



## **CURCUMA LONGA AMELIORATES; AMORPHOUS, APOPTOTIC, INFLAMMATORY AND NUCLEAR CHANGES CAUSED BY 2G CELL PHONE RADIATION EXPOSURE IN MYOCARDIUM OF ALBINO RATS.**

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### **ABSTRACT**

This study on sixty albino rats divided in four groups. Group A was control, B exposed to radiations one hour daily (Cell phone 2G 900-1900 MHz), C given Curcuma longa (turmeric) orally (166.5mg/kg/day) emulsified with olive oil and D exposed to both radiations and Curcuma longa orally. After 2 month of exposure animals, sacrificed by cervical dislocation then heart dissected out, preserved, processed and stained with H & E examined under microscope. Observations of myocardium in group B shown amorphous deposits, inflammation and mononuclear infiltration, congestion, karyopyknosis. while structural enhancement in group C than group A and minimal effects in group D than group B. Concluded that Regular cell phone exposure has produced, alteration in cellular and nuclear structure which could be minimized by using turmeric in proper manner.

**Keywords:** Cell phone, Radiation, Myocardium, Inflammation, Curcuma longa.

### **INTRODUCTION**

The cell phone (mobile phone) use has been the fastest form of communication in the form of continuous regular mobile use. Exposure of radiofrequency radiation having that use of electronic communication is not limited to mobile phone only but also extended to FM towers, base stations, TV towers, AM tower, Wi-Fi hot spots, MRI, microwave oven and cell towers producing similar exposure to radiofrequency radiation. Higher the frequency, and power of exposure greater danger will be the radiation exposure. The radiation pattern of a cell tower is highest at its horizontal frontal regions of dish antenna. Antennas on cell tower transmit in the frequency range of 869-890 MHz (CDMA), 935-960 MHz (GSM 900), 1805-1880 MHz (GSM 1800), 2110-2170 MHz (3G) Every day, we are swimming in a sea of electromagnetic radiation (EMR) produced by electrical appliances, power lines, and wiring in buildings that are part of modern life. RF signals are certainly an invisible form of pollution, From the dishwasher and microwave oven in the kitchen and the clock radio next to your bed, to the cellular phone you hold to your ear, and heart sometimes for hours each day, exposure to EMR is growing and becoming a serious health

threat. (Cox, D.R. et al 2003). Most common complaints and symptoms are fatigue, dizziness, buzzing in the head, forgetful memory, headache, loss of concentration, visual disorders, palpitations of the heart, sleep disturbances, depression, and cardiovascular problems. Many of these related to changes in electrical activity of brain and heart. Specific Absorption Rate (SAR) is the rate at which the radiation energy is absorbed by the body. The SAR limit stated in ICNIRP guide lines should not exceed 2.0 watts/kg averaged over 10gms of human tissue. The SAR value of the device may change depending upon the factors such as use of accessories or enhancements and device proximity to a network. It is prefer to use your device when the signal quantity is good. People having active medical implants should preferably keep the device at least 15 cm away from the implant and maintain at least 15 mm distance from the device. One well-understood effect of microwave radiation is dielectric heating, in which any dielectric material (such as living tissue) is heated by rotations of polar molecules induced by the electromagnetic field. The brain's blood circulation is capable of disposing of excess heat by increasing local blood flow. Studies have shown that exposure to the RF waves emitted from mobiles can cause (Dasdag S. et al 2000) slightly raised blood pressure at the time of use, pressure returning to normal when use is stopped direct brain warming after prolonged use, mild fatigue after prolonged use. Our bodies recognize the information carrying wave as an "invader," setting in place protective biochemical reactions that alter physiology and cause biological problems that include intracellular free-radical build up, leakage in the blood-brain barrier, genetic damage, disruption of intercellular communication, and an increase in the risk of tumours. The health dangers of recognizing the signal, therefore, aren't from direct damage, but rather are due to the biochemical responses in the cell .Cellular energy is now used for protection rather than metabolism. Cell membranes harden, keeping nutrients out and waste products in. Waste accumulating inside the cells creates a higher concentration of free radicals, leading to both disruption of DNA repair (micronuclei) and cellular dysfunction.(Diema Elisabeth, 2005) Unwanted cell death occurs, releasing the micronuclei from the disrupted DNA repair into the fluid between cells (interstitial fluid), where they are free to replicate and proliferate. Damage occurs to proteins on the cell membrane, resulting in disruption of intercellular communication. Increased blood brain barrier permeability, allowing unwanted dangerous chemicals reaching into the brain tissue, resulting in damage.

