



THE HEPATOTOXIC EFFECTS OF MOBILE PHONE RADIATION (900 MHZ) ON MALE MICE AND THE HEPATOPROTECTIVE POTENTIALS OF ARCHITECTURAL SHAPES OF CAGES

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Abstract

Advances in technology, industry, economy and researches forced all people to continuous use of rapidly increased application of microwave (MW) radiation especially Wireless communication systems that is used daily in telecommunication, on line learning, medicine and even for animal farms management, these radiation uses always happen inside the buildings such as houses, schools, hospitals, offices, farms and public places leading to the threaten people's and animals' health especially vital organs and so this will reflect negatively on investment. Our study aimed to evaluate the possibility of new trends in hepatoprotection by potentiality of some famous historical architectural shapes as a physical protector against the harmful effects of the mobile phone radiation MPR, (900 MHz) for 8 weeks and to create healthy and high efficient architectural environments. Thirty-six (36) Swiss Albino male mice were randomly divided into 6 groups (n = 6), they housed in 6 cages with various shapes to assess the hepatoprotective effects of against MPR. Group I & II housed in a traditional cage, Group I served as a control which did not subjected to mobile phone but groups (II-VI) are exposed to mobile phone radiations. Our result revealed that these changes in architectural shapes (especially pyramid, bio-geometry and hexagonal shapes) can decreased the elevated hepatic enzymes either serum transaminases (ALT, AST) or alkaline phosphatase (ALP) in comparison to positive control groups and also restore the antioxidant capacity (total antioxidant (TAC), malondialdehyde (MDA) and nitric oxide (NO), reduced glutathione (GSH), catalase (CAT) plus retain the normal hepatic architecture in histopathology, it concluded that some specific architectural shapes may protect the liver from hazard of electromagnetic waves and this study can be useful for architects and advised to be used in the creation of healthy architecture buildings for either human or animal farms.

Key Words: Architectural shapes, bio geometry, Electromagnetic radiation, hepatotoxicity, Mice, Mobile phone radiation.

Introduction

Liver is a vital organ, it plays a principal role in the maintenance of metabolic functions, detoxification and elimination of foreign matters (Sharma and Sharma, 2010), Liver injury (liver dysfunction) is a principal life-threatening problem that oppose not only health care professionals but also the pharmaceutical industry and veterinarians where liver injury has linked with nutrient malabsorption leading to loss of animal body weight. (Mohamed Saleem *et al.*, 2010; Klaassen, 2008), There is many environmental factors leading to liver injury as

infection, hepatotoxic compound, but the most surrounded ones are painting materials and radiation (Yu *et al.*, 2010; bashandy *et al.*, 2020, Qi *et al.*, 2015).

In latest decade uses of technologies in all fields are increasingly day after day, especially the use of mobile phones, its application and networking that subjecting our environment to huge source of electromagnetic radiation (EMR) that in turn negatively affect human health (Adebayo *et al.*, 2015), so number of studies have concerned to report EMR hazard effects and displayed that EMR affect mainly brain causing nerve cell damage (Salford *et al.*, 2003), altering blood-brain barrier

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permeability (S1rav and Seyhan, 2016), impaired memory performance (Ahmadi *et al.*, 2018), deterioration in behavioral and cognitive processes in both humans and prolonged exposure of animals (Cassel *et al.*, 2004; Söderqvist *et al.*, 2015; Zhao *et al.*, 2012), Increasing incidence of the heart and brain tumors (Falcioni *et al.*, 2018; Finnie *et al.*, 2006) but also due to its oxidizing effects can impair oxidant and antioxidant balance (Irmak *et al.*, 2002), decrease the reproductive capacity (Chavdoula *et al.*, 2010), hormonal disturbance (Yüksel *et al.*, 2016; Lin *et al.*, 2018) and hepatic damage (Qi *et al.*, 2015).

All these diseases and potential symptoms and others that related to radiation have led scientists to serious search for safe sources of medication or solutions to reduce these negative effects, recently use term of “substitution therapy” for reliable treatment that can replace the undesirable or side effects which forced the patients to stop the medication, these substitutes may be in form of plant extracts (Mohamed and Fayed, 2020), physical changes in nano form (Abdallah *et al.*, 2020) or shape power and architectural spaces (RAO, 1997).

As mentioned above people cannot dispense about mobile phone radiation and they spend most of their time within an architectural interior spaces, surrounded by radiation sources in addition to the appearance of Sick Building Syndrome (Redlich *et al.*, 1997), the architect in turn, concerned in creating a safe and healthy space for the occupants of the buildings, Therefore, if there is any possibility that the shape, proportions, or angles of the space may have an effective role in the solve of these problems, some previous studies have shown that the architectural shapes have a healthy role in: healing the occupants (RAO, 1997), also Elbauomy *et al.*, 2017 affirmed obvious relationships between the inhabitants of the architectural spaces with different geometric forms and their construction materials and their awareness. Likewise, living within a pyramid shape houses has resulted in a decrease in the incidence of cancer as well as a slowdown in the process of damage (Nahed *et al.*, 2010) and used as milk preservation free from bacterial growth for a long time (Gopinath *et al.*, 2008). In this respect, Karim, 2010 and Sharaf *et al.*, 2014 concluded that living in bio-geometrical spaces strengthened the immune system and accelerated self-healing, respectively.

