

Amelioration of Cell Phone and Wi Fi induced Pancreatic damage and Hyperglycemia (Diabetes Mellitus) with Pomegranate and Vit E in rats.

ABSTRACT:

Background. Type 2 Diabetes Mellitus has become a global concern. To date numerous studies have been conducted but little literature is available to explain the effects of mobile phone radiation on pancreas, where from Insulin is secreted. In Some studies, effects of ionizing radiation have been examined and established the relationship between cell phone exposure and cell damage. Objectives: Objectives of study were to observe the effects of mobile phones, connected with WiFi on the pancreas. Methods: 40 male Wistar Albino rats were exposed to mobile phones connected with Wi-Fi for eight weeks. Results: The histopathological examination of the rat pancreas revealed that, exposure of rats to cell phones and Wi-Fi causes significant damage to the rat pancreas. Conclusion: The ionizing radiation emitted from cell phones and WiFi causes increase in oxidative stress leading to inflammation and pancreatic cell death that may affect glucose homeostasis.

Key Words: Mobile Phone, WiFi, Oxidative stress, Diabetes Mellitus, Pancreas

INTRODUCTION:

Type 2 Diabetes mellitus has become leading cause of mortality and morbidity in recent decades globally. It has been identified as one of the top 10 causes of death, worldwide [1]. International Diabetes Federation (IDF) data shows that around 451 million world population suffered from diabetes in 2017 and the number is estimated to increase to 693 million by 2,045 [2]. Type 2 DM increases the morbidity and mortality rate manifold due to its complications like, infections, ischemic heart disease, stroke, nephropathy, chronic liver disease, and angiopathy [3-5]. Insulin resistance i.e. when the pancreas produces a little or no insulin at all is mainly responsible for occurrence of Type 2 DM. Due to deficiency of Insulin, cells can no longer take up glucose from the blood, resulting in, hyperglycemia and consequently Hyperglycemia causes complications associated with diabetes [6]. In pathogenesis of Diabetes Mellitus oxidative stress plays a vital role. Reactive oxygen species (ROS) and reactive nitrogen species play double role as both harmful and beneficial species. Overproduction of ROS lead to oxidative stress [7]. Several studies have concentrated on the characterization of the reactive oxygen species (ROS) source, its mechanism, scavenging and antioxidant substances in diabetes [8,9]. Glucose homeostasis is mainly dependent on the normal functioning of beta islets of pancreas, which secrete insulin. Over production of ROS by the transfer of their free unpaired electron causes the oxidation of cellular machinery and affect the normal functioning of all the body cells including beta cells of pancreas leading to deficiency of Insulin [10,11]. Role of sedentary life style causing Type 2 DM is very well established. In recent times. Use of cell phone and Wi fi has increased many fold. Sedentary life style causes obesity and obesity leads to increase in oxidative stress. Several researchers have found hazardous effects of Wi fi on different organs like the following but not limited to, Oxidative stress [12], Brain damage [13], decreased fertility [14], Cellular DNA damage [15], Calcium overload [16], Endocrine effects [17] etc. In recent times cell phones have become part and parcel of daily life, worldwide. The cell phone use is dependent on Lithium batteries plus its connection with WiFi. Lithium batteries have been identified in research to

contain potential risk to human health [18,19]. Several researchers consider Oxidative stress and lipid peroxidation as important factor in development of various diseases, and consequently antioxidant role is given considerable importance in the prophylaxis and treatment of these diseases especially, the effects of vitamin E, the most important lipophilic radical-scavenging antioxidant, have been extensively investigated [20,21]. Components of pomegranate such as polyphenols, have been found to possess several health benefits due to their antioxidant effects. Therefore, pomegranate use is considered helpful in treatment of many ailment risk factors including high blood pressure, high cholesterol, oxidative stress, hyperglycemia, and inflammatory activities [22,23].

MATERIALS AND METHODS:

Animals:

Forty Male Wistar Albino rats, weighing 240-260 g and 8 weeks old, obtained from the animal unit in college of pharmacy, NBU Border University were used in the study. The rats were housed in polycarbonate cages. Rats were kept in the environment of controlled temperature (25-26 °C), humidity (55-60%), and controlled light and dark for a period of 5 days before beginning the experiment. Standard balanced diet and tap water were provided to the animals.

Experimental Design:

After 5 days of acclimatization, the 40 rats were randomized based on body weight into different groups. Prior to test item administration, the animals were randomized into four groups viz., G1 (Vehicle control), whereas G2 is a treatment control exposed to mobile phone for 8 weeks. Groups, G3 and G4 were administered with pomegranate juice orally for 4 weeks with a dose of 0.4 ml/200g/kg/rat and 0.8ml/200g/kg/rat, respectively. Similarly, group G5 was administered with Vitamin E 50 IU/kg of body weight for 4 weeks. These groups G3, G4 and G5 were exposed to mobile phones daily 24 hours for 8 weeks.

Similarly, groups G6, G7 and G8 were exposed to mobile phones daily 24 hours for 8 weeks. Whereas, groups, G6 and G7 were administered with pomegranate juice orally for 4 weeks with a dose of 0.4 ml/200g/kg/rat and 0.8ml/200g/kg/rat, respectively and group G8 was administered with Vitamin E 50 IU/kg of bodyweight for 4 weeks.

All the animals were observed daily twice for signs of morbidity and mortality during the experimental period.