The electromagnetic wave spectrum is divided into ionizing radiation such as ultraviolet and X-rays and non-ionizing radiation such as radiofrequency (RF), which includes WiFi, cell phones, and Smart Meter wireless communication. No one learned from the lessons of Madam and Pierre Curie who, tinkered by radium hundred years ago and died from radiation poisoning. It has long been recognized that ionizing radiation can have a negative impact on health. However, the effects of non-ionizing radiation on human health recently have been seen. The radiation effect on health are being investigated at molecular level, when a cell is exposed to radiation its DNA may be damaged and cell with damaged DNA either die (due to apoptosis under oxidative cell stress due to free radical injury caused by radiation exposure) or attempt to repair the damage may resulting into normal recovery if repair is not accurate or disrepair cell may develop into a cancer depending on the site of DNA damage. The cells responsible for immunity (lymphocyte) decreases as a result resistant to viruses and pathogens decreases resulting into persistent inflammation and accelerated aging. Thus, a chain reaction of free radicals occurs, leading to damaging biological systems and tissues. To some extent this free radical injury can be prevented by antioxidants.(Mehmet OkanOzkaya 2013) Genotoxic effects from RF exposure, including studies of non-thermal levels of exposure, consistently and specifically show chromosomal instability, altered gene expression, gene mutations, DNA fragmentation and DNA structural breaks. (Löscher W et al 1998) The World Health Organization has classified mobile phone RF emissions as group 2 B carcinogens. Areas of close proximity to towers was also shown to be associated with an increased risk for cancer. The fact that RF exposure causes neurological damage has been documented repeatedly. Increased blood-brain barrier permeability and oxidative

damage, which are associated with brain cancer and neurodegenerative diseases, have been found. This is where antioxidants enter the scene to provide protection or primary prevention from free radical induced damage.

### **ANTI-OXIDANT ROLE OF CURCUMIN**

*Curcuma longa* (turmeric) acts as free radical scavengers and effective antioxidant. In addition, they exhibit oxidative DNA damage and relieve oxidative stress. *Curcuma longa* (turmeric) is a great anti-oxidant since it is able to inhibit the formation of nitric oxide and reactive oxygen species (ROS), (Sreejayan RM et al 1997, Joe B et al 1994) which plays a key role in inflammation and carcinogenesis. *Curcuma longa* (turmeric) potency is comparable to vitamin C and E. Curcumin was shown to be eight times more potent than Vitamin E in lipid peroxidation, and three times more powerful than Vitamin C in neutralizing free radicals. The present study investigates the possible histological effects of non-ionizing electromagnetic radiations and curcumin of albino rats. The turmeric (*Curcuma longa*) have various phytoalkaloids commonly termed "Curcumin" which is found to inhibit formation of amyloid beta oligomers and fibrils binds plaques and reduces amyloid *in vivo* (Yang et al 2005) On the other hand recent scientific studies have been focusing on the use of plant products as therapeutic agents. Curcumin acts as free radical scavengers and make for effective antioxidants. In addition, they inhibit oxidative DNA damage and relieve oxidative stress. Curcumin is a great antioxidant since it is able to regulate the formation of nitric oxide which plays a key role in inflammation and carcinogenesis. Oxidative stress plays a major role in the pathogenesis of various diseases including cancer, diabetes, cardiovascular diseases, neuronal cell injury, and hypoxia and many experimental models, particularly in the field of injuries to nervous system, have been introduced to investigate the therapeutic effects of different materials as well as curcumin. (Ebrahimi S. et al 2012) The most common experimental studies on curcumin, aside from providing new derivatives, are those of its antioxidant potentials. The biological classification of curcumin as both pro-oxidant and antioxidant, is well supported by studies (Jovanovic S. et al 2001) showing curcumin as a free radical scavenger, a reducing agent, and a DNA damage inhibitor, especially in the presence of Cu or Fe ions. Curcumin is able to bind to Fe, Mn and Cu that was reported to modulate the antioxidant properties. (Antunes LMG et al 2005)