Historically, housing has long been associated with health according to The World Health Organization (Howden-Chapman *et al.*, 2017). Therefore, engineers, architects, planners and others have been challenged with research to address potential damage to wireless

technology or reduce the disease burden associated with RFR exposure.

Therefore, the present study concerned to investigate this new trends to assess the ability of the number of famous historical architectural forms to protect against hepatotoxic effects of RFR produced by a mobile phone (900 MHz) using biochemical parameters, oxidative parameters and histopathological results and adult male mice as a model of human health.

Material and Methods

Animals

Healthy adult male Swiss Albino mice weighing 24 ± 2 g, were purchased from the Animal Breeding House of the National Research Centre (NRC), Dokki, Giza, Egypt. Animals were housed in clean acrylic cages in the laboratory animal room ($23 \pm 2^\circ\text{C}$), on standard pellet diet and tap water *ad-libitum*, a minimum relative humidity of 40 % and a 12 h dark/light cycle. Mice were allowed to acclimate to laboratory conditions for one week.

Ethics statement




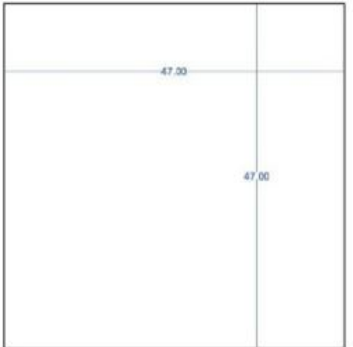

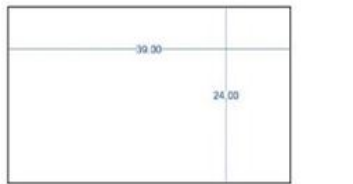

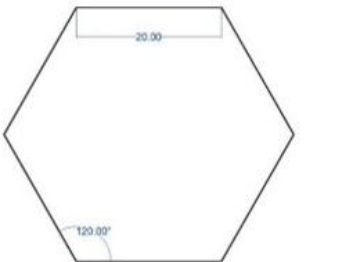

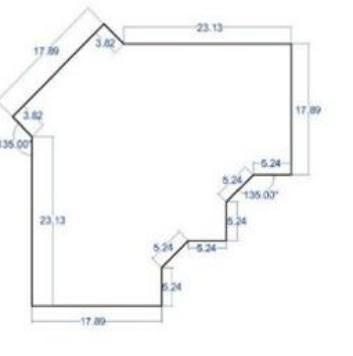
The experimental work on mice was performed with the approval of the Animal Care & Experimental Committee, National Research Centre, Giza, Egypt and the international guidelines for the care and use of laboratory animals of the National Institutes of Health (NIH No. 85:23 revised 1985).

The cage design

All the cages used in our study had nearly the same volume and made from acrylic material. The color of the acrylic material was white to neutralize or to avoid the influence of the colors in our paradigm. Two of the shapes (G I & II) were identical and looked like the traditional laboratory cages with a volume of 22040 cm^3 ($40\text{cm} \times 29\text{cm} \times 19\text{cm}$). While the other architectural forms selected were known to contain special capabilities across different ages, civilizations and cultures for health. The names and shapes of cages were depicted in Fig. 1.

Animal grouping

The experimental study aimed to assess the effect of the exposure to MFR on the oxidative stress parameters, liver functions biomarkers and histopathological observations of male mice and to evaluate the hepatoprotective of the geometric shapes of architectural voids in terms of shape, angle and proportions. Thirty-six (36) adult male mice were randomly divided into 6 groups (6 mice/cage). The groups were housed in cages with various architectural shapes as follows Fig. 1:

<p>GI & GII: Ordinary Laboratory cage.</p> <p>Height of the cage: 19cm.</p> <p>Volume of the cage: 22,040 cm³</p>		
<p>G III: Pyramid shape cage.</p> <p>Height of the cage: 30cm.</p> <p>Volume of the cage: 22,090 cm³</p>		
<p>G IV: Cage with a Golden rectangle base.</p> <p>Height of the cage: 24cm.</p> <p>Volume of the cage: 22,464 cm³</p>		
<p>G V: Cage with a hexagonal base.</p> <p>Height of the cage: 22cm.</p> <p>Volume of the cage: 22,862 cm³</p>		
<p>GVI: Cage with a base designed according to the Biogeometry principles</p> <p>Height of the cage: 21.18cm.</p> <p>Volume of the cage: 22,074 cm³</p>		

· G I: served as a control, mice housed in a traditional cage at a separate room with the same conditions, but without MPR.

· G II: mice housed in a traditional cage.

· G III: mice housed in Pyramidal shape cage (with the same proportions of the great pyramids).

· G IV: mice housed in a cage with a gold ratio rectangle base.

· G V: mice housed in a cage with a hexagonal base.

· G VI: mice housed in a cage with a base designed according to the biogeometry principles.

