

## **PHYSIOLOGICAL CHANGES IN LIVER AND KIDNEY OF RATS EXPOSED TO MOBILE PHONE: PROTECTIVE ROLE OF ANTIOXIDANT VITAMINS**

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### **ABSTRACT**

Modern technology creates different instruments emitted electromagnetic waves such as Mobile phone, microwaves, television set, and computer. Epidemiological and biological studies have suggested that exposure to extremely low and high (ELF- EMF) affects living cells and tissues.

The present study was planned to assess the effects of electromagnetic wave's emitted Mobile phone on biochemical variables in serum, liver and kidney. Also the histological effects and the role of antioxidant some vitamins such as Vit C and E were investigated.

Wistar albino rats were divided into (12) groups. Group (1); control group, group (2) received vitamin C (0.04mg V.C / kg b. wt ), group (3) received vitamin E (0.027 mg V.E / kg b. wt ), groups 4; 7 & 10 are exposed to Electromagnetic waves emitted from ringing mobile phone at intervals (1/4,1/2 & 1 hr/day for 2-weeks ) , groups 5 ,8 & 11 are exposed to Electromagnetic waves emitted from ringing Mobile phone at intervals (1/4,1/2&1 hr/day for 2-weeks ) + Vit. C; groups 6, 9 & 12 were exposed to Electromagnetic waves emitted from ringing mobile phone at intervals (1/4, 1/2&1 hr/day for 2-weeks) + Vit. E. The mobile phones are hanging at a distance about 50 cm.

The results revealed that, exposure to Mobile phone lead to degenerative morphological changes in liver and kidney. A significant difference was found in the levels of hydrogen peroxide, Glutathione, glutathione peroxidase, conjugated diene, and lipid hydro peroxide in serum, liver and kidney when compared to the control group. No significant changes in serum GOT ,ALP, Urea, Creatinine, Uric acid, Total protein ,Albumin , Globulin and minerals (Na,K,Ca,Ph) but a significant increase in serum glucose in rats exposed to ringing mobile phone for ¼ hr and Vit C&E, however, significant decrease in GPT was observed in rats

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exposed to ringing mobile phone for ½ and 1 hr. Administration of Vitamin C & E caused a significant decrease in the degenerative changes, hydrogen peroxide, conjugated diene, and lipid hydro peroxide and a significant increase in the activities of Glutathione, glutathione peroxidase when compared to the control group of serum, liver, and kidney.

In Conclusion the potent free radical scavenger and antioxidant agent's vitamins C and E seem to be highly promising agents for protecting liver and kidney tissues from oxidative damage and preventing organ dysfunction as a result of exposure to ringing mobile phone.

**Key words:** Mobile phone, liver, kidney, Vitamin C, Vitamin E

## **INTRODUCTION**

Modern technology allowed the development of many different instruments which emitted electromagnetic waves such as Mobile phone, microwaves, television set, and computer. Epidemiological and biological studies have suggested that exposure to extremely low and high (ELF- EMF) affects living cells and tissues. The mechanism by which ELF-EMF interacts with living cells remains undefined. (Tenforde, 1991 and Hendee et. al, 1996)

The use of cellular phones in the last few years has raised many questions about their use and their safety, because the operator is exposed to electromagnetic (radio frequency) radiation (EMR) in ultra-high-frequency range (i.e. 300-3000 MHz), the effect of which depends on its frequency and power. There has been increasing interest in the biological effects and possible health outcomes of weak, high frequency electric and magnetic fields (Knave, 2001). Studies on the effect of magnetic fields, on cancer, reproduction and neurobehavioral reactions were reported by some investigators (Leszczynski, et al., 2002; Bortkiewicz, 2001 & Riu et al., 1997)

The kidney is a major potential route for the absorption of hazardous materials encountered in the environment (Irmak, MK.et al., 2002). The Mobile telephones emitting 900 MHz EMR may be absorbed by kidney more than other internal organs since the Mobile phones are often carried in belts. (Ozguner, et al. 2005)

Electromagnetic radiation (EMR) or radiofrequency fields of cellular Mobile phones may affect biological systems by increasing free radicals, which appear mainly to enhance lipid peroxidation, and by changing the antioxidant defense systems of human tissues, thus leading to oxidative stress [Ozguner, et al. 2005].

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Evidences that Mobile phones induce free radical formation in other tissues have been reported (Irmak, et al. 2002 & Irmak, et al. 2003; Iihan, et al. 2004). Biological systems may interact resonantly with EMR but there is as yet no robust evidence to support this suggestion. The role of reactive oxygen species (ROS) have been implicated in tissue injury. The main ROS that have to be considered are superoxide anion ( $O_2^-$ ), which is predominantly generated by the mitochondria; hydrogen peroxide ( $H_2O_2$ ) produced from  $O_2^-$  by the action of superoxide dismutase (SOD), and peroxynitrite ( $ONOO^-$ ), formed when  $O_2^-$  couples with nitric oxide (NO).

These continuously produced ROS are scavenged by SOD, glutathione peroxidase (GSH-Px) and catalase (CAT). Under some circumstances, these endogenous antioxidant defenses are likely to be perturbed because of overproduction of oxygen radicals, inactivation of detoxification systems, consumption of antioxidants, and failure to adequately replenish antioxidants in tissue. It has been demonstrated in numerous studies that ROS are directly involved in oxidative damage of cellular macromolecules such as lipids, proteins, and nucleic acids in tissues (Ozguner, et al. 2005)

Malondialdehyde (MDA) is the breakdown product of the major chain reactions leading to oxidation of polyunsaturated fatty acids and thus serves as a reliable marker of oxidative stress-mediated lipid peroxidation (LPO) (Serel, et al. 2004). Levels of these endogenous indices of oxidative stress have not yet been reported in kidney tissue of EMR-exposed rats (Ozguner, et al. 2005)

Nonenzymatic antioxidants such as vitamins E and C may act to overcome oxidative stress because they are part of the antioxidant system. Antioxidants play an important role in preventing free radical-mediated damage by directly scavenging free radicals.  $\alpha$ -Tocopherol is one of the most widely distributed naturally occurring and biologically active antioxidants in the biologic system. It protects against lipid peroxidation (LPO) most efficiently through its chain-breaking antioxidant action. Intracellularly, it is associated with lipid-rich membranes such as mitochondria and microsomes. In contrast to  $\alpha$ -tocopherol, ascorbic acid is hydrophilic and functions better in the aqueous environment than does  $\alpha$ -tocopherol. Moreover, it can restore the antioxidant properties of oxidized tocopherol, suggesting that a major function of ascorbic acid is to recycle the tocopheroxyl radical. Some studies have reported that a combination of vitamins E and C reduces LPO and apoptosis caused by toxic substances (Ramanathan, et al. 2005 and Serbecic, & Beutelspacher, 2005).

Previous studies have emphasized on the protective effect of melatonin and caffeic acid phenethyl ester on the endogenous indices of oxidative stress in kidney tissue after long-term 900 MHz EMR-exposed animals [12, 16]

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(Ozgunger et al., 2005 & oktem et al., 2005).

The present study was planned to assess the effects of electromagnetic waves emitted from ringing Mobile phone on biochemical variables and histopathological changes in serum, liver and kidney of albino rats. Also the role of antioxidant vitamins such as Vit C and E were investigated.

### **MATERIALS AND METHODS**

Male Wistar albino rats weighing 250 -350g obtained from the Experimental Animal Center of College of Pharmacy, King Saud University, in Riyadh, Saudi Arabia were used. Animal were housed, and fed with pellet chow and tap water ad libitum. Every six rats were placed in a separated cage to avoid stress of isolation or overcrowded. Seventy – two rats were randomly divided into 12 groups. Group 1(n =6) *control group* (received distilled water), group (2) received vitamin C in a dose (0.04mg V.C / kg b. wt ), group (3) received vitamin E in a dose (0.027 mg V.E / kg b. wt ), groups 4; 7 & 10 are exposed to Electromagnetic waves emitted from ringing Mobile phone at intervals (1/4,1/2&1 hr/day for 2-weeks), groups 5 ,8 & 11 are exposed to Electromagnetic waves emitted from Mobile phone at intervals (1/4,1/2&1 hr /day for 2-weeks) + Vit. C; groups 6, 9 & 12 are exposed to Electromagnetic waves emitted from Mobile phone at intervals (1/4, 1/2&1 hr/day for 2-weeks) + Vit. E . The Mobile phones are hanging at a distance about 50 cm. (nearly distance between Mobile phone and human being during ringing).