### **CARDIOPROTECTIVE ROLE OF CURCUMIN**

Numerous reports have indicated that inflammation plays a major role in most Cardiovascular diseases. First, it is widely appreciated that inflammation and oxidant stress contribute to atherogenesis. Second, following cardiopulmonary bypass (CPB) and cardiac global ischemia and reperfusion (I/R), pro-inflammatory cytokines regulated by NF- $\kappa$ B are activated and cause cardiomyocytic injury. Third, chronic transmural inflammation and proteolytic destruction of medial elastin are key mechanisms in the development of abdominal aortic aneurysms (AAAs). Fourth, CRP, which is also regulated by NF- $\kappa$ B, is an inflammatory marker and a well-known predictor of CVD. Several studies have suggested that curcumin protects the heart from I/R injury (Srivastava et al 1985). The effect of curcumin on myocardial ischemia induced by the ligation of the left descending coronary artery. Curcumin was administered 30 min before ligation, and the hearts were removed 4 h prior to coronary artery ligation. Curcumin protected the animals against decreases in the heart rate, blood pressure and enzymatic changes following ischemia. Histopathologic studies of the infarcted rat heart also showed a decrease in necrosis after curcumin treatment. Vascular smooth muscle cell (VSMC) migration, proliferation, and collagen synthesis are key events in the pathogenesis of CVD. Growth factors, such as platelet-derived growth factor (PDGF) and fibroblast growth factor, which are released during vascular injury, play a pivotal role in regulating these events. Many studies have pointed out that immune or inducible (iNOS), and endothelial (eNOS) nitric oxide synthase play a crucial part in the pathogenesis of cardiovascular disorders, such as cardiomyopathy, due to diabetes. (Farhangkhoe H et al 2006) Curcumin was

shown to down regulate NOS and decrease NO oxidation, it may have inhibitory effect on the development of cardiovascular disorders in hyper oxidative diseases such as diabetes.(Brouet I. et al 1995) The parameters of inflammatory process play an essential part in the pathogenesis of many cardiovascular complications, like atherosclerotic process, acute coronary syndrome, and atrial arrhythmias. Curcumin also exhibited anti-proliferative effect which is remarkably associated to its power to induce OH-1 (Pae HO et al 2007) It is well known that the OH-1 owns important antioxidative and anti-inflammatory functions

### AIMS & OBJECTIVE

The aim of present study is to observe the histological changes due to electromagnetic radiations on the heart of albino rats and combined effect of turmeric and radiations on the heart of albino rats. This study highlights some adverse effects of radiations and benefits of turmeric for primary prevention and treatment of cell damage due to regular use of Cell phones to provide acceptable cost effective medicines, as well as lowering adverse effects with some natural plant component. The study investigates the possible histological effects of isothermal non-ionizing electromagnetic radiations on the Heart of Albino Rats and role of curcuma longa to minimize adverse effects of electromagnetic radiations.

**MATERIAL AND METHOD:-** This study was conducted on sixty albino rats of both sex in The Department of Anatomy Dr. S. N. Medical College Jodhpur. All the animals housed in a standard animal facility with a controlled temperature 25° -27° C and 5-10% humidity. Animals divided in four groups.

Group A - Taken as control.