Histopathological Examination:

At the end of 8th week (end of the treatment period, 24 hrs after the last administration) the rats were sacrificed, after intra-peritoneal administration of sodium pentobarbital solution (40 mg/kg) as an anesthetic, and the peritoneal cavity was opened with a lower transverse abdominal incision. After removing the pancreas from abdomen, pancreas was sectioned sagittally. The removed pancreas was then fixed with a buffered 10% formalin solution for 24 h and embedded in paraffin. Tissues were then sectioned, stained with hematoxylin and eosin (H&E) and examined for histopathology changes using light microscope.

Blood Glucose Determination:

Blood samples were collected from the tail vein of the rats. Basal glucose levels were determined prior to mobile phone exposure. Samples were then taken after 4 weeks of exposure to mobile phones and after treatment with substances used in the study.

RESULTS:

Comparison of total body weights at different periods in different groups were shown in table (1). At 1st day, the total body weights in G2, G5 and G8 groups were significantly increased versus G1. Compared with G2, the total body weights were significantly reduced in G3, G4, G6, G7 but were significantly increased in G8 (figure1). At 14th day, the total body weights in G2, G5 and G8 groups were significantly increased as compared to G1. Compared with G2, the total body weights were significantly reduced in G3, G4, G5, G6, G7 but were significantly increased in G8. At 28th day, the total body weights in G2, G5 and G8 groups were significantly increased as compared to G1. Compared with G2, the total body weights were significantly reduced in G3, G4, G5, G6, and G7, but were significantly increased in G8. At 56th day, the total body weights in G2, G5 and G8 groups were significantly increased versus G1. Compared with G2, the total body weights were significantly decreased in G3, G4, G5, G6, G7 but were significantly increased in G8. At 84th day, the total body weights in G2 and G8 groups were significantly increased versus G1. Compared with G2, the total body weights were significantly reduced in G3, G4, G5, G6, G7 but were significantly increased in G8 (figure2).

Comparison of blood glucose at different periods in different groups is displayed in table 2. At the first day, the blood glucose in G3, G4 and G6 groups were significantly increased as compared to G1 (figure 3). At 14th day, the blood glucose level in G2, G6, and G8 groups were significantly increased versus G1 but were significantly decreased in G7 versus G2. At 28th day, the blood glucose in G2, G5 and G8 groups were significantly increased versus G1. Compared with G2, blood glucose levels were significantly decreased in G5 but were significantly increased in G3. At 56th day, the blood glucose in G6 group was significantly increased versus G1. At 84th day, the blood glucose in G6 and G7 groups were significantly increased versus G1. Compared with G2, the blood glucose levels were significantly decreased in G4 and G5 (figure4).

Figures (5 to 12) show the different histological effects on pancreas sections for different groups. Morphology of the beta islets of langerhans in pancreas changed significantly with increase in duration of exposure to WiFi and Cell Phones. Damage to the cells was found less, in the treated groups and after exposure treated groups showed significant repair and recovery.

Table (1): Comparison of the body weight (grams) in different studied groups at different days.

Groups	1st day	14th day	28th day	56th day	84th day
G1 (Normal control)	113.17±5.08	115.00±5.83	119.83±5.74	123.33±5.28	128.50±3.15
G2 (EMR only)	175.50±7.18	178.17±6.65	179.83±9.20	180.83±10.87	182.83±11.34
Significance	1P <0.0001	1P <0.0001	1P <0.0001	1P <0.0001	1P <0.0001
G3 (EMR 900 MHz EMR (1hr/Day) + PM (0.4ml/200g)	120.17±4.07	121.33±3.98	123.00±5.87	126.50±5.68	136.50±9.65
Significance	1P=0.558, 2P <0.0001	1P=0.661, 2P <0.0001	1P=0.995, 2P <0.0001	1P=0.994, 2P <0.0001	1P=0.854, 2P <0.0001
G4 (EMR 900MHz EMR (1hr/Day) + PM + 0.8ml/200g)	122.83±5.12	126.17±6.21	133.00±5.80	136.00±5.44	141.00±5.62
Significance	1P=0.177, 2P <0.0001	1P=0.068, 2P <0.0001	1P=0.062, 2P <0.0001	1P=0.068, 2P <0.0001	1P=0.384, 2P <0.0001
G5 (EMR 900MHz EMR + Vit E 50 IU/kg)	166.17±8.82	159.00±7.24	147.00±10.56	142.83±9.28	131.00±11.54
Significance	1P <0.0001 , 2P=0.211	1P <0.0001 , 2P<0.0001	1P <0.0001 , 2P<0.0001	1P =0.001 , 2P<0.0001	1P =1.000, 2P<0.0001
G6 (EMR for 56 days) + then PM (0.4ml/200g/day for 28 days)	114.33±4.72	114.00±4.98	113.50±3.33	112.00±3.58	114.50±12.11
Significance	1P=1.000, 2P <0.0001	1P=1.000, 2P <0.0001	1P=0.807, 2P <0.0001	1P=0.139, 2P <0.0001	1P=0.250, 2P <0.0001
G7 (EMR for 56 days) + then PM (0.8ml/200g/day for 28 days)	108.00±7.92	111.50±7.09	236.83±8.54	118.83±7.11	124.50±14.15
Significance	1P=0.851, 2P <0.0001	1P=0.977, 2P <0.0001	1P=0.968, 2P <0.0001	1P=0.955, 2P <0.0001	1P=0.997, 2P <0.0001
G8 (EMR for 56 days + then PM (0.8ml/200g/day) + VitE(50 IU/kg) for 28 days)	251.67±6.53	247.67±7.58	247.67±7.58	234.50±7.18	228.83±6.71
Significance	1P<0.0001 , 2P <0.0001	1P<0.0001 , 2P <0.0001	1P<0.0001 , 2P <0.0001	1P<0.0001 , 2P <0.0001	1P<0.0001 , 2P <0.0001

Data are expressed as mean +/- standard error. 1P: significance versus G1; 2P: significance versus G2; using OneWay ANOVA test (Turkey test).