At the end of the period of this study, the animals were anesthetized by ether. Blood samples were obtained from retro-orbital venous plexus using capillary pipette method (Halpern & Pacaud, 1951) then sacrificed.

Fasting blood sample (5ml) was taken from each rats, and left for 15min to clot and centrifuged at 3500 r.p.m. for 15 min to separate serum. Serum samples were stored at -20°C in deep freeze until analysis.

#### **(1) Sampling of Organs:**

The kidneys and liver tissues were dissected out, washed with cold normal saline and divided into two parts. One part was homogenized in five volumes of phosphate buffer (0.1 M- pH 7.4) containing 1 mM EDTA with a motor-driven Teflon glass tissue homogenizer (Wills, 1966). The homogenate was centrifuged at 1200 g for 15 minutes. The supernatant was used for determination of the different biochemical parameters.

The second part was cut into two portions and prepared for histological examination. (Fixed in 10% formalin).

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### (2) Analytical Procedures:

(1) **Histological Examination:** sections were stained with hematoxylin and eosin (Hx & E) according to (Drury & Wallington, 1980) and investigated in Histology Department- National Research Center -Egypt

### (2) Biochemical assays:

#### (a) In serum:

i) Serum liver function (SGOT, SGPT, and ALP) & serum kidney function test (urea, creatinine, and uric acid) serum glucose, total protein, Albumin, Globulin and minerals ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{++}$  and  $\text{Ph}^{+++}$ ) were done in King Fahd Specialist Hospital.

ii) Hydrogen peroxide was determined by the spectrophotometric method of the spot test (Machly & Chance 1954) and which was modified by Feigl (1958).

iii) Glutathione was determined according to Beutler et al. (1963).

iv) Glutathione peroxidase was determined by the procedure of Flohe and Gunzler (1984).

v) Conjugated dienes were measured according to Ohakawa et al. (1976).

vi) Lipid hydro peroxides were measured by the method of (Buege and Aust, 1978).

#### b) In tissues:-

The levels of hydrogen peroxide, glutathione, glutathione peroxidase, conjugated diene, and lipid hydro peroxide were determined in liver, kidney as described above.

#### Statistical Analysis:-

All data of the experimental results were expressed as mean  $\pm$  S.E and statistically analysed using SPSS program.

## RESULTS

### (A) Biochemical changes

The effects of vitamin C (0.04 mg V.C/kg b.wt) and vitamin E (0.027 mg V.E /kg b.wt) pretreatment on serum, liver and kidneys of control and rats exposed to ringing Mobile phone for  $\frac{1}{4}$ ,  $\frac{1}{2}$  and 1 hr were shown in tables (1-3). As shown in these tables a significant increase in the levels of hydrogen peroxide, lipid hydro peroxide, and conjugated dienes while a significant decrease was recorded in the activities of glutathione and glutathione peroxidase when

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compared to the control group. When the rats exposed to mobile phone and treated with vitamin C & E a significant decrease in the levels of hydrogen peroxide, lipid hydroperoxide and conjugated dienes while a significant increase was observed in the activities of glutathione and glutathione peroxidase was observed.

The effects of Vitamin C (0.04 mg /Kg b.wt ) and Vitamin E (0.027mg/Kg b.wt) pretreatment on serum liver function test in control and rats exposed to ringing mobile phone for ¼, ½ and 1 hr was shown in table(4). As shown in this table no significant changes in the activities of SGOT and ALP in serum of rats exposed to ringing mobile phone for ¼, ½ and 1 hr. While a significant decrease in the activity of SGPT in rats exposed to ringing mobile phone for ½ and 1 hr when compared to control group.

The effects of Vitamin C (0.04 mg /Kg b.wt ) and Vitamin E (0.027mg/Kg b.wt) pretreatment on biochemical changes in serum of control and rats exposed to ringing Mobile phone for ¼, ½ and 1 hr was shown in tables (5,6,7). As shown in this table a significant increase in the level of serum glucose in rats exposed to ringing mobile phone for ¼ hr and Vit.C and E while no significant changes were recorded when rats exposed for ½ and 1 hr to ringing Mobile phone when compared to control group. No significant changes in kidney function test (urea, creatinine, and uric acid), total proteins, albumin and globulin in rats exposed to ringing mobile phone for ¼, ½ and 1 hr when compared to control group.

The effects of Vitamin C (0.04 mg /Kg b.wt) and Vitamin E (0.027mg/Kg b.wt) pretreatment on serum minerals in control and rats exposed to ringing mobile phone for ¼, ½ and 1 hr was shown in table(8). As shown in this table no significant changes in serum sodium, potassium, calcium and phosphorous were observed in rats exposed to ringing Mobile phone for ¼, ½ and 1 hr when compared to control group.

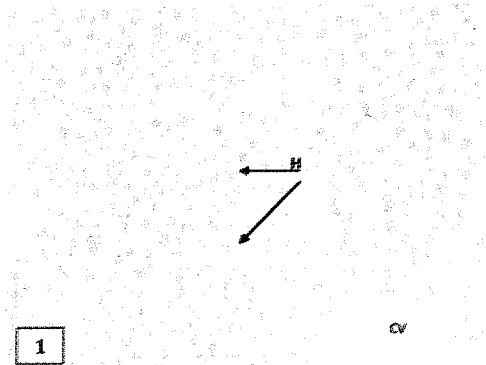
### **(B) Histopathological changes**

#### **Liver:**

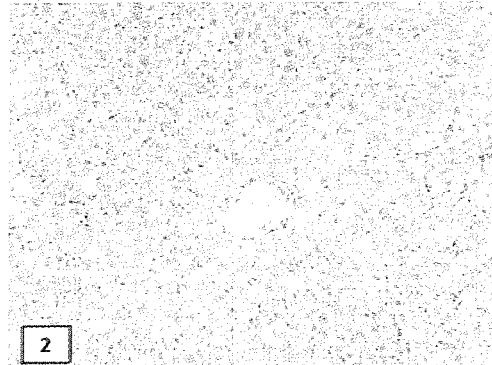
Examination of sections of liver of control and rat's received Vitamin C&E showed the normal architecture of the hepatic lobule (Figures 1-3).

Sections of rat's liver exposed to ringing mobile phone for ¼ hr showed cytoplasmic vacuolar degeneration with hyperchromatic nuclei, focal necrosis, dilatation, coagulation, hemorrhage and thickening of the central vein, together with necrosis and inflammatory cells surround it. (Figures 4-6). Sections of rat liver (exposure. ¼ Hr+ vit C&E.) showed hepatocytes and central vein structure (more or less normal hepatocytes with vesiculated nuclei similar to control). (Figures 7-8).