Group B - Exposed to radiations (10cm away) by cell phone(Samsung Galaxy Y S5360-2G GSM890-960 Mhz) pd -82to-86 dbm SAR -U.S. -0.57 w/kg (Head) 0.64 w/kg(body)

Group C - Given pulv. Curcuma longa (166.5 mg/kg/day) orally emulsified with olive oil to enhance bioavailability of curcumin.

Group D - Exposed to Curcuma longa and radiations.

After 2 months of exposure subjects sacrificed by cervical dislocation and their hearts preserved in 10% formalin, processed, stained with H&E for observing histological changes in these organs.

**OBSERVATION AND RESULTS:-** The present study was conducted with 60 cases of Albino rats. All rats of control, radiation and curcuma exposed group were included in the study. The distribution of cases according to age, weight, dose of curcuma and histological findings as encountered in present study are presented in a tabulated form diagrams.

### Mean Weight Changes (gms) in different groups of Albino Rats

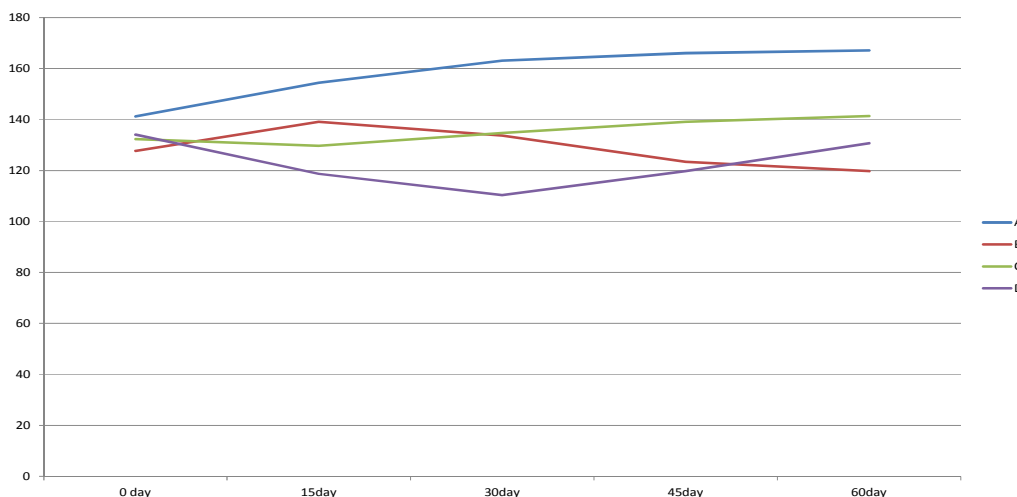


Fig.1 Weight changes group A showing normal growth pattern, Group B showing hampered growth with regular decrease in weight, group C showing controlled stationary pattern while group D showing initial decrease in weight with regain of weight in later period.