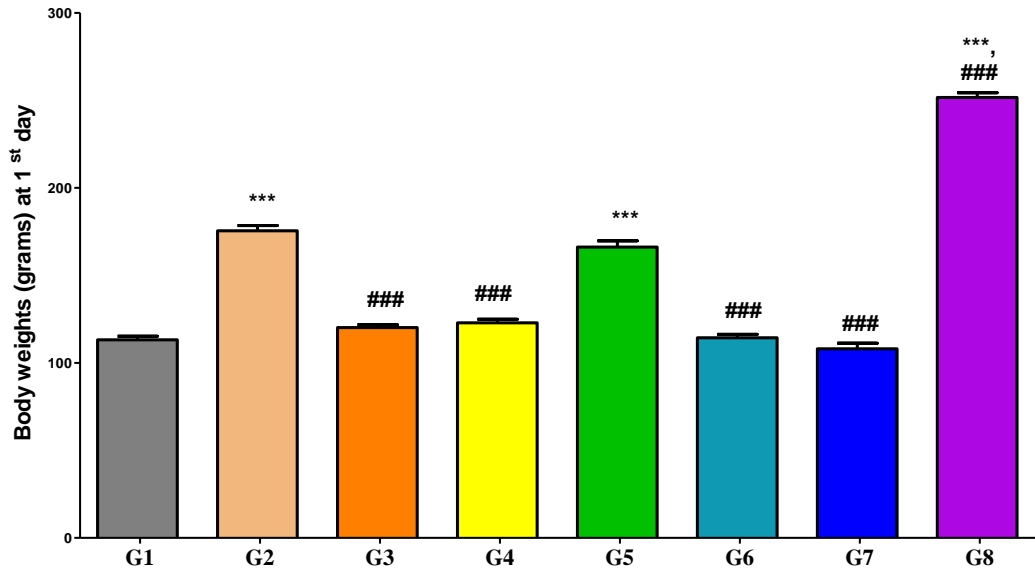


Figure (1): Comparison of the body weight (grams) in different studied groups at 1st day. *: Significance versus G1; #: significance versus G2. *: P < 0.05, **: P < 0.010; ***: P < 0.0001.

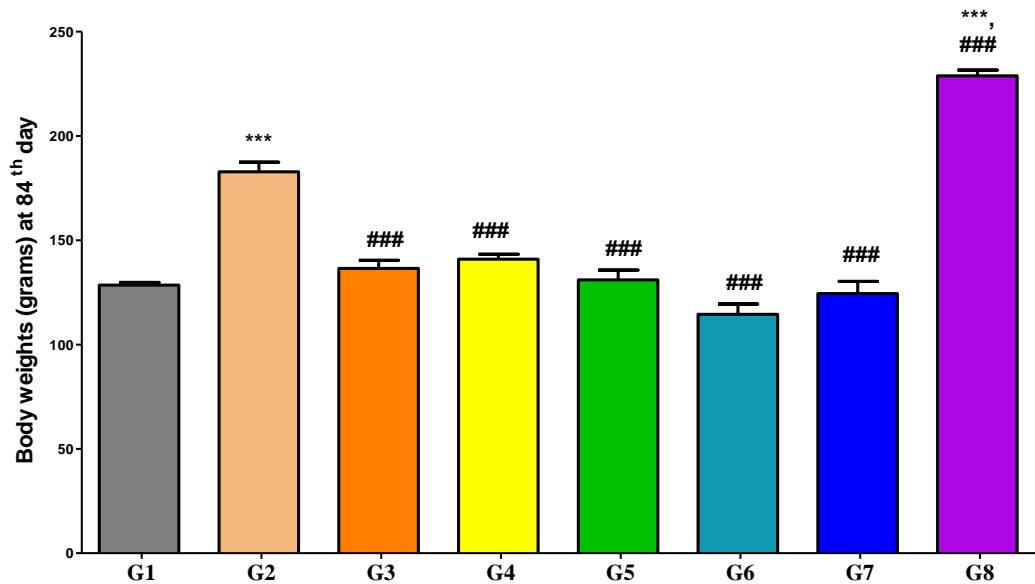


Figure (2): Comparison of the body weight (grams) in different studied groups at 84th day. *: Significance versus G1; #: significance versus G2. *: P < 0.05, **: P < 0.010; ***: P < 0.0001.

Table (2): Comparison of the blood glucose levels (mg/dl) in different studied groups at different days.