Experimental protocol

According to our laboratory, the control group (G I) was placed in a separate room under the same conditions, but without the mobile phone. However, the mice in the experimental groups (G II- G VI) were exposed to a mobile phone as a source of Radiofrequency Electromagnetic Radiation (900 MHz) from an active GSM (Global system for mobile communications) for 24 hours per day for eight weeks with a daily 50 missed calls. The missed call duration equaled 45 seconds while the intervals between the two successive missed calls equaled 15 seconds. Besides, the missed calls were set on a silent non-vibrating mode to avoid disturbance or stress.

The cages were placed at axes corresponding to the four coordinate directions, with an average distance of at least one and a half meters from each other as shown in Fig. 2. Besides, the two phones were placed in the middle of the shapes at equal distances (1.38 m) from all shapes as represented in Fig. 2.

The radiation source used in our study came from two commercial identical mobile phones (ALCATEL 1066G, GSM 900 MHz). Thus, instead of using models of digital mobile phone signals with constant parameters (frequency, power), we used real GSM signals (Vodafone,

Fig. 1: Architectural shapes of cages designed for mice exposed to a mobile phone radiation (900 MHz) protocol.

Egypt) which are never constant since there are continuous changes in their intensity.

Electromagnetic field (EMF) measurements-dosimetry

The electrical field produced by the mobile phone was monitored by the Smart Fieldmeter, EMC Test Design RPF-04, LLC test lab, National Physical Laboratory, UK,

having a band of 900 MHz and the reading was 29-32 V/m within the various cages, depending on sound level or distance variation. The shape places were changed periodically every three days to ensure equal exposure to radiation. The specific absorption rate (SAR) for the whole body of the exposed mice can be approximately calculated according to the equation:

$$\text{SAR} = \sigma E^2 / \rho$$

Where E is the root mean square value of the electrical field measured within the cages, σ is the mean electrical conductivity of the tissues and ρ is the mass density (21, 22). The SAR is a parameter widely used by most authors to compare the absorbed energy in different biological tissues. The SAR values ranging from 0.65 to 0.84 W/kg were calculated using the above equation by applying the measured electrical field density 29–33 V/m, $\sigma = 0.8$ S/m and mass density $\rho = 1040$ kg/m³.

Blood collection and tissue preparation

Blood samples were collected from the retro-orbital venous plexus of mice under light ether anesthesia and collected in clean test tubes, allowed to clot, then centrifuged for 10 minutes at 3000 r.p.m. Serum samples were separated and stored into Eppendorf tubes at -20°C to be used for biochemical analysis. After collection of blood samples, mice were sacrificed by cervical dislocation and their livers were immediately removed. Livers of mice were divided into 2 portions; the first portions were kept at (-80°C) for the determination of the hepatic levels of MDA, GSH, NO and CAT. The second portions were preserved in phosphate buffered formalin 10% for further histopathological investigation.

Biochemical analysis of serum samples

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were determined by using Reitman and Frankel methods (Reitman and Frankel, 1957). Alkaline Phosphate (ALP) was determined as outlined by Belfield and