**HISTOLOGICAL CHANGES SEEN IN VARIOUS GROUPS (A,B,C,&D)**

**Comparative Heart 20x**

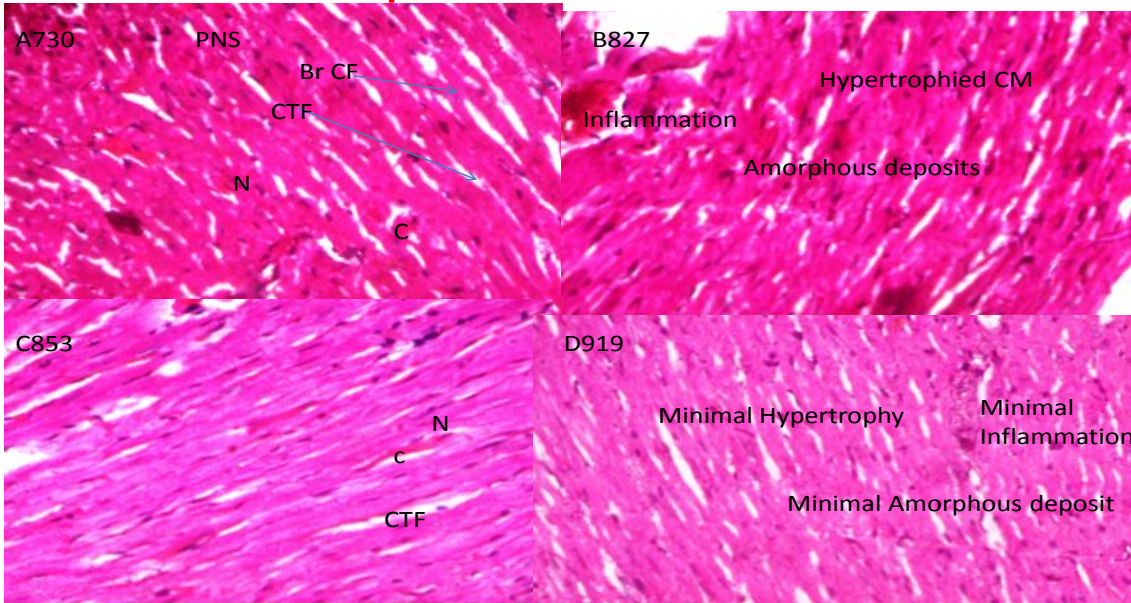


Fig.2 showing C(capillary) N(nucleus CTF(connective tissue fibre)PNS(perinuclear space)BrCF(branched cardiac fibre)

**Comparative Heart 40x**

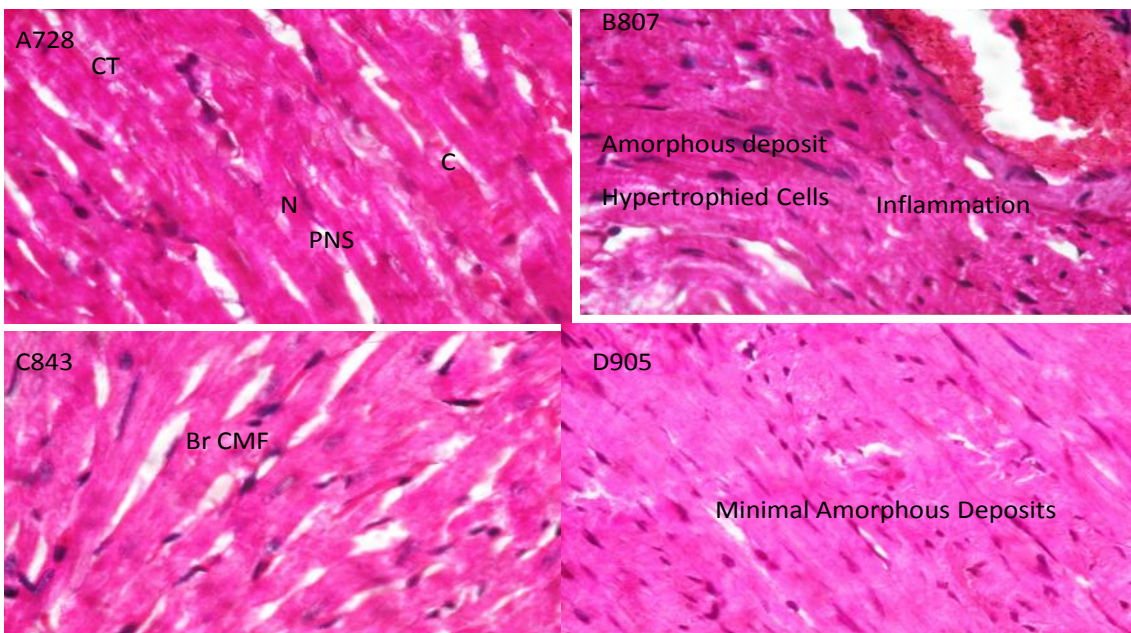
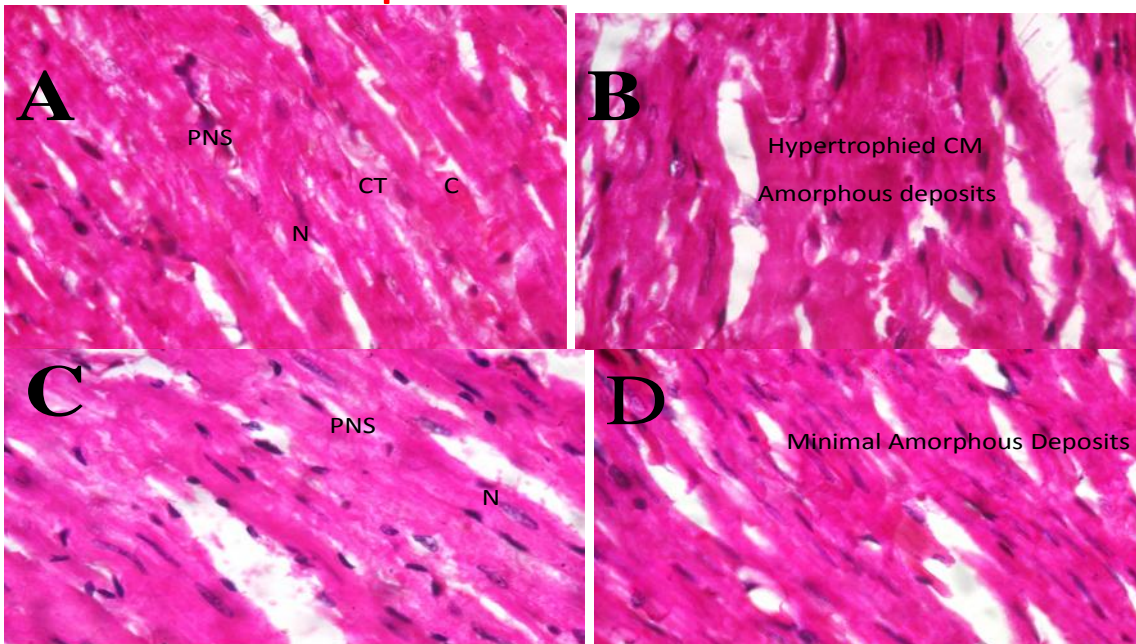