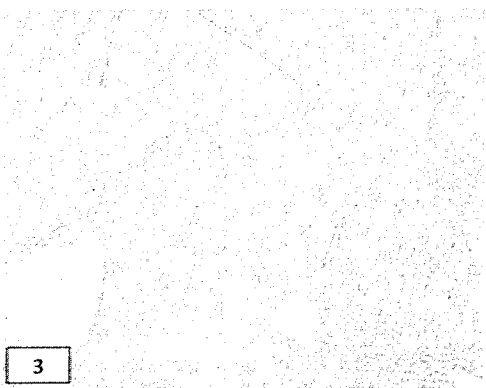
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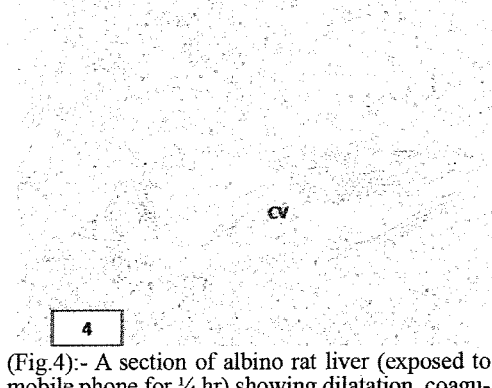
(Fig.1):- A section of albino rat liver showing the normal hepatocytes (H) architecture and the central vein (CV). (HX & E. X200)



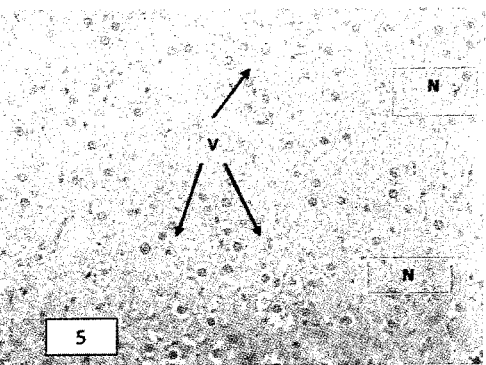
(Fig.2):- A section of albino rat liver treated with Vit-C showing normal hepatocytes architecture and the central vein. (HX& E. X200)



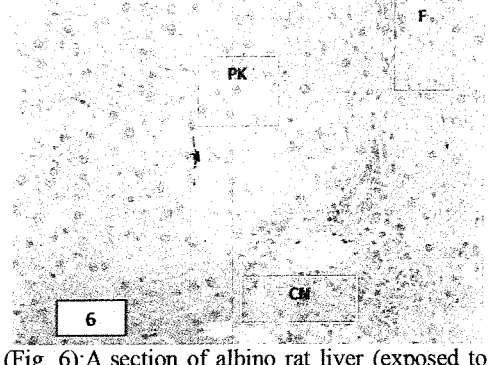
(Fig.3):- A section of albino rat liver treated with Vit-E showing more or less normal hepatocytes architecture and central veins. (HX & E. X100)



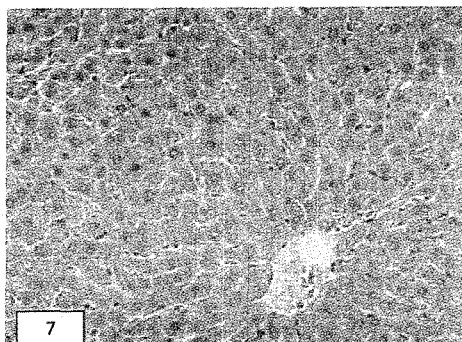
(Fig.4):- A section of albino rat liver (exposed to mobile phone for ¼ hr) showing dilatation, coagulation, hemorrhage and thickening of the central vein (CV), together with necrosis and inflammatory cells surround it. (HX & E. X200)



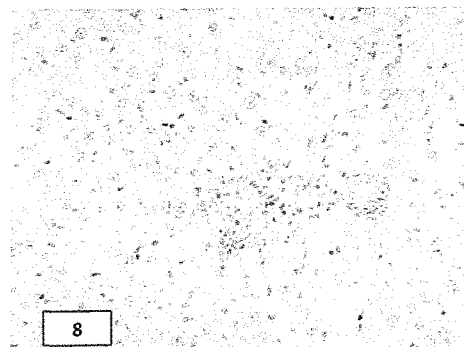
(Fig. 5): High magnification in a section of albino rat liver (exposed to mobile phone for ¼ hr) showing hepatocytes vacuolar degeneration with hyperchromatic nuclei V. Focal necrosis also present N. (HX & E. X400)



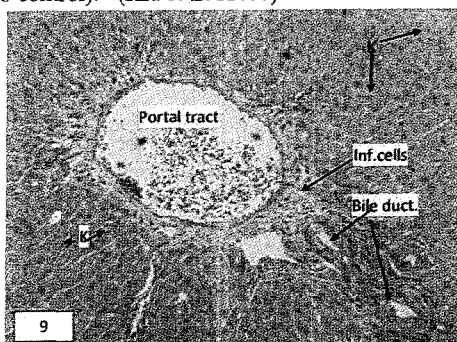
(Fig. 6): A section of albino rat liver (exposed to mobile phone for ¼ hr) showing thickening of the portal tract, elongated bile canaliculi, per portal fibrosis (F) and coagulative necrosis CN. The hepatocytes nuclei are pyknotic in periportal area PK. (HX & E. X400)



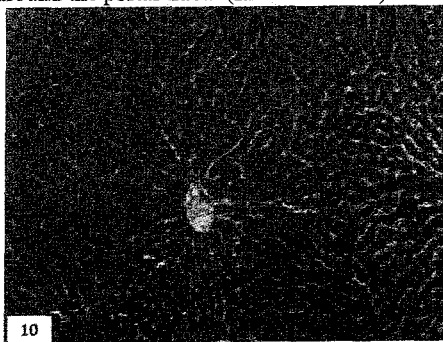
(Fig.7):- A section of albino rat liver (exposed to mobile phone for ¼ hr +Vit C) showing hepatocytes and central vein structure. (More or less normal hepatocytes with vesiculated nuclei similar to control). (HX & E. X400)



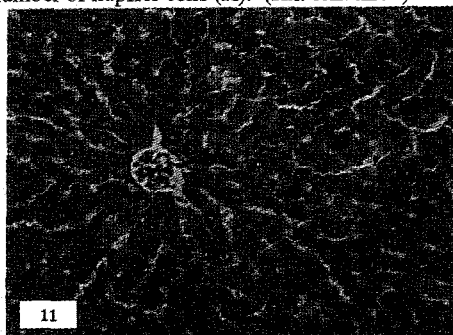
(Fig.8):-A section of albino rat liver (exposed to mobile phone for ¼ hr+ Vit E.) showing more or less normal hepatocytes with vesiculated nuclei similar to control . Few inflammatory cells are around the portal tract. (HX & E. X200)



(Fig.9):- A section of liver from a rat (exposed to mobile phone for ½ hr) showing dilatation, congestion and thickening of portal tract and other blood vessels around. Severe necrosis cellular changes and cellular infiltration at the portal tract areas the majority of bile ducts are affected. Marked increase in number of kupffer cells (K). (Hx. &E. x200)



(Fig.10) A section of liver from a rat(exposed to mobile phone for ½ hr +Vit C) showing histological structure of hepatic cells and central vein. (Hx. &E. x200)



(Fig.11):- A section of liver from a rat (exposed to mobile phone for ½ hr +Vit.E) showing improvement in histological structure of hepatic cells and central vein. The hepatic cells nuclei are vesiculated. (Hx. &E. x400)

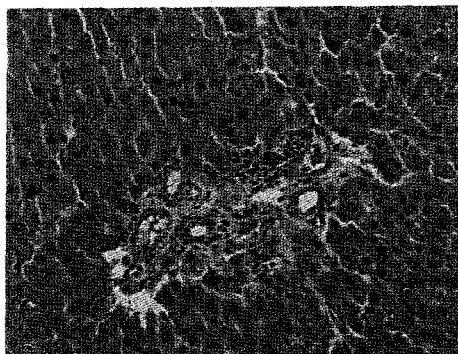


Fig. (12): A section of liver (exposed to mobile phone for 1 hr) showing per portal necrosis and the replaced by fibrous tissues and inflammatory cells. The hepatocytes reveal acidophilic necrosis and pyknotic nuclei. (Hx. &E. X 400)



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Sections of liver of rats exposed to ringing mobile phone for ½ hr showing dilatation, congestion, thickening of portal tract and other blood vessels around. Severe necrosis and cellular infiltration was observed. The majority of bile ducts are affected. Marked increase in number of kupffer cells(Figure 9). Sections in a section of rat liver (exposure. ½ hr+ Vit C&E.) revealed an improvement in histological structure of hepatic cell and central vein structure. (Figures 10-11).

Sections of liver of rats exposed to ringing mobile phone 1hr showed portal necrosis and inflammatory cells. The hepatocytes revealed acidophilic necrosis and pyknotic nuclei. (Figure 12). Sections of rat liver (exposure. 1hr+ vit C&E.) showed the normal hepatocyte and a congested central vein. (Figures 13-14).