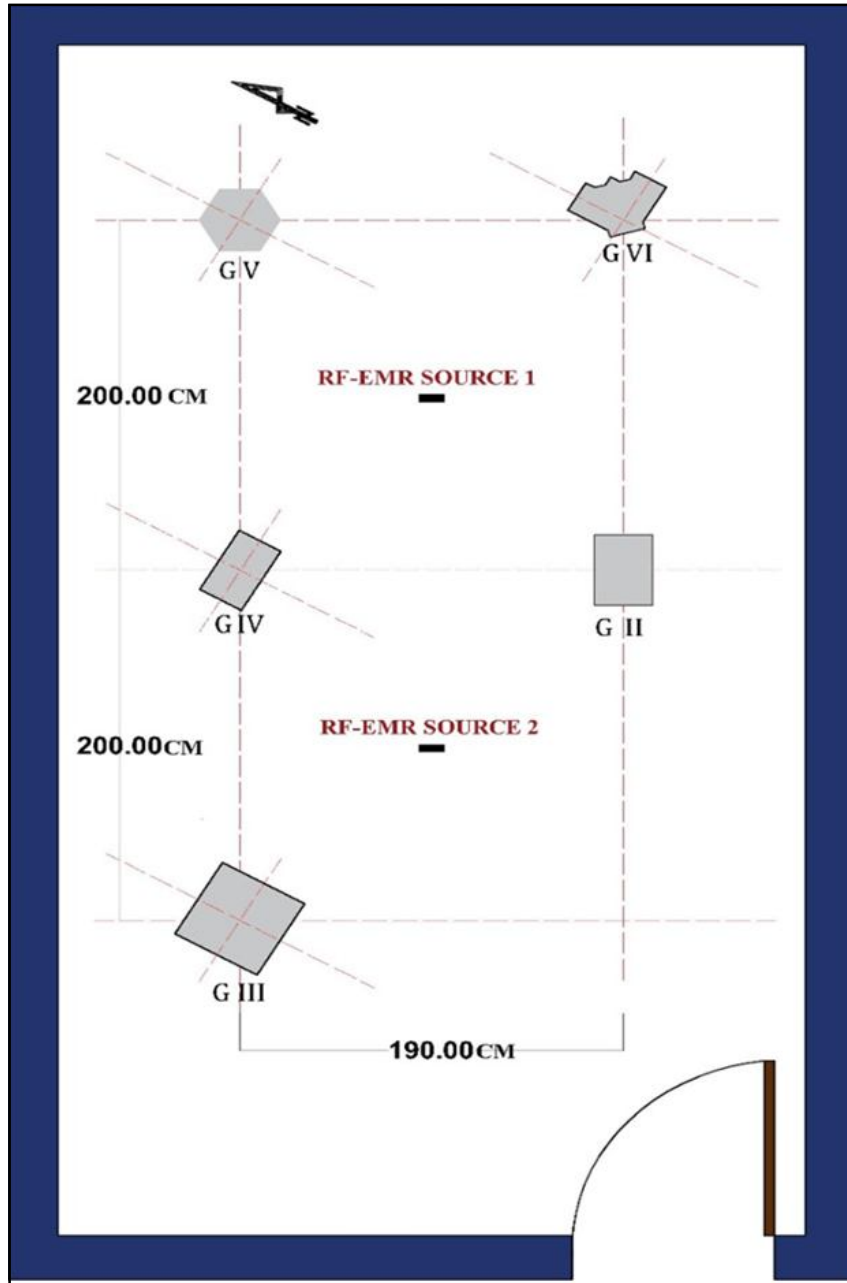


Fig. 2: The top view of exposure system setup used in the study. Two mobile phones, as sources of Radiofrequency Electromagnetic Radiation (RF-EMR) placed at the center surrounded by the mice residing in the various cages. The mice were exposed to RF-EMR of 900 MHz frequency for 24 h/day for 8 weeks at SAR of 1.1 W/kg.

G I: control (Traditional cage); G II: Traditional cage; G III: Pyramid shape cage; G IV: Golden ratio rectangle cage; G V: Hexagonal cage; G VI: Bio geometry cage.

Goldberg (Belfield and Goldberg, 1971), and total antioxidant capacity (TAC) was determined according to the method described by Koracevic *et al.*, (2001).

GSH was estimated in hepatic tissue according to the method described by Beutler *et al.*, (1963). CAT activity was evaluated in liver according to the methods of Aebi, (1984). MDA was estimated as a marker for lipid peroxidation in hepatic tissue according to method suggested by Ohkawa *et al.*, (1979). NO was evaluated by the method described by Montgomery and Dymock, (1961). All the above biochemical parameters were assayed by using local commercial kits purchased from Biodiagnostic, local distributor, Giza, Egypt.

Histopathological examination

For histopathological study, small pieces of left lobes of livers were excised, fixed in 10% neutral buffered formalin solution, prepared in paraffin blocks, cut into sections of 5-6 μm in thickness and stained with haematoxylin-eosin (Carleton *et al.*, 1976).

Statistical analysis

In the present study, all results were expressed as mean ± standard error of the mean. Data analysis was achieved by one-way analysis of variance (ANOVA) followed by Tukey comparison test using software program ASSISTAT (Version 7.7 beta). Difference was set at P<0.001.

Result

Exposure of male mice to GSM-900-MHz mobile phones radio-frequency electromagnetic radiation resulted in numbers of biological effects. Except for discomfort, there was no obvious signs of toxicity observed in

Table 1: Effects of architecture shapes on liver function enzymes biomarkers of male mice exposed to mobile phone radiation (900 MHz).

Test groups	Biochemical parameters			
	ALT (U/ml)	AST (U/ml)	ALP (U/L)	TAC(mM/L)
GI	114.83±9.82	119.68±5.89	52.66±2.96	1.55±0.09
GII	207.88±11.24 ^a	240.02±14.25 ^a	109.30±10.02 ^a	0.48±0.12 ^a
GIII	149.63±5.02 ^{ab}	187.66±11.55 ^{ab}	60.96±2.24 ^b	0.98±0.04 ^{ab}
GIV	175.23±1.14 ^{ab}	198.96±5.60 ^{ab}	89.47±3.02 ^a	0.91±0.06 ^{ab}
GV	129.53±4.58 ^b	170.98±13.72 ^{ab}	53.76±1.31 ^b	1.38±0.11 ^b
GVI	119.68±5.89 ^b	158.60±10.60 ^{ab}	52.17±2.51 ^b	1.53±0.06 ^b

Data were expressed as mean ± SE (n=6). Statistical analysis was carried out by one-way ANOVA followed by Tukey’s multiple comparisons test. a = significantly different from control at P<0.001 & b = significantly different from G II at P<0.001.

G I: control (Traditional cage); G II: Traditional cage; G III: Pyramid shape cage; G IV: Golden ratio rectangle cage; G V: Hexagonal cage; G VI: Biogeometry cage.

Table 2: Architectural cages shapes against severity scoring of histopathological examination in mice livers exposed to mobile phone radiation (900 MHz).

Histopathological observation	Groups					
	GI	GII	GIII	GIV	GV	GVI
Degenerative changes	-	+++	+	+	+	+
Inflammatory cells infiltrates	-	+	+	+	+	+
Congestion of Blood vessels	-	+++	-	-	+	+
Necrotic changes	-	++	-	+	-	-

G I: control (Traditional cage); G II: Traditional cage; G III: Pyramid shape cage; G IV: Golden ratio rectangle cage; G V: Hexagonal cage; G VI: Bio geometry cage. (-) indicates nil, (+) indicates mild, (++) indicates moderate, (+++) indicates severe, and (+++++) indicates extremely severe.

experimental animals. However, there was no a significant difference in body weight of the treated groups compare with control group (un-tabulated data).