Fig.3 showing C(capillary)N(nucleus)CT(connective tissue)PNS(peri nuclear space)BrCMF(branched cardiac muscle fibre)

## Comparative Heart 40x



**Fig.4** showing N(nucleus), CT(connective tissue), C(capillary), PNS(perinuclear space)

In the present study light microscopic examination of sections from heart of Albino rats exposed to mobile phone radiations one hour /day for two months with calculated standard dose of curcuma longa showed significant reduction in morphological alteration in nuclear membrane, pyknotic changes in nucleus, darkening of nuclear material, Amorphous deposits , degeneration and apoptotic changes in myocardium with, polymorphonuclear infiltrations , congestion and dilatation of blood vessels.

**Table no.1** distribution of histological changes in heart in control and EMR exposed group

Experimental group	Histological changes in myocardium		
	Normal	Amorphous deposits	Total
control	15(9.0)[4.0]	0(6.0)[6.0]	15(100)
EMR	3(9.0)[4.0]	12(6.0)[6.0]	15(100)

$\chi^2 = 20$ ,  $df=1$ ,  $p$  value=0.00008 Result is significant at  $P < .05$  Table no. 1 show the total number of control and electromagnetic radiation exposed experimental albino rats out of 60 cases studied. In control group out of 15 experimental animals was most common histopathological observation constituting 15(100%) normal cases and no case of Amorphous deposits(0%) in heart changes was observed. In EMR exposed group out of 15 experimental animals was most common histopathological examination constituting Amorphous deposits in heart 12(80%) cases followed by normal 3(20%). Two parameters amorphous deposit changes and normal histological changes of control and electromagnetic radiation exposed group were compared and chi square test was employed for the comparison of parameters. As a result of application of chi square test the values obtained was 20,  $df$  value was 1 and  $p$  value is equal to 0.000008.

