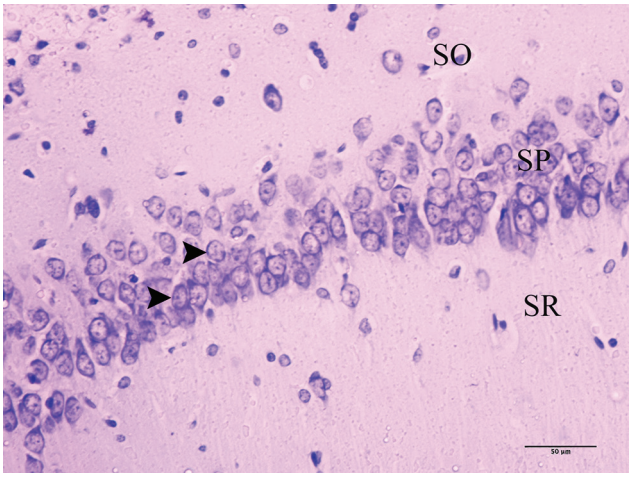
A semithin section of CA1 field of an adult rat treated with cadmium. It shows that many of the pyramidal cells in the stratum pyramidale (SP) have darkly stained nuclei (arrows). Some cells have pyknotic nuclei (open arrows). Toluidine blue, ×400.

Figure 19



An electron micrograph of CA1 pyramidal cell in adult rat treated with cadmium showing the nucleus (N) with peripheral chromatin condensation and marked loss of free ribosomes (R) and damaged mitochondria (M) in the vacuolated cytoplasm (V). ×3600.

Figure 20



A coronal section of CA1 field of an adult rat treated with L-carnitine showing the stratum pyramidale (SP) with its pyramidal cells are large rounded (arrow heads) with prominent nucleoli. Stratum oriens (SO) and stratum radiatum (SR). Gallocyanin, ×400.

neuron showed the presence of numerous synaptic vesicles and mitochondria with well-defined cristae (Fig. 25).

CA1 field

Thickness: there is decrease in the thickness of the stratum pyramidale of CA1 field in the adult rats treated with cadmium. This decrease in the thickness is statistically highly significant ($P < 0.01$) (Table 5 and Histogram 5).

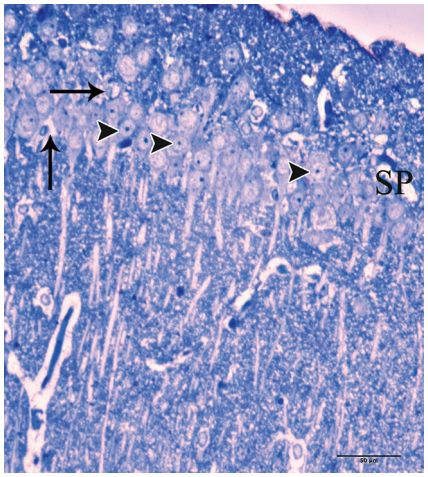
There is decrease in the thickness of the stratum pyramidale of CA1 field in the adult rats treated with L-carnitine. This decrease in the thickness is statistically insignificant ($P > 0.05$) (Table 5 and Histogram 5).

There is decrease in the thickness of the stratum pyramidale of CA1 field in the adult rats treated with both cadmium and L-carnitine in comparison with those of the control group. This decrease in the thickness is statistically highly significant ($P < 0.01$). However, the thickness of the stratum pyramidale of CA1 field of this group in comparison with those treated with cadmium is increased. This increase in thickness is highly significant ($P < 0.01$) (Table 5 and Histogram 5).

Cell count

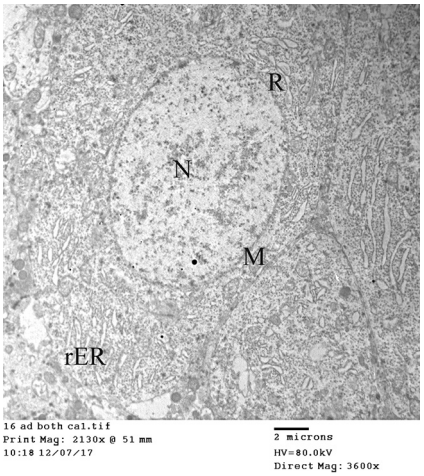
There is decrease in mean number of the pyramidal cells of CA1 in the adult rats treated with cadmium. This decrease in the mean number is statistically highly significant ($P < 0.01$) (Table 6 and Histogram 6).