Liver function enzymes for biomarkers were shown in the serum of mice subjected to mobile phone radiation in table 1. Compared to the control group (GI), the exposure of mice to mobile phone radiation led to a significant rise (P <0.001) in the serum involved in enzyme activities (ALT, AST, ALP) For a conventional cage group (G II), while certain effects were reduced in cages of particular shape especially in the GV and G VI groups.

Compared to G I, the total antioxidant content in the serum of group II decreased significantly (P <0.001) due to mobile phone radiation. However, the G VI group reduced these adjustments to the normal value table 1. Furthermore, accompanying pathological results demonstrated in mice liver such as hepatic degenerative changes, inflammatory cell infiltration, blood cell congestion as well as necrotic changes were depicted in Fig. 4 and their severity was shown in table 2.

Mice exposure to mobile phone radiation in G II group resulted in a significant increase (p <0.001) in the NO content Fig. 3D and lipid peroxide Fig. 3C as evidenced by the increase in MDA levels in liver tissue compared to G I. However, housing mice in cages of various architectural forms mitigated these changes in liver tissue in exposed mice. GSH works in reduced form as one of the most important antioxidant in the body. Compared to the control group, a significant decrease (P<0.001) was found in the GSH content Fig. 3B) and CAT activity in liver tissue of mice subjected to mobile radiation G II Fig. 3A. Whereas, the use of cages of different architectural shapes improved the

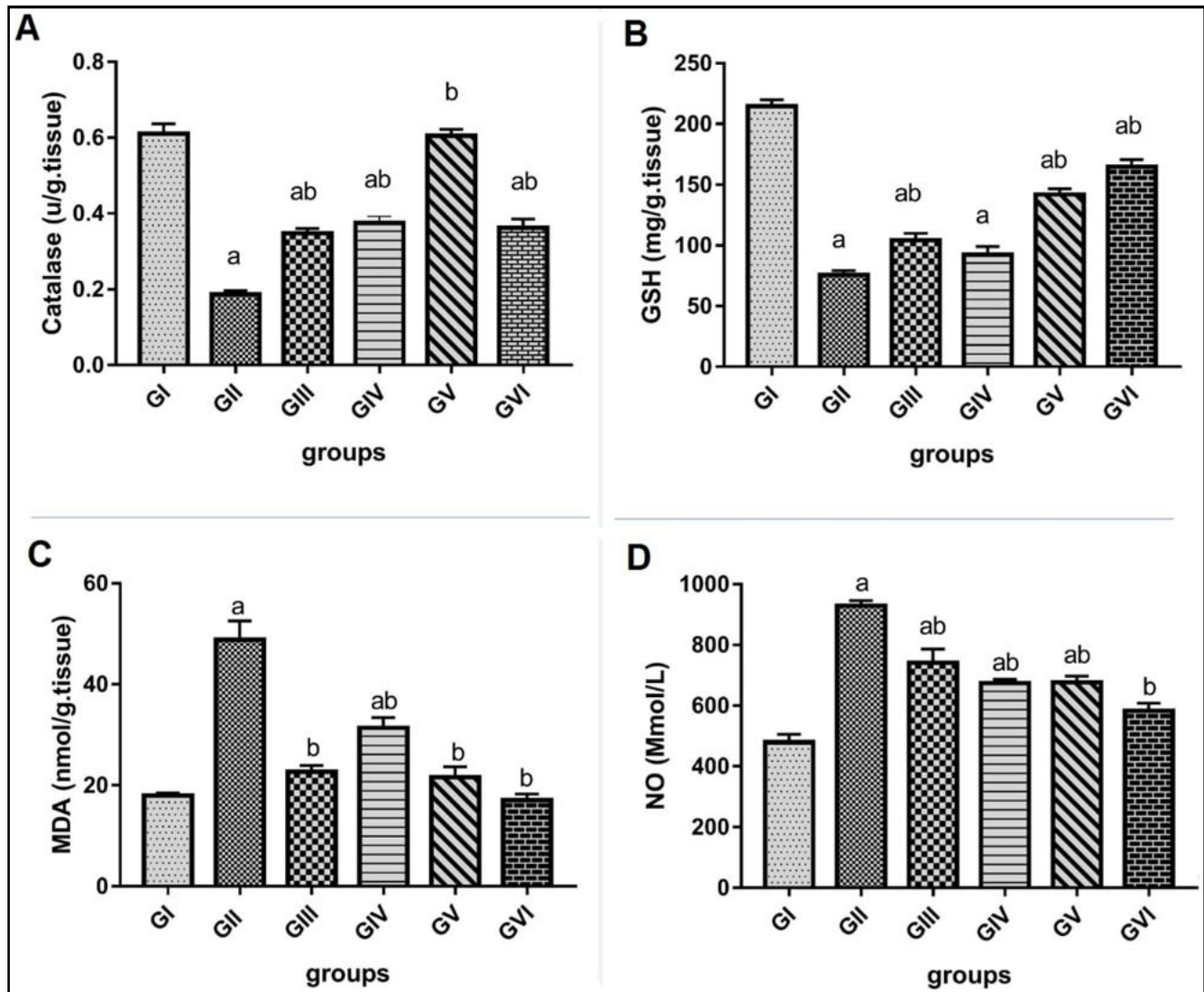


Fig. 3: Effects of architecture shapes on antioxidant status (MDA, GSH, CAT, and NO) in liver tissues of male mice exposed to mobile phone radiation (900 MHz).