**Table no. 2** distribution of histological changes in heart in control and curcuma exposed group

Experimental Group	Histological changes in myocardium		
	normal	Amorphous deposits	Total
control	15(14.5)[0.02]	0(0.5)[0.5]	15(100)
curcuma	14(14.5)[0.02]	1(0.5)[0.5]	15(100)

$\chi^2=1.0345$ ,  $df=1$ ,  $p$  value =0.309108 The result is not significant at  $P < .05$

Table no 2 shows the total number of control and curcuma exposed experimental albino rats out of 60 cases studied. In control group out of 15 experimental animals was most common histopathological examination constituting 15(100%) normal cases and 0 (0%) cases of amorphous deposits changes was observed. In curcuma exposed group out of 15 experimental animals was most common histopathological examination constituting 14 (93.33) normal and 1(6.67) Amorphous deposits changes. Two amorphous deposits changes and normal histological changes of control and curcuma radiation exposed group were compared and chi square test was employed for the comparison of parameters .As a result of application of chi square test the values obtained was 1.0345,  $df$  value was 1 and  $p$  value is equal to 0.309108 was not significant.

**Table no: 3** distribution of histological changes in heart in control and EMR+curcuma exposed group

Experimental group	Histological changes in myocardium		
	normal	Amorphous deposits	Total
Control	15(14.0)[0.07]	0(1.0)[1.0]	15(100)
EMR+curcuma	13(14.0)[0.07]	2(1.0)[1.0]	15(100)

$\chi^2=2.1429$ ,  $df=1$ ,  $p$  value=0.143235 The result was not significant at  $P < .05$

Table no: 3 shows the total number of control and electromagnetic radiation curcuma exposed experimental albino rats out of 60 cases studied. In control group out of 15 experimental animals was most common histopathological examination constituting 15(100%) normal cases and no case of Amorphous deposits (0%) changes. In EMR +curcuma group out of 15 experimental animals was most common histopathological observation constituting 13(86.66%) normal cases and 2(13.33) Amorphous deposits changes. Two parameters normal and Amorphous deposits changes of control and electromagnetic radiation+curcuma exposed group were compared and chi square test was employed for the comparison of parameters. As a result of application of chi square test the values obtained was 2.143,  $df$  value was 1 and  $p$  value is equal to 0.143235 was not significant at  $P < .05$

**Table no: 4** Distribution of histological changes in heart in control group A and EMR exposed group B

Experimental group	Histological changes in myocardium		
	Normal	Morphological alteration in nuclear membrane and nucleus	Necrotic, degenerative and apoptotic changes
Control	13(86.66)	1(6.66)	1(6.66)
EMR	4(26.67)	10(66.66)	3(20)

Figures in parenthesis indicate percentage. Table no. 4 shows the total number of control and EMR exposed cases studied out of total 60 cases. In control group out of 15 the most common histological observation constituted normal cases 13(86.66%), followed by Morphological alteration in nuclear membrane in 1case (6.66%) and Necrotic, degenerative and apoptotic changes in 1(6.66%) case. In EMR exposed group normal histology was seen in 4(26.67%), Morphological alteration in nuclear membrane and nucleus 10(66.66%) cases and Necrotic, degenerative and apoptotic changes in 3(20%) cases.

**Table no: 5** Distribution of histological changes in Heart in control and curcuma exposed group(C)

Experimental group	Histological changes in myocardium		
	Normal	Morphological alteration in nuclear membrane and nucleus	Necrotic, degenerative and apoptotic change
Control	13(86.66)	1(6.66)	1(6.66)
Curcuma	14(93.33)	0(00)	1(6.66)

Table no. 5 shows the total number of control and curcuma exposed cases studied out of total 60 cases. In control group out of 15 the most common histological diagnosis constituted normal cases 13(86.66%), followed by Morphological alteration in nuclear membrane and nucleus in 1 case (6.66%) and in 1(6.66%) case. In curcuma exposed group normal histology was seen in 14(93.33%), Morphological alteration in nuclear membrane and nucleus 0(0%) cases and Necrotic, degenerative and apoptotic change in 1(6.66%) cases.