Figure 21



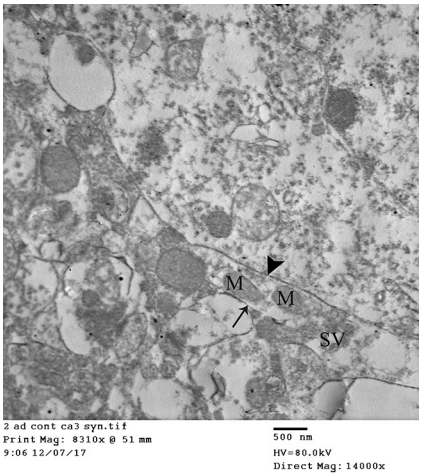
A semithin section of CA1 field of an adult rat treated with both cadmium and L-carnitine. It shows normal pyramidal neurons (arrow heads) in the stratum pyramidale (SP). Some cells with vacuolated cytoplasm and darkly stained nuclei (arrows). Toluidine blue, ×400.

Figure 22



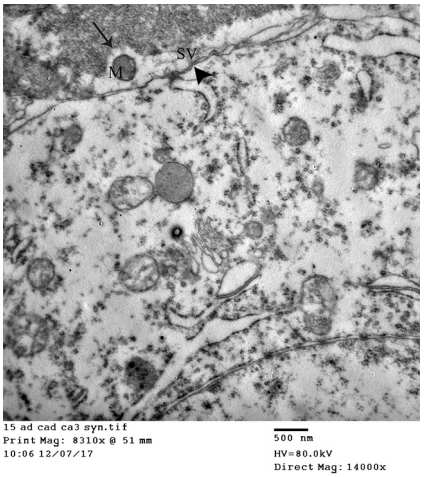
An electron photomicrograph of CA1 pyramidal cells of an adult rat treated with both cadmium and L-carnitine. The pyramidal cell has oval nucleus (N) with fine chromatin. The cytoplasm contains mitochondria (M), ribosomes (R), and dilated rough endoplasmic reticulum (rER). ×3600.

Figure 23



An electron photomicrograph showing synaptic contact (arrow head) on the pyramidal cells of the hippocampus of an adult control rat. The presynaptic terminal (arrow) has a lot of synaptic vesicles (SV) and mitochondria (M). ×14 000.

Figure 24



An electron micrograph of the pyramidal cell in an adult rat treated with cadmium. It shows synaptic contact (arrow head) between the pyramidal cells and presynaptic terminal (arrow). Note damaged mitochondria (M) and marked loss of the synaptic vesicles (SV). ×14 000.

There is increase in the mean number of the pyramidal cells of CA1 in the adult rats treated with L-carnitine. This increase in the mean number is statistically highly significant ($P < 0.01$) (Table 6 and Histogram 6).

There is increase in the mean number of the pyramidal cells of CA1 in the adult rats treated with both cadmium and L-carnitine in comparison with those of the control mothers. This increase in the mean number is statistically insignificant ($P > 0.05$). However, the mean number of the pyramidal cells of CA1 of this group in comparison with those of the cadmium-treated adult rats is increased. This increase in the mean number is statistically highly significant ($P < 0.01$) (Table 6 and Histogram 6).

Discussion

In this work, cadmium was studied because it is one of the most toxic heavy metals [11]. On entering the body, cadmium has detrimental effects on lung [12], reproductive system [13], liver [14], bone [15], blood [16], nervous system [16], and kidney [17].

For the control group of the adult age, our results were similar to that reported by El-Sokkary and Awadalla [18].

Electron microscopic examination revealed the normal structure of the granule and pyramidal cells. These results came in accordance with Helal *et al.* [19]. The

Table 5 CA1 thickness in the albino rats (in μm)

Adult	Control	Cadmium	L-carnitine	Cadmium+L-carnitine
Mean±SD	50.60±3.67	44.04±2.97	50.59±3.97	47.35±4.01
P^1		0.000*	1.000	0.001*
P^2			0.000*	0.001*

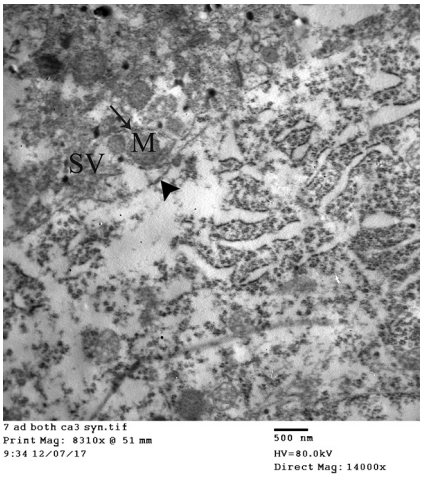
*Significant.