Groups	1 st day	14 th day	28 th day	56 th day	84 th day
G1 (Normal control)	99.00±7.80	100.83±8.08	104.50±9.01	105.33±8.45	107.83±7.55
G2 (EMR only)	113.00±5.93	115.17±3.66	116.83±3.43	115.33±6.38	116.50±4.14
Significance	1P =0.181	1P =0.016	1P =0.019	1P =0.256	1P =0.212
G3 (EMR 900 MHz EMR (1hr/Day) + PM (0.4ml/200g)	124.83±16.19	122.67±7.92	120.00±2.83	118.00±3.58	113.50±7.50
Significance	1P=0.001 , 2P =0.368	1P=0.016 , 2P =0.558	1P=0.001 , 2P =0.982	1P=0.066, 2P =0.998	1P=0.715, 2P =0.987
G4 (EMR 900MHz EMR (1hr/Day) + PM + 0.8ml/200g)	118.00±2.19	116.17±1.72	113.17±2.99	110.67±4.59	103.00±2.90
Significance	1P=0.020 , 2P =0.981	1P<0.0001 , 2P =0.558	1P =0.217, 2P=0.960	1P=0.895, 2P =0.945	1P=0.847, 2P =0.007
G5 (EMR 900MHz EMR + Vit E 50 IU/kg)	106.33±12.19	104.83±10.67	103.17±9.20	102.33±8.19	100.67±9.71
Significance	1P =0.865, 2P=0.913	1P =0.008 , 2P=1.000	1P=1.000, 2P =0.006	1P=0.996, 2P =0.055	1P =0.437, 2P=0.001
G6 (EMR for 56 days) + then PM (0.4ml/200g/day for 28 days)	112.00±12.87	119.00±1.41	120.17±1.94	119.00±3.63	120.50±3.21
Significance	1P=0.004 ,2P =0.789	1P=0.970,2P =0.179	1P=0.001 ,2P =0.976	1P=0.037 , 2P =0.985	1P=0.014 ,2P =0.936
G7 (EMR for 56 days) + then PM (0.8ml/200g/day for 28 days)	112.33±2.58	111.17±10.03	110.33±8.59	108.00±7.54	119.17±3.92
Significance	1P=0.256,2P =1.000	1P=0.001 ,2P =0.976	1P=0.690, 2P =0.566	1P=0.998, 2P =0.636	1P=1.000,2P =0.095
G8 EMR for 56 days + then PM (0.8ml/200g/day) + VitE(50 IU/kg) for 28 days	251.67±6.53	114.33±3.56	116.67±3.50	117.00±11.12	228.83±6.71
Significance	1P=0.229,2P =1.000	1P=0.179, 2P =0.970	1P=0.021 , 2P =1.000	1P=0.115, 2P =1.000	1P=0.038 ,2P =0.993

Data are expressed as mean +/- standard error. 1P: significance versus G1; 2P: significance versus G2; using OneWay ANOVA test (Turkey test).

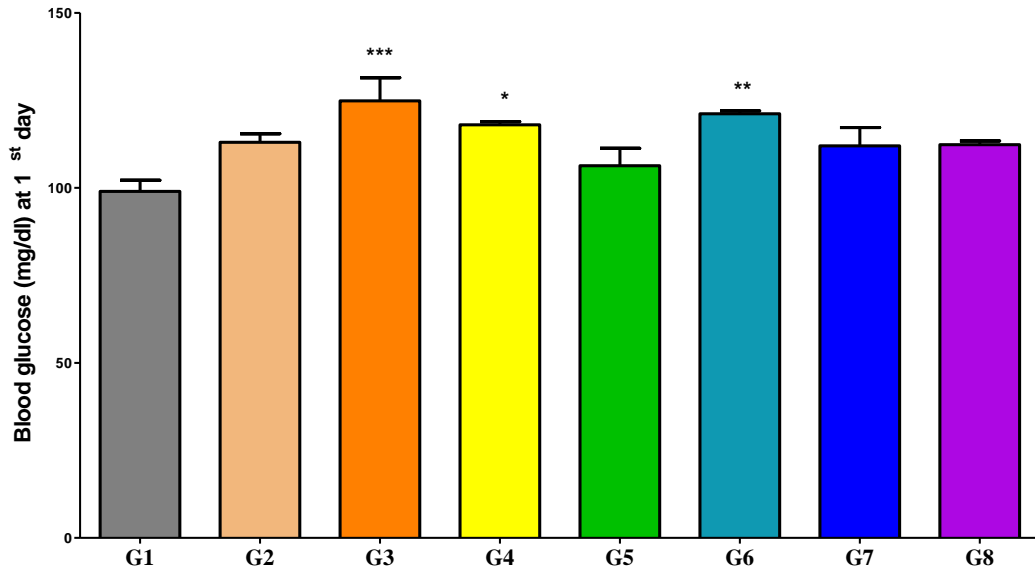


Figure (3): Comparison of the blood glucose (mg/dl) in different studied groups at 1st day. *: Significance versus G1; #: significance versus G2. *: P <0.05, **: P <0.010; ***: P <0.0001.