### **Kidney:**

Examination of sections of kidney of control and rat's received Vitamin C&E showed the normal architecture of renal tubules and glomeruli (Figures 15-17).

Sections of kidney of rats exposed to ringing mobile phone ¼ hr showed renal tubules with hyaline casts in their lumen and interstitial inflammatory cells. Renal tubular with necrotic damage and pyknotic nuclei were seen in the epithelial cell lining. Glomerular mesangial cell proliferation with pyknotic nuclei, matrix expansion, glomerular necrosis and dilated blood vessels were also observed (Figure 18-20). Sections of rat kidney (exposure. ¼hr+ vit C&E.) showing a normal renal tubules and glumerulus in rats treated with Vitamin C but a few tubular damage and interstitial hemorrhage in rats treated with Vitamin E(Figures 21-22).

Sections of kidney from a rat exposed to ringing mobile phone for ½ Hr showing renal tubular damage (completely necrotic) and glomerular degeneration (Figures 23-24). Also, section of rat kidney (exposure. ½hr+ Vit C&E.) showed that the renal tubules epithelial cells appeared with cloudy swelling and the glomeruli expanded and there are extravasations of blood in between renal tubules in rats treated with Vitamin C. While the renal tubules and glomerular are nearly normal in rats treated with Vitamin E. (Figures 25-26)

Sections of kidney from a rat exposed to ringing mobile phone for 1 Hr showed completely tubular damage (necrosis) and replaced by fibrous tissues and pyknotic nuclei (Figures 27-28). Section of rat kidney (exposure. 1hr+ vit C&E.) showed normal renal tubules in rats treated with Vitamin c, while few cloudy swelling in epithelia of renal tubes were observed in rats treated with Vitamin E. (Figures 29-30).

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Table (1): Effects of vitamin C (0.04mg V.C / kg b. wt) and vitamin E (0.027 mg V.E / kg b. wt) pretreatment on biochemical parameters of serum of control and rats exposed to ringing mobile phone for ¼, ½ and 1 hr/day for 2-weeks.

Duration Of Exposure	Experimental groups	H <sub>2</sub> O <sub>2</sub>	GSH	GSH-Px	CONJ.DI	LIP.HY
		μ mol/ml	μ mol/g	nmol/mg protein	mM/ml	mM/ml
		mean ± SE	mean ± SE	mean±SE	mean± SE	mean± SE
	1-Control Distilled water	0.49±0.08	3.90±0.30	15.80±1.1	2.18 ±0.22	3.76±0.48
	2-Vitamin C	0.54±0.09	3.55±0.32	15.58±1.14	2.06 ±0.20	3.70±0.44
	3-Vitamin E	0.56±0.097	3.48±0.30	15.01±0.77	1.82 ±0.22	3.70±0.45
¼ hr	4-Mobile phone	1.01 ±0.09	2.11±0.09*	11.38 ±1.04*	3.40 ±0.42	5.25 ±0.66
	5-Mobile phone + V.C	0.72 ±0.61	3.11 ±0.19	14.25 ±1.07 <sup>a</sup>	2.40 ±0.21	5.03 ±0.44
	6-Mobile phone + V.E	0.74 ±0.04	2.96 ±0.20	12.91 ±0.97*	2.25 ±0.16	4.63 ±0.44
½ hr	7-Mobile phone	2.13 ±0.24*	1.45±0.11*	9.00 ±0.67*	4.60 ±0.54	5.70 ±0.62*
	8-Mobile phone + V.C	0.71 ±0.10 <sup>b</sup>	3.03 ±0.22 <sup>b</sup>	12.88±0.80* <sup>b</sup>	2.66 ±0.29	5.05 ±0.70
	9-Mobile phone + V.E	0.79 ±0.02 <sup>b</sup>	3.01 ±0.15 <sup>b</sup>	13.30±0.82* <sup>b</sup>	3.08 ±0.26	4.96 ±0.63
1 hr	10-Mobile phone	3.39 ±0.33*	1.08±0.08*	6.60 ±0.45*	6.00 ±0.60*	6.63 ±0.67*
	11-Mobile phone + V.C	0.94 ±0.14 <sup>c</sup>	2.76 ±0.15 <sup>c</sup>	10.63±0.48* <sup>c</sup>	3.50 ±0.06 <sup>c</sup>	5.51 ±0.68*
	12-Mobile phone + V.E	1.38 ±0.05 <sup>c</sup>	2.76 ±0.27 <sup>c</sup>	10.60±0.48* <sup>c</sup>	3.71 ±0.04 <sup>c</sup>	5.28 ±0.45

- The results are given as the mean ± SE of 6 rats.

-\*,a, b,c represent significant change in comparison with the normal control or ringing Mobile phone treated rats respectively at P <0.05 .

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Table (2): Effects of vitamin C (0.04mg V.C / kg b. wt) and vitamin E (0.027 mg V.E / kg b. wt) pretreatment on liver biochemical parameters of control and rats exposed to ringing Mobile phone for ¼, ½ and 1 hr/day for 2-weeks.

Duration Of Exposure	Experimental groups	H <sub>2</sub> O <sub>2</sub>	GSH	GSH-Px	CONJ.DI	LIP.HY
		µ mol/100ml Wet.wt	µ mol/g Wet.wt	nmol/mg protein	mM/100ml Wet.wt	mM/100ml Wet.wt
		mean ± SE	mean ± SE	mean ± SE	mean ± SE	mean ± SE
	1-Control Distilled water	0.79± 0.109	4.41± 0.56	18.38± 0.92	1.18± 0.082	0.70± 0.087
	2-Vitamin C	0.85± 0.10	4.61± 0.55	16.68± 1.01	1.13± 0.074	0.82± 0.099
	3-Vitamin E	0.95± 0.13	4.66± 0.53	18.91± 0.77	1.27± 0.081	0.87± 0.11
¼ hr	4-Mobile phone	1.68± 0.29	3.66± 0.53*	12.30± 0.92*	2.21± 0.16*	1.41± 0.13*
	5-Mobile phone + V.C	1.10± 0.15	3.20± 0.30	15.96± 1.10* <sup>a</sup>	1.47± 0.13	1.28± 0.060*
	6-Mobile phone + V.E	1.10± 0.12	3.58± 0.28*	15.18± 0.98* <sup>a</sup>	1.53± 0.12	1.49± 0.070*
½ hr	7-Mobile phone	2.73± 0.18*	2.95± 0.46*	9.45± 0.58*	4.33± 0.51*	3.20± 0.45*
	8-Mobile phone + V.C	1.87± 0.09*	3.08± 0.12*	13.70± 0.78* <sup>b</sup>	1.83± 0.091*	1.64± 0.055*
	9-Mobile phone + V.E	1.92± 0.14*	2.54± 0.24*	11.99± 0.63* <sup>b</sup>	1.96± 0.13	1.66± 0.068*
1 hr	10-Mobile phone	4.64± 0.58*	1.74± 0.32*	8.71± 0.35*	6.04± 0.37*	6.85± 0.85*
	11-Mobile phone + V.C	1.30± 0.18 <sup>c</sup>	3.30± 0.42 <sup>c</sup>	15.61± 0.86* <sup>c</sup>	2.56± 0.30 <sup>c</sup>	1.87± 0.23 <sup>c</sup>
	12-Mobile phone + V.E	1.56± 0.06 <sup>c</sup>	3.02± 0.36* <sup>c</sup>	16.30± 0.86 <sup>c</sup>	2.57± 0.31 <sup>c</sup>	1.91± 0.22 <sup>c</sup>

- The results are given as the mean ± SE of 6 rats.

-\*, a, b, c represent significant change in comparison with the normal control or ringing Mobile phone treated rats respectively at P <0.05 .

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Table (3): Effects of vitamin C (0.04mg V.C / kg b. wt) and vitamin E (0.027 mg V.E / kg b. wt) pretreatment on kidney of control and rats exposed to ringing Mobile phone for ¼, ½ and 1 hr.