Data were expressed as mean \pm SE (n=6). Statistical analysis was carried out by one-way ANOVA followed by Tukey's multiple comparisons test. a = significantly different from normal control at $P < 0.001$ b = significantly different from positive control at $P < 0.001$. CAT: catalase; MDA: Malondialdehyde; GSH: reduced glutathione; NO: nitric oxide.

GI: control (Traditional cage); GII: Traditional cage; GIII: Pyramid shape cage; GIV: Golden ratio rectangle cage; GV: Hexagonal cage; GVI: Bio geometry cage.

decline in the live tissue of exposed mice Fig. 3.

Mice exposure to mobile phone radiation in G II group resulted in a significant decrease in live body weight while housing in different architectural shapes significantly improved the decreased weight in comparison to GII especially bio-geometry shapes (GVI), hexagonal shapes (GV), Fig. 5.

Discussion

The main purpose of our study was to investigate the ability of the housing in number of famous historical architectural shapes to protect against the hepatotoxic effects induced by exposure effects of RFR produced

by mobile phone radiation (900 MHz) on mice liver, the choice of liver as assessment of healthy is due to several points i, liver is the site of detoxification (Sharma and Sharma, 2010), ii highly susceptible to the magnetic fields due to its high iron content (Ngelucci *et al.*, 2010), iii it is the major site affected by oxidative stress which is the main mechanism of mobile phone radiation (Irmak *et al.*, 2002).

The results presented in this study provide evidence that mobile phone radiation (900 MHz) may induce oxidative damage in mice liver of G II. The oxidative damage was mediated by increased lipid peroxidation and nitric oxide and by decreased enzymatic antioxidant