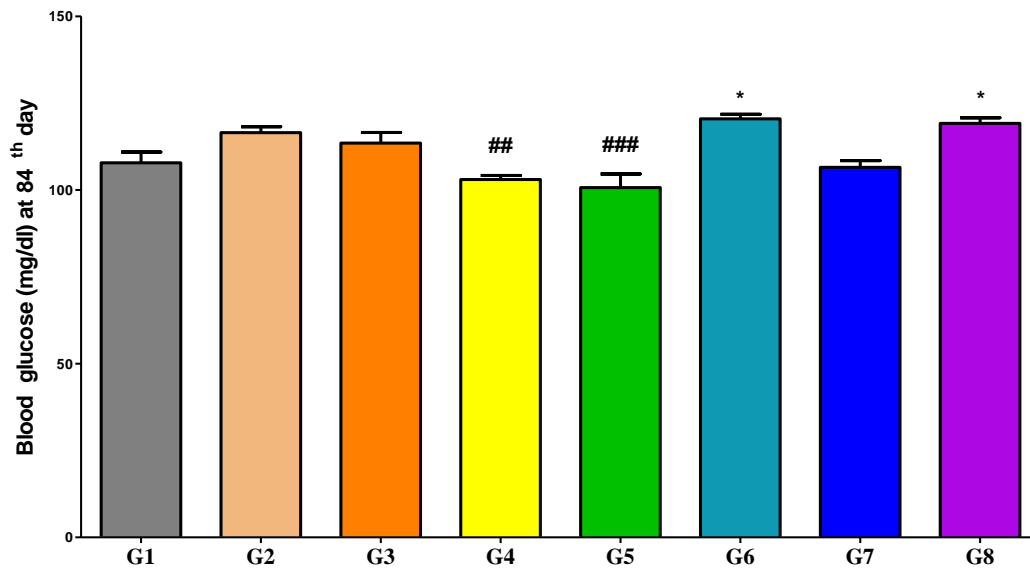
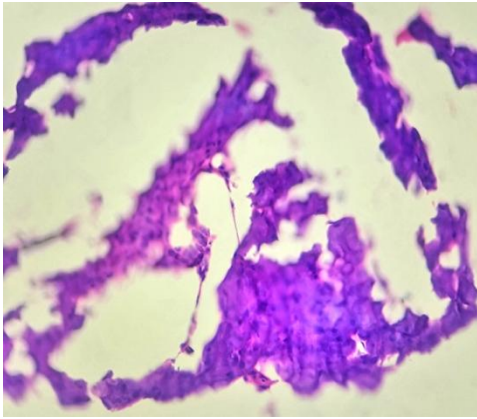
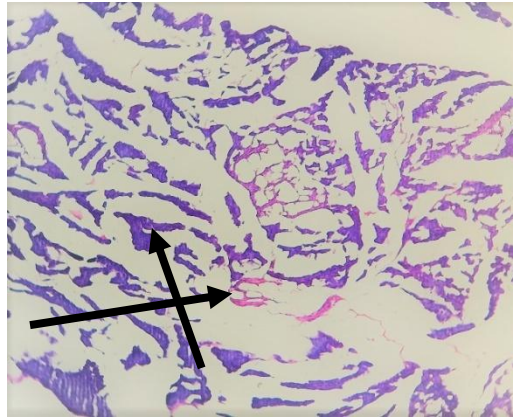


Figure (4): Comparison of the blood glucose (mg/dl) in different studied groups at 84th day. *: Significance versus G1; #: significance versus G2. *: P <0.05, **: P <0.010; ***: P <0.0001.

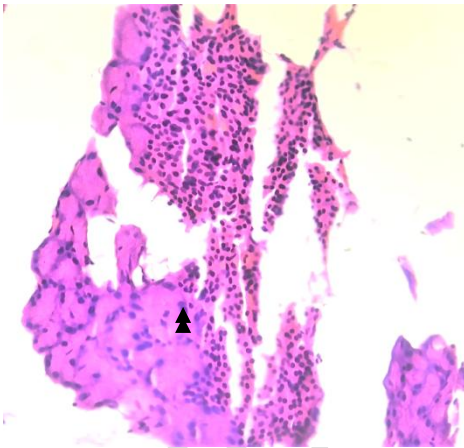


H&E, x400

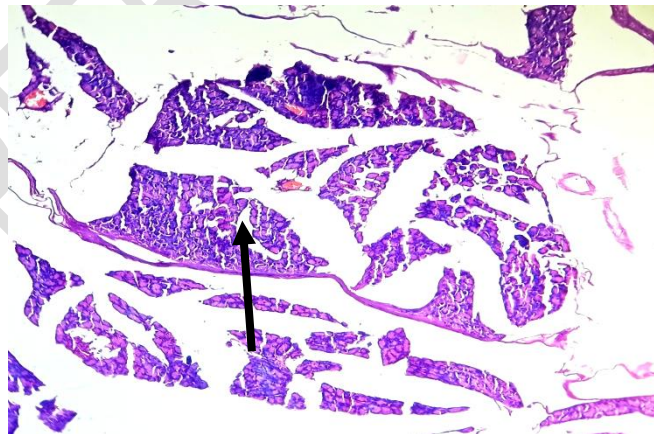


H&E, x50

Figure (5) Group – 1 Microscopy: Section studied shows pancreatic lobules separated by connective tissue septa. The number of islets appears intact in number. The center of islet cells consist of Beta-cells (60%), while the periphery comprises of large Alpha-cells (35%). The intervening septae shows congested vessels.