Duration Of Exposure	Experimental groups	H2O2	GSH	GSH-Px	CONJ.DI	LIP.HY
		$\mu$ mol/100ml Wet.wt	$\mu$ mol/g Wet.wt	nmol/mg protein	mM/100ml Wet.wt	mM/100ml Wet.wt
		mean $\pm$ SE	mean $\pm$ SE	mean $\pm$ SE	mean $\pm$ SE	mean $\pm$ SE
	1-Control Distilled water	4.61 $\pm$ 0.39	0.75 $\pm$ 0.042	7.83 $\pm$ 0.42	2.06 $\pm$ 0.103	1.21 $\pm$ 0.092
	2-Vitamin C	4.66 $\pm$ 0.44	0.76 $\pm$ 0.043	7.95 $\pm$ 0.44	2.08 $\pm$ 0.16	1.28 $\pm$ 0.093
	3-Vitamin E	4.91 $\pm$ 0.37	0.75 $\pm$ 0.040	7.94 $\pm$ 0.59	2.11 $\pm$ 0.15	1.16 $\pm$ 0.12
¼ hr	4-Mobile phone	4.95 $\pm$ 0.37	0.77 $\pm$ 0.044	8.11 $\pm$ 0.47	2.25 $\pm$ 0.19	1.21 $\pm$ 0.15
	5-Mobile phone + V.C	5.10 $\pm$ 0.32	0.82 $\pm$ 0.043	7.98 $\pm$ 0.41	2.13 $\pm$ 0.18	1.09 $\pm$ 0.11
	6-Mobile phone + V.E	5.60 $\pm$ 0.25	0.82 $\pm$ 0.040	7.52 $\pm$ 0.34	2.25 $\pm$ 0.13	1.06 $\pm$ 0.084
½ hr	7-Mobile phone	11.12 $\pm$ 0.66*	0.42 $\pm$ 0.030*	4.22 $\pm$ 0.34*	5.60 $\pm$ 0.36*	3.41 $\pm$ 0.39*
	8-Mobile phone + V.C	8.91 $\pm$ 0.43* <sup>b</sup>	0.77 $\pm$ 0.021 <sup>b</sup>	6.63 $\pm$ 0.24* <sup>b</sup>	3.86 $\pm$ 0.28* <sup>b</sup>	2.21 $\pm$ 0.30
	9-Mobile phone + V.E	8.38 $\pm$ 0.29* <sup>b</sup>	0.80 $\pm$ 0.017 <sup>b</sup>	6.48 $\pm$ 0.27* <sup>b</sup>	3.91 $\pm$ 0.23* <sup>b</sup>	2.06 $\pm$ 0.32
1 hr	10-Mobile phone	15.76 $\pm$ 0.79*	0.42 $\pm$ 0.093*	2.68 $\pm$ 0.24*	7.15 $\pm$ 0.29*	4.36 $\pm$ 0.49*
	11-Mobile phone + V.C	9.63 $\pm$ 0.23* <sup>c</sup>	0.62 $\pm$ 0.028* <sup>c</sup>	5.29 $\pm$ 0.17* <sup>c</sup>	3.70 $\pm$ 0.22* <sup>c</sup>	2.68 $\pm$ 0.40
	12-Mobile phone + V.E	9.46 $\pm$ 0.35* <sup>c</sup>	0.68 $\pm$ 0.032 <sup>c</sup>	5.78 $\pm$ 0.26* <sup>c</sup>	4.16 $\pm$ 0.27* <sup>c</sup>	3.70 $\pm$ 0.40*

- The results are given as the mean  $\pm$  SE of 6 rats.

-\*,a, b,c represent significant change in comparison with the normal control or ringing Mobile phone treated rats respectively at P <0.05 .

## PHYSIOLOGICAL CHANGES IN LIVER AND KIDNEY OF RATS

Table (4): Effect of vitamin c (0.04 mg v. c / kg b. wt) and vitamin E (0.027 mg V.E / kg b. wt) pretreatment on liver function enzyme of control and rat exposed to ringing mobile phone for ¼, ½ and 1 hr.

Duration Of Exposure	Experimental groups	SGPT U/L	SGOT U/L	ALP U/L
		mean ±SE	mean ±SE	mean ±SE
	1-Control Distilled water	295.33 ±20.83	238.5 ±49.99	225 ±23.85
	2-Vitamin C	255 ±17.18	256 ±10.39	164.83 ±14.24
	3-Vitamin E	286.17 ±29.46	286.2 ±22.21	162.17 ±6.61
¼ hr	4-Mobile phone	246 ±34.48	292 ±26.99	188 ±22.14
	5-Mobile phone + V.C	204 ±19.62	258.17 ±30.23	159 ±23.88
	6-Mobile phone + V.E	199 ±15.42	301 ±13.66	182.60 ±16.12
½ hr	7-Mobile phone	145.67 ±10.12*	273.67 ±24.27	196.67 ±15.19
	8-Mobile phone + V.C	173.33 ±7.08*	344.67 ±18.89	212.67 ±22.38
	9-Mobile phone + V.E	135.83 ±10.25*	307.67 ±13.63	204.33 ±11.42
1 hr	10-Mobile phone	116.2 ±4.0*	229 ±12.31	230 ±21.3
	11-Mobile phone + V.C	108.80 ±5.41*	193.2 ±7.70	171.4 ±18.74
	12-Mobile phone + V.E	137.80 ±9.85*	249.80 ±41.90	205 ±33.29

- The results are given as the mean ±SE of 6 rats.
- \*,a, b, c represent significant change in comparison with the normal control or ringing Mobile phone treated rats respectively at P <0.05 .

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Table (5): Effects of vitamin C (0.04mg V.C / kg b. wt) and vitamin E (0.027 mg V.E / kg b. wt) pretreatment on serum glucose of control and rats exposed to ringing Mobile phone for ¼, ½ and 1 hr.

Duration Of Exposure	Experimental groups	Glucose m mol/L
		mean ±SE
	1-Control Distilled water	3.65±.673
	2-Vitamin C	6.34±0.31*
	3-Vitamin E	7.32±0.17*
¼ hr	4-Mobile phone	10.88±0.87*
	5-Mobile phone + V.C	8.93±0.58*
	6-Mobile phone + V.E	6.24±0.03*
½ hr	7-Mobile phone	3.90±0.80
	8-Mobile phone + V.C	4.95±0.80
	9-Mobile phone + V.E	4.49±0.87
1 hr	10-Mobile phone	5.85±0.45
	11-Mobile phone + V.C	4.75±0.64
	12-Mobile phone + V.E	6.39±0.4

-The results are given as the mean ±SE of 6 rats.

-\*, a, b, C represent significant change in comparison with the normal control or ringing Mobile phone treated rats respectively at P <0.05

## PHYSIOLOGICAL CHANGES IN LIVER AND KIDNEY OF RATS

Table (6): Effects of vitamin C (0.04mg V.C / kg b. wt) and vitamin E (0.027 mg V.E / kg b. wt) pretreatment on kidney function parameters of control and rats exposed to ringing Mobile phone for ¼, ½ and 1 hr.

Duration Of Exposure	Experimental groups	Urea	Creatnin	Uric acid
		m mol/L mean ±SE	μ mol/L mean ±SE	μ mol/L mean ±SE
	1-Control Distilled water	10.79 ± 1.04	54.83 ± 2.37	181.33 ± 20.56
	2-Vitamin C	9.12 ± 0.84	54.83 ± 3.48	155.17 ± 22.34
	3-Vitamin E	9.55 ± 2.21	60.67 ± 1.58	174.33 ± 15.43
¼ hr	4-Mobile phone	7.54 ± 0.11	55.67 ± 67	213.67 ± 50.44
	5-Mobile phone + V.C	8.52 ± 0.23	53.16 ± 3.51	213.83 ± 67.91
	6-Mobile phone + V.E	6.48 ± 0.34	53.40 ± 2.84	162.60 ± 22.67
½ hr	7-Mobile phone	6.15 ± 0.17	46.00 ± 1.00	165.33 ± 19.02
	8-Mobile phone + V.C	6.94 ± 0.48	42.67 ± 1.69	181.00 ± 23.51
	9-Mobile phone + V.E	7.62 ± 0.81	42.17 ± 1.64	258.83 ± 41.75
1 hr	10-Mobile phone	6.51 ± 0.21	40.20 ± 1.62	155.20 ± 28.28
	11-Mobile phone + V.C	6.15 ± 0.55	39.80 ± 1.80	139.40 ± 20.88
	12-Mobile phone + V.E	6.58 ± 0.69	42.60 ± 1.03	196.40 ± 35.65

-The results are given as the mean ±SE of 6 rats.