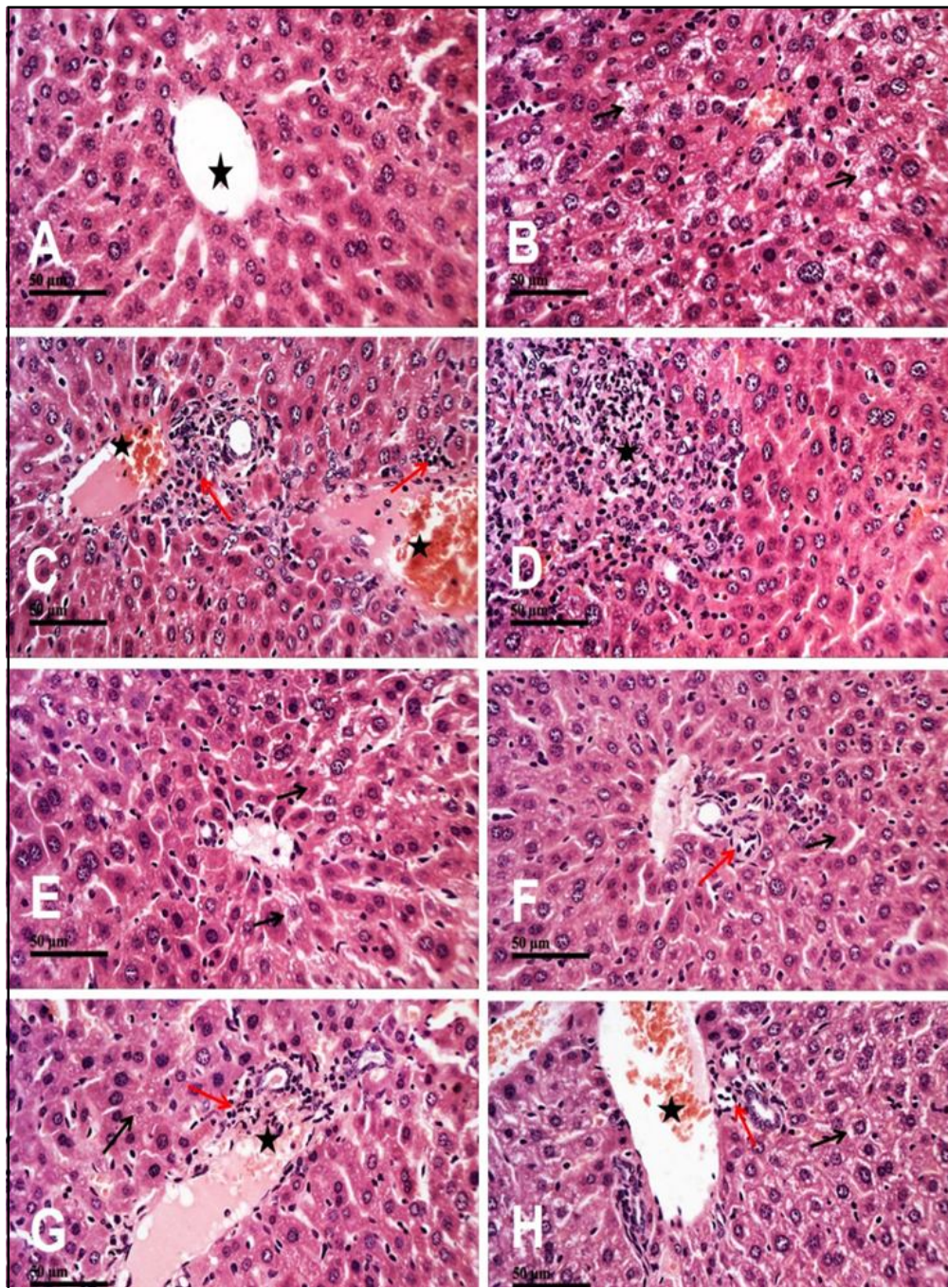


Fig. 4: Photomicrographs of liver sections of mice exposed to radiofrequencies (900 MHz) in absence and presence of various architecture shapes cages. Showing normal morphological features of hepatic parenchyma with almost intact hepatocytes... ..having large vesicular nuclei, intact sinusoids and vasculatures (star) (A, control group, GI), vacuolar degenerative records of hepatocytes (B, blackstar), with moderate congestion of blood vessels (black star) accompanied with periportal inflammatory cells infiltrates (red arrow) (C) and Focal areas of necrosis replaced by inflammatory cells (D, black star) (GII), mild few records of hepatocellular degenerative changes (E, black arrow) (GIII), similarly, hepatocellular degenerative changes (black arrow) with mild occasional periportal inflammatory cells infiltrates (red arrow) (F, GIV), few records of vacuolar degenerative changes of hepatocytes as in GII with few records of inflammatory cells infiltrates (red arrow), as well as dilatation and congestion of hepatic blood vessels (star) (G, GV), very few degenerative changes hepatocytes, with low records of inflammatory cells infiltrates compared with group 3 or 4 (red arrow) and moderate dilatation and congestion of hepatic blood vessels (star) (GV) and picture of (G VI) also turned to normal as showed the same records as (G III).

G I: control (Traditional cage); G II: Traditional cage; GIII: Pyramid shape cage; GIV: Golden ratio rectangle cage; GV: Hexagonal cage; GVI: Bio geometry cage.

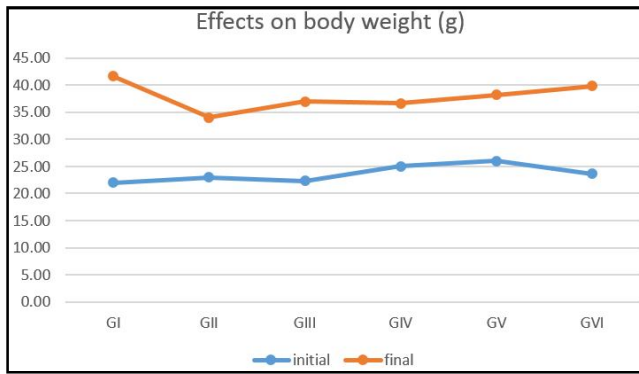


Fig. 5: Effects of architecture shapes on body weight from starting time and final time of male mice exposed to mobile phone radiation (900 MHz).

Data were expressed as mean \pm SE (n=6). Statistical analysis was carried out by one-way ANOVA followed by Tukey's multiple comparisons test. a = significantly different from normal control at $P < 0.001$ b = significantly different from positive control at $P < 0.001$. CAT: catalase; MDA: Malondialdehyde; GSH: reduced glutathione; NO: nitric oxide.

G I: control (Traditional cage); G II: Traditional cage; GIII: Pyramid shape cage; GIV: Golden ratio rectangle cage; GV: Hexagonal cage; GVI: Bio geometry cage.

(CAT) and non-enzymatic antioxidant (GSH) levels (Eid *et al.*, 2015).

The current observations are indicative of oxidative stress parameters which are in line with many previous investigators, who have been observed a correlation between exposure to EMFs and formation of reactive oxygen species either *in vitro* (Zmylony *et al.*, 2004; Yao *et al.*, 2008; Lai and Singh, 2004; Oktem *et al.*, 2005; Tkalec *et al.*, 2007; Esmekaya *et al.*, 2016). Lifetime exposures to EMF cause crucial alterations and deleterious effects in biological systems (Tkalec *et al.*, 2007; Moulder *et al.*, 2005; Sephrimanesh *et al.*, 2014; Shehu *et al.*, 2016; Buckus *et al.*, 2017).

Given that RFR is a part of the electromagnetic spectrum; however, unlike ionizing radiation, electromagnetic at frequencies applied in mobile phones (900-2100 MHz) do not have sufficient energy to break the chemical bonds or ionize molecules (Moulder *et al.*, 1999). So, the biological impacts of EMR can be classified as thermal and non-thermal effects. Although, the non-thermal effects do not raise the body temperature sufficiently to impair the structure of tissues, their effects can still be seen as an increase in free radical production in tissues (Challis, 2005). Yet, reports of clear perturbations of biological systems at levels near or even below $1000 \mu\text{W}/\text{m}^2$ (BWG, 2012) were explained by an exacerbation in electron and proton transfers supporting ATP production in mitochondria (Sanders *et al.*, 1985) exposed to RFR signals (Li and Héroux, 2014).