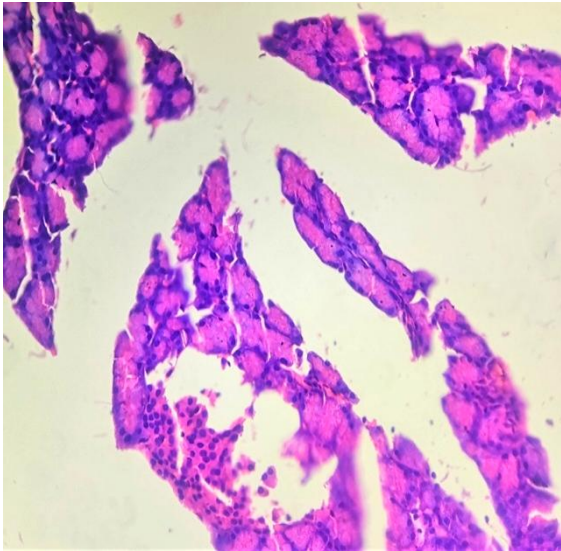


H&E, x400

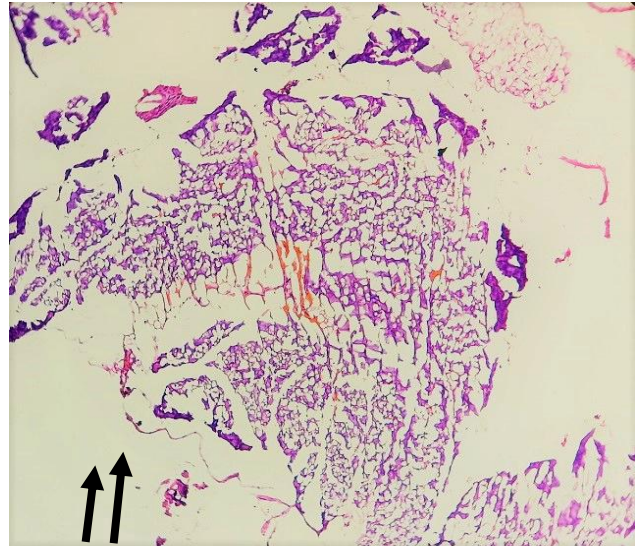


H&E, x50

Figure (6) Group-2 EMR 900MHz (1hr/day) only Section studied shows pancreatic lobules separated by connective tissue septa. The center of islet cells consist of quantitative increase in small Beta-cells (75%, compared to control group), while the periphery comprises of large Alpha-cells (20%). Intervening these cells are seen vascular spaces.

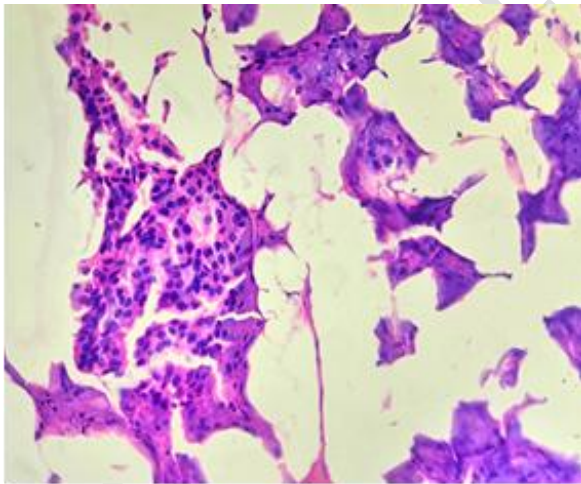


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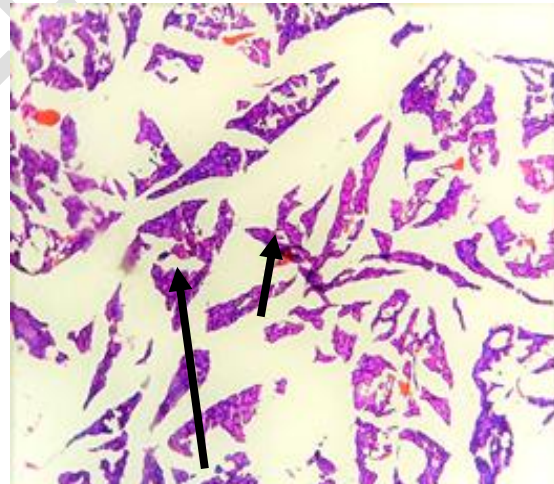


H&E, x50

Figure (7) group 3. EMR 900MHz (1hr/day) + PM (0.4ml/200g). Section studied shows pancreatic lobules separated by connective tissue septa. The pancreatic lobules consist largely of the exocrine acini and their intralobular ducts. Most of the lobules show small, round, light-staining islets of Langerhans. The center of islet cells consist of aggregates of small Beta-cells (70%, Fig., Long-arrow), while the periphery comprises of large Alpha-cells (25% Fig., Short-arrow).