-,\*,a, b ,C represent significant change in comparison with the normal control or ringing Mobile phone treated rats respectively at P <0.05

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Table (7): Effects of vitamin C (0.04mg V.C / kg b. wt) and vitamin E (0.027 mg V.E / kg b. wt) pretreatment on serum biochemical parameters of control and rats exposed to ringing Mobile phone for ¼, ½ and 1 hr.

Duration Of Exposure	Experimental groups	T. protein	Albumin	Globulin
		g/L	g/L	g/L
		mean ±SE	mean ±SE	mean ±SE
	1-Control Distilled water	75.66±4.57	40.33±.938	35.33±4.55
	2-Vitamin C	77.88±0.59	35.62±0.97	42.26±0.56
	3-Vitamin E	82.68±2.67	36.81±0.66	45.87±6.19
¼ hr	4-Mobile phone	58.75±3.19	32.44±1.32	26.31±1.96
	5-Mobile phone + V.C	65.43±2.84	33.78±1.33	31.64±1.61
	6-Mobile phone + V.E	63.70±2.61	32.45±.60	31.24±3.18
½ hr	7-Mobile phone	61.57±.92	34.10±.56	27.47±1.12
	8-Mobile phone + V.C	62.25±2.08	33.84±1.09	27.92±1.50
	9-Mobile phone + V.E	64.73±1.59	35.69±.649	29.02±1.08
1 hr	10-Mobile phone	62.76±1.41	35.91±.760	26.84±1.02
	11-Mobile phone + V.C	61.20±1.53	33.42±.691	27.79±1.39
	12-Mobile phone + V.E	62.48±1.57	34.81±1.35	27.68±1.22

-The results are given as the mean ±SE of 6 rats.

-,\*,a, b ,C represent significant change in comparison with the normal control or ringing Mobile phone treated rats respectively at P <0.05



**PHYSIOLOGICAL CHANGES IN LIVER AND KIDNEY OF RATS**

Table (8): Effect of vitamin c (0.04 mg v. c / kg b. wt) and vitamin E (0.027 mg V.E / kg b. wt) pretreatment on serum minerals of control and rat exposed to ringing mobile phone for ¼, ½ and 1 hr.

Duration Of Exposure	Experimental groups	$Na^+$	$K^+$	$Ca^{++}$	$Ph^{+++}$
		m mol/L	m mol/L	mol/L	mol/L
		mean ±SE	mean ±SE	mean ±SE	mean ±SE
	1-Control Distilled water	157.17 ±0.90	5.34 ±0.13	3.04 ±0.03	2.98 ±0.16
	2-Vitamin C	152.70 ±0.84	6.20 ±0.69	2.89 ±0.02	2.83 ±0.17
	3-Vitamin E	162.50 ±6.30	5.81 ±0.23	2.96 ±0.06	3.32 ±0.27
¼ hr	4-Mobile phone	149.50 ±1.78	5.862±0.41	2.62 ±0.05	3.88 ±0.33
	5-Mobile phone + V.C	151.83 ±1.42	6.32 ±0.37	2.78 ±0.04	3.19 ±0.25
	6-Mobile phone + V.E	150.40 ±1.80	6.40 ±0.23	2.68 ±0.02	3.62 ±0.38
½ hr	7-Mobile phone	148.17 ±1.30	5.19 ±0.32	2.71 ±0.04	3.55 ±0.11
	8-Mobile phone + V.C	148.33 ±1.63	5.82 ±0.30	2.66 ±0.04	3.44 ±0.14
	9-Mobile phone + V.E	151.67 ±1.98	6.87 ±0.59	2.76 ±0.09	3.99 ±0.22
1 hr	10-Mobile phone	150.00 ±1.09	6.47 ±0.43	2.67 ±0.04	3.87 ±0.17
	11-Mobile phone + V.C	147.80 ±0.58	5.66 ±0.28	2.53 ±0.06	3.37 ±0.20
	12-Mobile phone + V.E	150.00 ±2.39	6.95 ±0.90	2.76 ±0.11	3.72 ±0.14

- The results are given as the mean ±SE of 6 rats.

\*,a, b, c represent significant change in comparison with the normal control or ringing Mobile phone treated rats respectively at P <0.05 .

## DISCUSSION

The use of Mobile phones is currently one of the fastest growing technological developments. The close proximity of the antenna of such advice to the abdominal organs has raised concerns about the biological interactions between EMR and the Kidney. The direct biological effects of exposure to Mobile phone have not been studied extensively.

The present study has shown that, exposure to EMR from ringing Mobile phone with a frequency of 900 MHz (for ¼, ½ and 1 Hr) has a significant increase in the levels of H<sub>2</sub>O<sub>2</sub>, Conjugated diene and lipid hydroperoxide in serum, liver and kidney of rats. While a significant decreased in the levels of glutathione and glutathione peroxidase was recorded in serum, liver and kidney of rats when compared to the control group.

The changes in activities of glutathione and glutathione peroxidase are in agreement with the results of some previous studies (Ozguner et.al, 2005), suggesting that ROS were generated under the experimental conditions employed.

Decreased GSH concentration may be due to higher consumption of GSH for scavenging the higher production of free radicals. The lower GSH concentration may have some relation on to the increased SOD activity. The endogenous GSH has a protective function in Scavenging radicals and in molecular repair. However, such scavenging can set up a superoxide dependent chain production of H<sub>2</sub>O<sub>2</sub> and oxidized glutathione, which would, oxidatively stress the cell. Therefore, the increased SOD activity may be a response to suppress the higher chain oxidation of GSH or a response to balance the decreased GSH concentration. Thus, the up regulated SOD activity converts O<sup>-2</sup> to H<sub>2</sub>O<sub>2</sub> and down regulated GSH concentration leads to the insufficient detoxification and accumulation of H<sub>2</sub>O<sub>2</sub> in the system. H<sub>2</sub>O<sub>2</sub> is known to be converted to hydroxyl radical in the presence of iron rapidly, which is the most damaging form of ROS. Note that the balance between GSH-Px and SOD appears to be important for the cellular resistance to oxidative stress (Amstad et.al, 1994).

GSH-Px is an important antioxidant enzyme that plays a role in elimination of H<sub>2</sub>O<sub>2</sub> and lipid hydro peroxides and reduces peroxides by using reduced glutathione as a hydrogen donor (Ilhan et.al, 2004 & Irmak et.al, 2002, 2003)

GSH-Px converts H<sub>2</sub>O<sub>2</sub> to water and oxygen. GSH-Px uses H<sub>2</sub>O<sub>2</sub> to oxidized reduced glutathione (GSH). Decreased activity of GSH-Px leads to accumulation of H<sub>2</sub>O<sub>2</sub>, which in the presence of iron and copper promotes the Fenton reaction to yield OH<sup>•</sup>. Hydroxyl radical is the most reactive form of oxygen radicals that can initiate a chain reaction to generate numerous toxic reactants (Coyle &Puttfarcken, 1993 &Stadtman, 1998). A histopathological changes in liver and kidney agree with the obtained results and proved a biochemical changes.