Table 6 CA1 cell count (per an area 12 360 μm²)

Adult	Control	Cadmium	L-carnitine	Cadmium+L-carnitine
Mean±SD	30.08±2.09	23.50±1.90	32.22±1.84	31.11±2.88
P^1		0.000*	0.000*	0.205
P^2			0.000*	0.000*

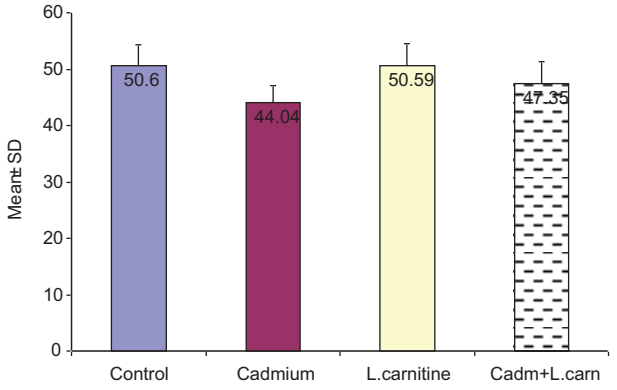
*Significant.

Figure 25



An electron photomicrograph showing synaptic contact (arrow head) between presynaptic terminal (arrow) and pyramidal cell in an adult rat that was treated with both cadmium and L-carnitine. Note the presence of mitochondria (M) and numerous synaptic vesicles (SV). ×14 000.

Histogram 5



Showing the variation of stratum pyramidale thickness in CA1 field (in μm) of the studied groups in adult albino rats.

synaptic terminals appeared to contain numerous vesicles responsible for neurotransmitters release as reported by Afifi and Embaby [20] and Chen *et al.* [21].

Histologic examination of the cadmium-treated group revealed the presence of degenerative changes in the principal cells and could be explained by the ability of cadmium to cross an intact blood barrier, and this agree with Goncalves *et al.* [6].

The mitochondrial damage was closely connected with a massive and rapid influx of calcium into the cells [22]. Vacuolations could be explained through lipid peroxidation theory, as stated by Afifi and Embaby [20]. The presence of dilated rough endoplasmic reticulum is attributed to lipid peroxidation, and this came in agreement with Afifi and Embaby [20].

In the hippocampal neurons synapses of rats treated with cadmium, it was observed marked decrease in the number of presynaptic vesicles and degeneration of the mitochondria. This came in accordance with Chen *et al.* [21].

On reaching the central nervous system, cadmium can induce microvessel injury which is attributed to oxidative stress [11]. In mitochondria, cadmium affects phosphorylation-oxidative enzymes and disrupts energy cycles [23]. Cadmium interferes with other metals such as calcium and zinc [11].

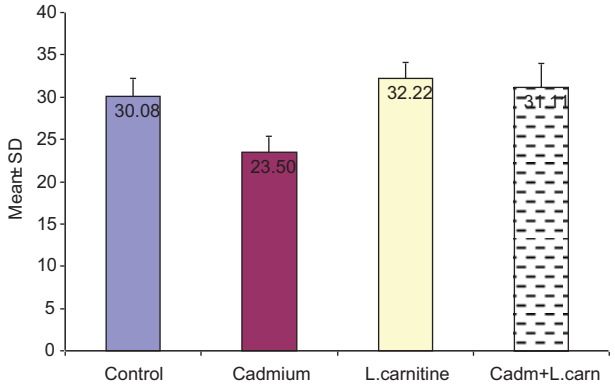
In addition, cadmium can impair neurogenesis, resulting in markedly reduced neuronal differentiation and axonogenesis, leading to neuronal cell death [24].

In this work, L-carnitine was given alone to the third experimental group (sham control), and by histological examination of this group, it was found that the results were more or less similar to those of the control group. This came in accordance with El-Masry *et al.* [10].

In this study, using L-carnitine together with cadmium revealed the protective effect of L-carnitine through histological study that revealed the normal appearance of the majority of the principal cells. The study of the ultrastructure of the principal cells revealed the improvement of the cells and in the synaptic terminals, and this agreed with Pettegrew *et al.* [25].

L-carnitine had an antioxidant effect, and this is attributed to its capability of fatty acid oxidation. This

Histogram 6



Showing the variation of pyramidal cell count in CA1 field per an area 12 360 μm^2 of the studied groups in adult albino rats.

agreed with Ozmen *et al*. [26]. These findings are also supported by reports of others [7,27,10].

The present morphometric study demonstrates that the thickness of the principal cell layers of the three studies areas of the adult group came in accordance with Hussein and George [28]. The morphometric results support the histologic studies coming in agreement with Ramezani *et al*. [27].

Acknowledgements

Drug source: imported from India.

The authors thank Assiut University for financial support for electron microscopic studies.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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