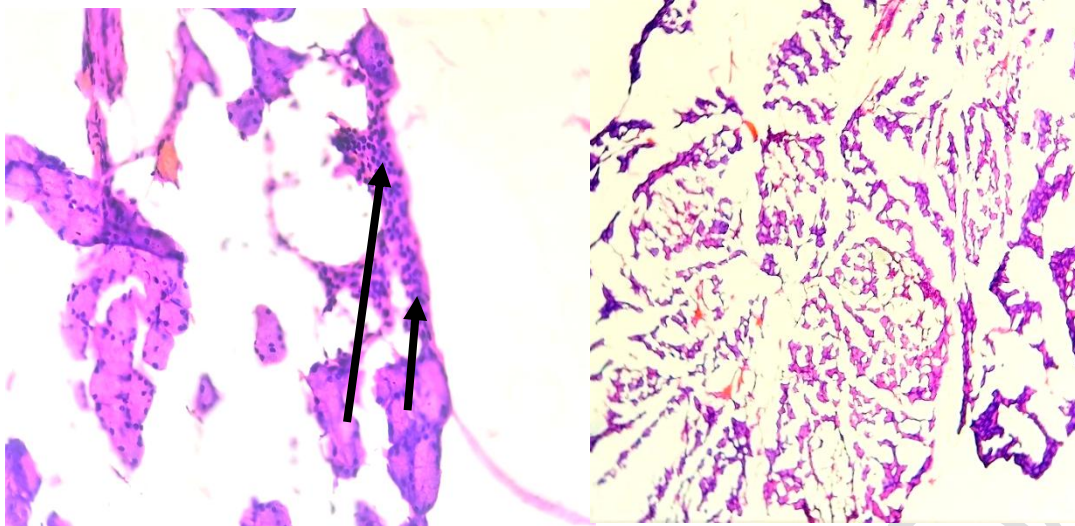


H&E, x400



H&E, x50

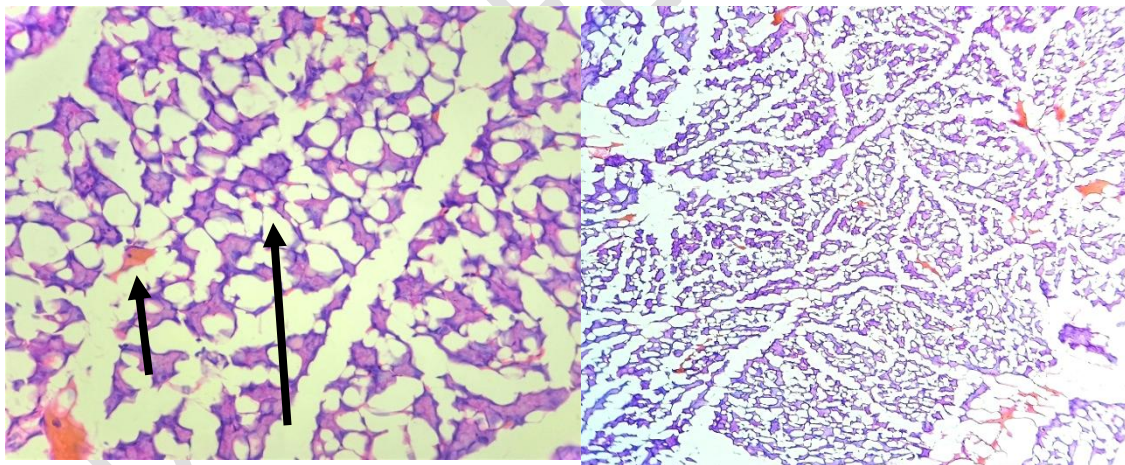
Figure (8) group 4. EMR 900MHz (1hr/day) + PM (0.8ml/200g). Section studied shows pancreatic lobules separated by connective tissue septa. The pancreatic lobules consist largely of the exocrine acini and their intralobular ducts. Most of the lobules show small, round, light-staining islets of Langerhans. The center of islet cells consist of aggregates of small Beta-cells (75%, Fig., Long-arrow), while the periphery comprises of large Alpha-cells (20% Fig., Short-arrow).



H&E, x400

H&E, x50

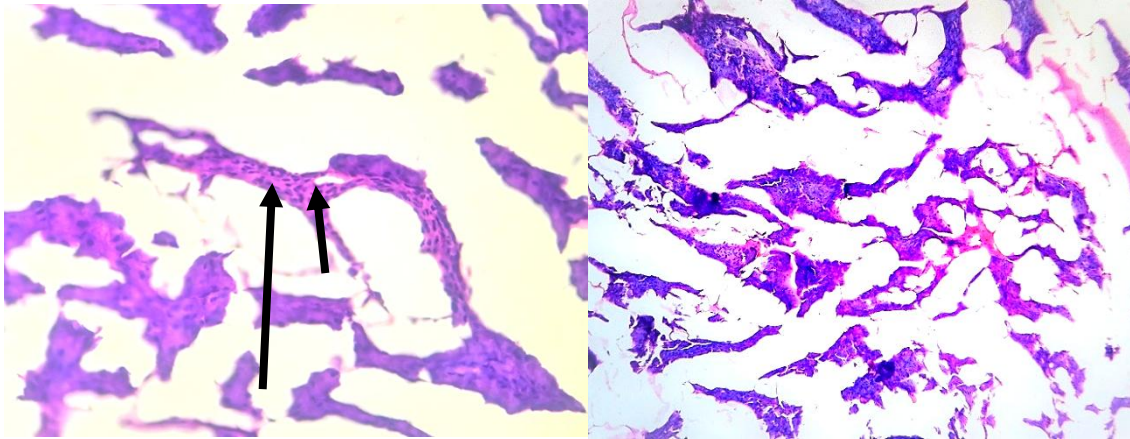
Figure (9) group 5. EMR 900MHz (1hr/day) + Vit. E (50 IU/kg). Section studied shows pancreatic lobules separated by connective tissue septa. The pancreatic lobules consist largely of the exocrine acini and their intralobular ducts. Most of the lobules show small, round, light-staining islets of Langerhans. The center of islet cells consist of aggregates of small Beta-cells (70%, Fig., Long-arrow), while the periphery comprises of large Alpha-cells (25% Fig., Short-arrow).