According to Heikal *et al.*, (2012) and Thampi *et*

al., (1991). malondialdehyde (MDA) is an important indicator of lipid peroxidation, which in turn explains many of deleterious effects in biological systems including increased membrane rigidity, decreased cellular deformation and membrane fluidity (Heikal *et al.*, (2012)). Consequently, the noticeable increase in the amount of lipid peroxidation observed in our study could have ultimately indicated oxidative stress and cellular damage that may be linked to the uncontrollable production of ROS within mice-exposed groups. Similarly, GSH is an important naturally occurring antioxidant that helps in detoxification by conjugating with free radicals (Heikal *et al.*, 2014). It can act either to detoxify ROS such as H_2O_2 or to reduce lipid peroxides themselves (Thampi *et al.*, (1991)). The increased level of NO in the present study was also indicative of increased oxidative stress in liver tissue. NO present could have reacted with superoxide to form peroxynitrite intermediate (ONOO⁻), which is a potent cellular oxidant (Clelland *et al.*, 1996) that can induce oxidation modification of proteins (Beckman, 1996). This disturbance of hepatic tissue antioxidant system may lead to hepatocyte destruction and leakage of internal cytosol enzymes (Jadhav *et al.*, 2010) causing serum transaminases (ALT, AST) level so they are important indicators of liver damage in clinic findings indicating necrosis and inflammatory effects (Hargus *et al.*, 1994).

In the current study, mice exposed to RFR for 8 weeks showed a significant increase ($P \leq 0.001$) in serum activities of ALT, AST and ALP when compared to negative control table 2. This is in the same line with Ragy, (2015). However, the housing of rats in the selected cage with different geometrical shapes attenuated such perturbations supposing the effect of angles distribution that may disturb or disperse the radiated waves as suggested with pyramid shape (El-Abiad *et al.*, 2010).

The change in the shape is meaning the change in both power or energy emitted from this surrounding shapes and angles distribution that may disperse or reflect the electromagnetic radiation (Karim, 2007), these states explained our result the significant retain of liver function and antioxidant capacity for rats that housed especially in cages assigned as bio-geometry shapes (GVI), hexagonal shapes (GV) and pyramid shapes (GIII) but these positive effects not reported in golden rectangle shapes that its angles distribution seems shape housed by the most deteriorated group (GII) these improvement in liver function (ALT, AST, ALP) and also antioxidant system also supported by histopathological observations such as very few degenerative changes hepatocytes, with low records of inflammatory cells infiltrates compared with vacuolar degenerative changes of hepatocytes, congestion of hepatic blood vessels, periportal inflammatory cells infiltrates and focal areas of necrosis

observed in mice-exposed group in ordinary shape (GII). Even our necrotic histopathological scoring affirmed the improvement for rats housed in the three selected geometrical shapes (bio-geometry based shapes (GVI), hexagonal shapes (GV) and pyramid shapes), these necrotic changes have linked with mentioned above about increment of liver function in GII and its normal level in the three selected geometrical shapes and explained that necrosis has been characterized by cell swelling and leakage of the cellular contents into the bloodstream, the elevation of hepatic enzymes in the serum considered to be the biomarker of liver damage and dysfunction (Salama *et al.*, 2018).

So the degenerated hepatocytes reported by histopathology in rats group housed in ordinary cage and subjected to MPR (GII) caused less nutrient absorption where liver is the site of absorption and has the central role in blood nutrient circulation (Klaassen, 2008) these assumes its role in lowering body weight in GII (Qi *et al.*, 2015) but the three selected geometrical shapes maintain non degenerative changes to hepatocyte and linked with normal body weight increase matching with normal growth of control group GI.

To the best of our knowledge, before this study, no attention has been paid to the indirect effects of RFR on liver function biomarkers.

However, housing the animals in cages of historical architectural shapes was capable of nearly induce significant alterations in the three selected shapes (bio-geometry based shapes (GVI), hexagonal shapes (GV) and pyramid shapes). The above results suggested that electromagnetic radiation from mobile phones caused increases in the levels of oxidative stress in the liver tissue of mice. However, the possible mechanism behind these alterations are still unclear and our study may be the pioneer in discussing these points.

Conclusion

Our data suggested that electromagnetic radiation from mobile phones induced perturbations in liver function biomarkers (ALT, AST, ALP) and oxidative stress parameters (MDA, NO, GSH, CAT, TAC) in the liver tissues of male mice. Of significance for health is seeking for solutions to attenuate these biological impacts. According to our study, housing the animals in cages of historical architectural forms attenuated most of the health impact outcomes. Moreover, the most noticeable mitigation had the right to bio geometry, hexagonal and then pyramid shapes, respectively. However, the precise mechanism underlying these effects is still unclear. Eventually, this study may provide guidance to the engineers and/or the architectures to use the above-mentioned shapes in construction for hepatic hospitals as well as buildings near

the radiofrequency station.

According to our study, housing of animals in cages of historical architectural forms alleviated most of the health impact outcomes. Moreover, the most prominent mitigation had the right to bioengineering, hexagonal and hierarchical forms, respectively

Conflict of Interest

The authors declare that they have no conflicts of interest.

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Authors' Contribution

All authors contributed to the design and implementation of the work.

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