**PHYSIOLOGICAL CHANGES IN LIVER AND KIDNEY OF RATS**

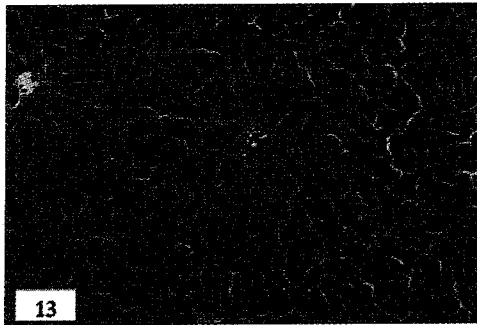


Fig. (13):- A section of liver from a rat (exposed to mobile phone for 1 hr + vitamin C) showing the normal hepatocytes and congested central veins (Hx. & E. X 100)

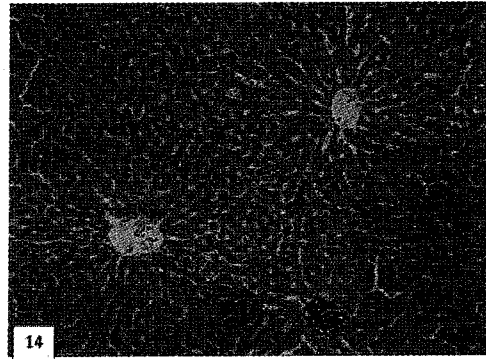
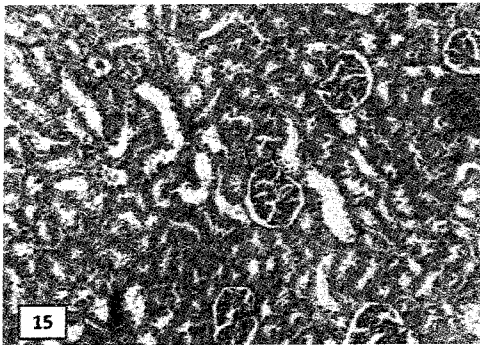
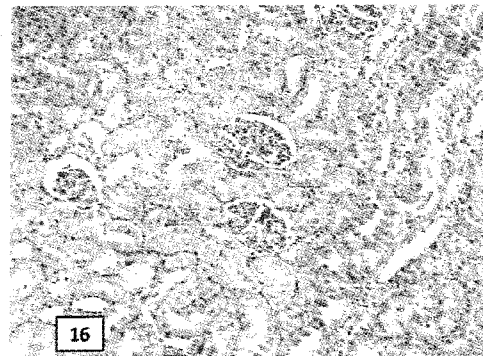


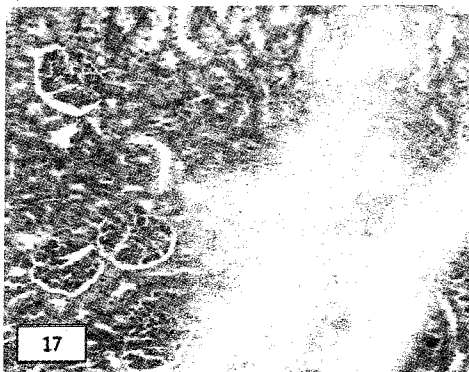
Fig. (14): A section of liver from a rat (exposed to mobile phone for 1hr +vitamin E) showing the normal hepatocytes and A congested central vein. (Hx. & E. X 100).



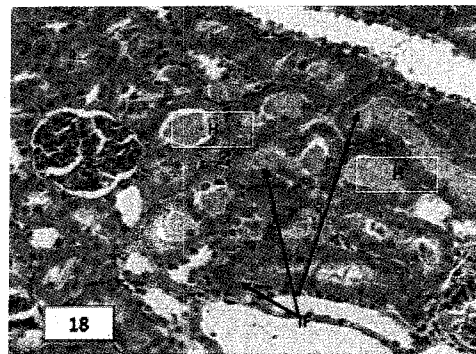
(Fig.15):- A section of a control albino rat kidney is showing the normal renal tubules (RT) and glomeruli (G). (Hx. & E. X 200).



( Fig.16):- A section of albino rat kidney treated with VIT-C showing more or less normal renal tubules and glomerul ( HX & E. X200).

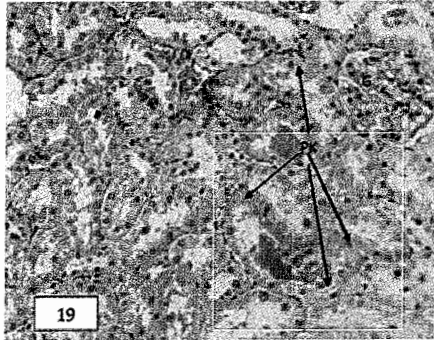


( Fig.17):- A section of albino rat kidney treated with VIT-E showing more or less normal renal tubules ( HX & E. X200 )

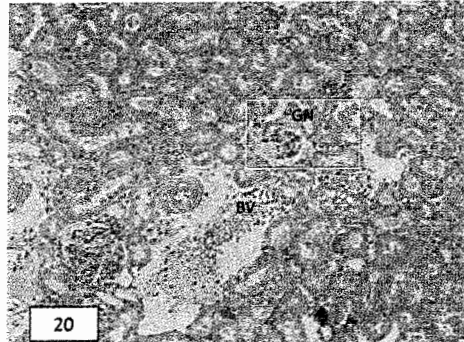


( Fig.18):- A section of albino rat kidney (exposed to mobile phone for ¼ hr ) showing Renal tubules with hyaline casts in their lumen (H) and interstitial inflammatory cells IF. (HX & E. X400)

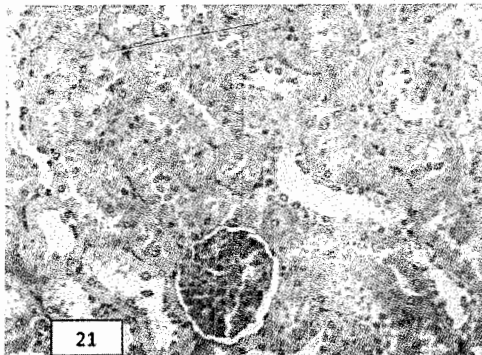
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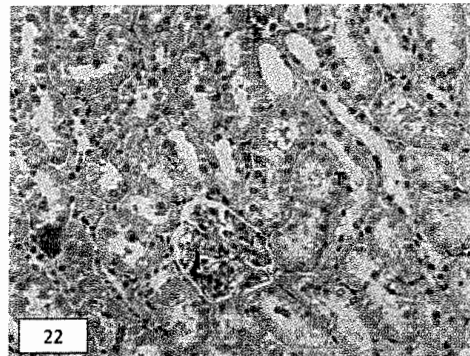
( Fig.19):- A ph section of albino rat kidney (exposed to mobile phone for ¼ hr) showing some renal tubular with necrotic damage and pyknotic nuclei (PK) in the epithelial cell lining (below right).Glomerular mesangial cell proliferation with pyknotic nuclei (G ) and matrix expansion .Notice the vacuolar degeneration in glomerular tufts and interstitial hemorrhage (HX & E. X400)



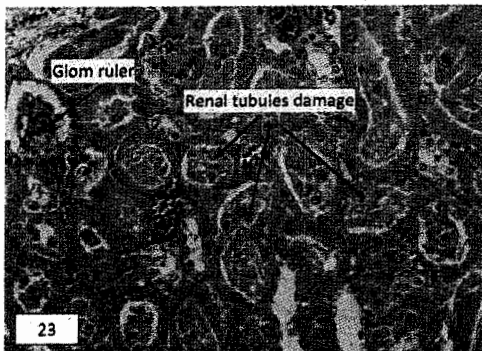
(Fig.20):- A section in albino rat kidney (exposed to mobile phone for ¼ hr) showing glomerular necrosis (GN) and dilated blood vessels B. (HX & E. X200)



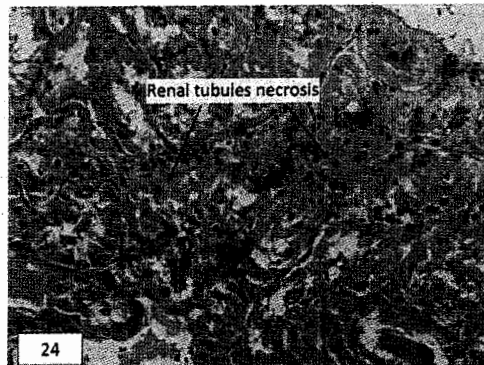
( Fig.21):- A section of albino rat kidney (exposed to mobile phone for ¼ hr +Vit C) showing renal tubules and glomerulus. (HX & E. X400)