**Table no: 6** Distribution of histological changes in Heart in control group (A) and curcuma+EMR exposed group (D)

Experimental group	Histological changes in myocardium		
	Normal	Morphological alteration in nuclear membrane and nucleus	Necrotic, degenerative and apoptotic change
Control	13(86.66)	1(6.66)	1(6.66)
Curcuma+EMR	10(66.67)	5(33.33)	4(26.66)

Table no. 6 shows the total number of control and curcuma exposed cases studied out of total 60 cases. In control group out of 15 the most common histological diagnosis constituted normal cases 13(86.66%), followed by Morphological alteration in nuclear membrane and nucleus in 1 case (6.66%) and in 1(6.66%) case. In curcuma+EMR exposed group normal histology was seen in 10(66.67%), Morphological alteration in nuclear membrane and nucleus 5(33.33%) cases and Necrotic, degenerative and apoptotic change in 4(26.66%) cases.

## DISCUSSION

The risks come from transient nervous system responses including peripheral (PNS) and central nerve stimulation(CNS), the induction of retinal phosphenes and possible effects on some aspects of brain function. In view of the considerations above for frequencies in the range 10 Hz to 25 Hz, occupational exposure should be limited to fields that induce electric field strengths in CNS tissue



consistently and specifically show chromosomal instability, altered gene expression, gene mutations, DNA fragmentation and DNA structural breaks.( Löscher W et al 1998) The present findings indicate that when albino rats of age group 40-120days when exposed to cell phone radiations showed morphological alteration in nuclear membrane, pyknotic changes in nucleus, darkening of nuclear material Amorphous deposits , degeneration and apoptotic changes in myocardium with, polymorphonuclear infiltrations , congestion and dilatation of blood vessels. In the present study light microscopic examination of sections from heart of Albino rats exposed to mobile phone radiations 10cm distance, one hour daily for two months with calculated standard dose of curcuma longa showed significant reduction in morphological alteration in nuclear membrane, pyknotic changes in nucleus, darkening of nuclear material, Amorphous deposits , degeneration and apoptotic changes in myocardium with, polymorphonuclear infiltrations , congestion and dilatation of blood vessels. Present study investigates that there were no significant histological changes observed in heart of Albino rats exposed to as EMR+curcuma longa showing protective effects of curcuma longa. Even reduction in number of Albino rats with Apoptosis and nuclear membrane alteration, darkening of nuclear material, pyknosis, congestion and dilatation of blood vessels in heart was observed in EMR and curcuma longa exposed group. In 2011, International Agency for Research on Cancer (IARC) has classified mobile phone radiation on the IARC scale into Group 2B - possibly carcinogenic. That means that there "could be some risk" of carcinogenicity, Pregnant mothers, foetus and children are at the greatest risk. However the regular and separate use of both mobile phone exposure and curcuma longa may cause abortion so their use can not recommended for the pregnant mothers.

#### **SUMMARY AND CONCLUSION**

This study concluding histological effects of electromagnetic radiations (2G mobile 900-1900 MHz) and combined effects of curcuma longa on myocardium of albino rats. EMR exposure (900-1900 MHz)in group B showed significant histological Observations in Heart group B showing inflammation, congestion, amyloid deposition, nuclear pyknosis while structural enhancement in group C and minimal effects in group D than group B. Effects of curcuma longa were significant in dose 166.5mg/kg/day to minimize histological changes in cardiac muscle and blood vessels. Thus curcuma longa act as an effective anti inflammatory and anti oxidant agent for prevention of mobile phone radiation injuries. On applying ANOVA there was no significant difference found between pre exposure mean weight of all four experimental groups but significant difference was observed in post exposure mean weight. So additional research into the long-term, regular use of mobile phones needs to be conducted.

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