(Fig.22):- A section of albino rat kidney (exposed to mobile phone for ¼ hr +Vit E) showing few tubular damage (T) and interstitial hemorrhage. (HX & E. X200)

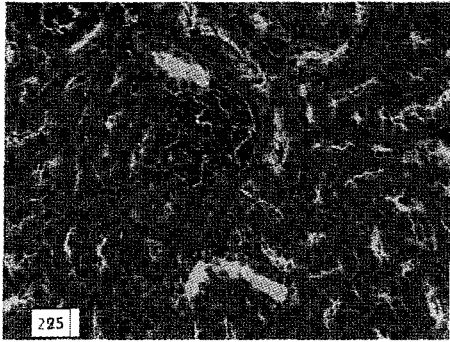


(Fig.23):- A section of kidney from a rat (exposed to mobile phone for ½ hr) showing renal tubular damage and glomerular degeneration. (Hx. & E. x400)

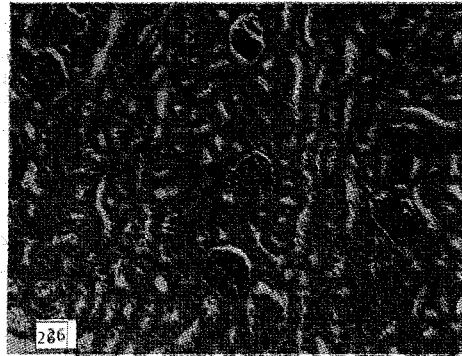


(Fig 24):- A section of kidney from a rat (exposed to mobile phone for ½ hr) showing renal tubular completely necrotic and replaced by inflammatory cells and homogenous acidophilic substances. (Hx. & E. x400)

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(Fig.25):- A section of kidney from a rat (exposed to Mobile phone for  $\frac{1}{4}$  hr +Vit C) showing the renal tubules and glomeruli. The renal tubules epithelial cells revealed cloudy swelling and the glomeruli expanded and there is extravasation of blood in between renal tubules. (Hx. &E. x400)



(Fig.26):- A section of kidney from a rat (exposed to mobile phone for  $\frac{1}{2}$  hr +Vit C) showing the renal tubules and glomeruli nearly normal. (Hx.&E. x200)

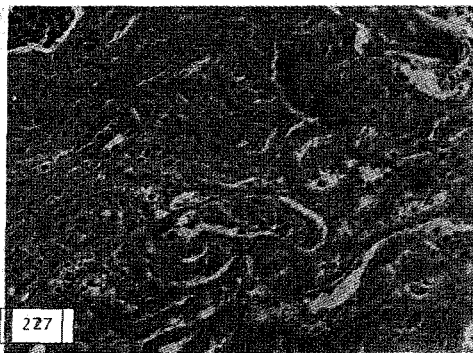


Fig. (27): A section of kidney from a rat (exposed to mobile phone for 1 hr) showing completely tubular damage and replaced by fibrous tissues and pyknotic nuclei. (Hx. &E. X 400)

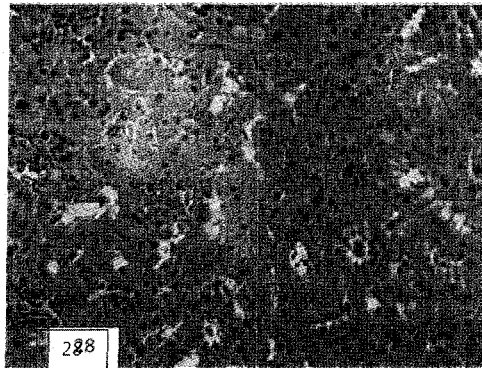


Fig. (28): A section of kidney from a rat (exposed to mobile phone for 1 hr) showing completely tubular necrosis and replaced by acidophilic materials and blood cells. (Hx. &E. X 400)

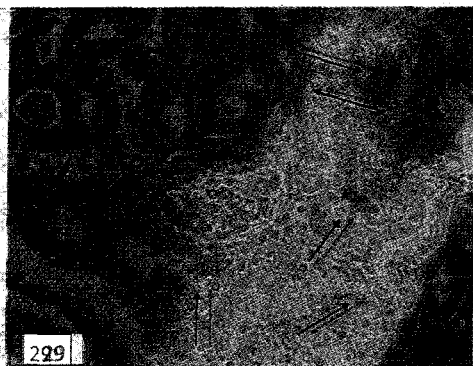


Fig. (29): A section of kidney from a rat (exposed to mobile phone for 1 hr + vitamin C) showing most of renal tubules are normal. (Hx. &E. X 100)

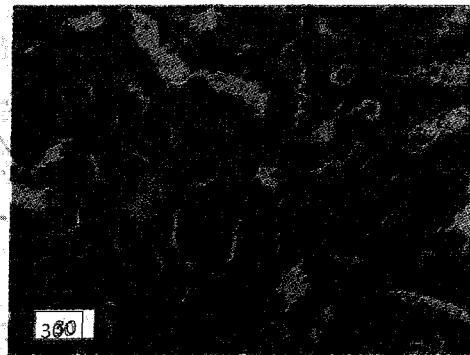


Fig. (30): A section of kidney from a rat (exposed to mobile phone for 1 hr +Vit E) showing the tubular cloudy swelling and few having hyaline casts. (Hx. &E. X 400)

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The present study also found that treatment of rats with mobile phone for ¼, ½, 1 hr with powerful antioxidants vitamins such as C &E was found to be blocking the adverse effect of EMR. Since vit. E, the most important lipophilic antioxidant resides mainly in the cell membranes, thus helping to maintain membrane stability [29] (Baker et.al, 1996). Vitamin C is the most important hydrophilic free radical scavenger in extracellular fluids ;it traps radicals in the aqueous phase and protects biomembranes from per oxidative damage (Harapanhall et.al, 1996). In addition to providing its antioxidant effects, Vit. C is involved in the regeneration of tocopherol from tocopheroxyl radicals in the membrane. Thus, vitamins E and C may have interactive effects (Stoyanovsky et.al, 1995). Normal histopathology of liver and kidney after treatment with Vit.C and E proved a role of Vit.C and E in the protection of tissue damage (liver and kidney) from exposure to mobile phone.

The present study has shown that, no significant changes in serum GOT, ALP, Urea, Creatinine, Uric acid, Total protein, Albumin, Globulin and minerals (Na, K, Ca, Ph). but a significant increase in serum glucose (rats exposed to ringing mobile phone for ¼ hr and Vit C&E) was recorded a significant decrease in GPT (rats exposed to ringing Mobile phone for ½ and 1 hr).

This study provides three important findings relating to oxidative damage in experimental exposure to Mobile phone. Firstly, Mobile phones cause oxidative damage biochemically by increasing the levels of H<sub>2</sub>O<sub>2</sub>, lipid hydroperoxide, and conjugated diene and decreasing the activities of Glutathione and Glutathione peroxidase in serum, liver and kidney of rats exposed to ringing mobile phone. Secondly, ringing Mobile exposure to liver and kidney of rats caused a histopathological change. Thirdly, oral treatment with the antioxidant vitamins such as C&E prevented oxidative damage and pathological changes in the liver and kidney tissue.

In Conclusion, our results may indicate a probable role of Ros in the adverse effects of EMR from mobile phone. The potent free radical scavenger and antioxidant agent's such as vitamins C and E seem to be highly promising agents for protecting liver and kidney tissues from oxidative damage and preventing organ dysfunction as a result of exposure to ringing Mobile phone.

## **RECOMMENDATIONS**

We recommended by the following:-

- Please, put the Mobile phone far the human being by a distance more than 50 cm.

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- Take care, when used Mobile phone uses vitamin C&E to ameliorate the deleterious effect of Mobile phone on serum, liver and kidney.

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