H&E, x400

H&E, x50

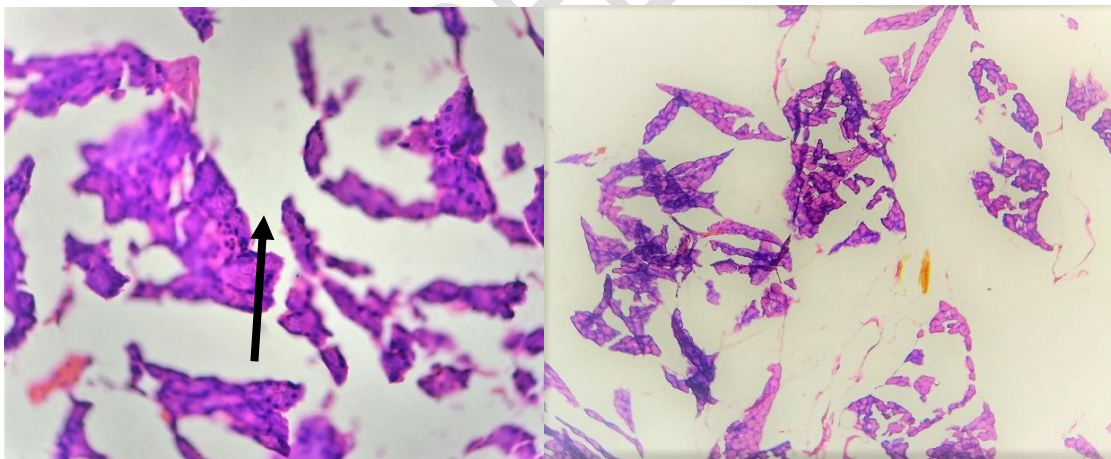
Figure (10) group 6. PM (0.4ml/200g/day). Section studied shows pancreatic lobules separated by connective tissue septa. The pancreatic lobules consist largely of the exocrine acini and their intralobular ducts (Fig., Long-arrow). The lobules appear deficient of islets of langerhans. The interlobular septae shows congested vessels (Fig., Short-arrow).



H&E, x400

H&E, x50

Figure (11) group 7. PM(0.8ml/200g/day). Section studied shows pancreatic lobules separated by connective tissue septa. The pancreatic lobules consist largely of the exocrine acini and their intralobular ducts. Some of the lobules show small, round, light-staining islets of langerhans. The center of islet cells consist of aggregates of small Beta-cells (60%, Fig., Long-arrow), while the periphery comprises of large Alpha-cells (35% Fig., Short-arrow).



H&E, x400

H&E, x50

Figure (12) group 8. PM (0.8ml/200g/day) + Vit. E (50 IU/kg). Section studied shows pancreatic lobules separated by connective tissue septa with decrease in islets. The center of islet cells consist of quantitative decrease in both the Beta-cells and alpha cells showing degenerative changes (compared to control group) Intervening these cells are seen vascular spaces.

DISCUSSION:

This is an era in which it is seen that medical science has developed a lot average age in terms of years has increased due to development and discovery of medications for the treatment of diseases. At the same time new challenges to human health are coming on surface in the shape of new viral infections, increase in the number of patients suffering from chronic diseases like hypertension and diabetes mellitus, increase in the number of cancer patients etc. All of these issues can be related to change of life style, environmental pollution etc. **Changes in** life style include dietary habits, lack of physical activity and dependence on cell phones, laptops connected with **Wi Fi**. Current study is first of its kind in which effects of **cell** phones and Wi fi have been studied particularly on **pancreas** and **serum** glucose levels. In our study all the groups exposed to cell phones connected with **Wi Fi** developed damage to pancreatic beta cells while alpha cells remained intact, this appears to be a strange phenomenon, it is seen especially in Type 1 DM. The α -cells secrete **glucagon**, which causes increase in serum glucose levels. Both damage to beta islets (insulin secreting cells of pancreas) and stability of alpha cells caused an increase in serum glucose levels. Regarding damage to the body cells i.e beta cells results of our study tally with the previous studies [24-26].

Pomegranate's anti-oxidant and anti-diabetic effects observed in this study are in conformity with the previous studies [27,28]. In previous studies it has been found that pomegranate is rich in flavonoids [29]. It is well documented in the research that flavonoids are effective in controlling **hyperglycemia** associated with Diabetes Mellitus [30,31]. Being rich in flavonoids can be the main reason behind the beneficial effects of pomegranate like decrease in serum glucose levels as well as prevention of damage to beta islets and their recovery after the damage.

Regarding Vit E effects on the pancreas and serum glucose levels of rats exposed to **cell phones** and **Wi Fi**, it was observed that Vit E could prevent damage to cells to some extent but Serum glucose levels remained higher in comparison to the control. These results are in agreement of the observations found in previous study [32].

CONCLUSION:

It was discovered in this study that **cell** phones and **Wi Fi** can cause pancreatic damage and hyperglycemia leading to Diabetes Mellitus and already existing Diabetes Mellitus may get aggravated. To some extent both the substances used in the study i.e. **pomegranate** and **vitamin E** were found effective in decreasing serum glucose levels as well as repair of the damage to the rat pancreas caused by mobile phones and **Wi Fi**. **while vitamin E** didn't produce significant reduction in serum glucose levels as well as couldn't repair damaged pancreas significantly. **It is** concluded that both cell phones and **Wi Fi** possess detrimental effects, causing damage to pancreas leading to hyperglycemia. Pomegranate repairs and controls pancreatic damage very well resulting in reduction in serum glucose levels. It may help manage Diabetes Mellitus. **Vitamin E** is found to possess preventive **effects** in pancreatic

damage. It is suggested that the research studies should be conducted with large sample size in humans to verify the harmful effects of cell phones and **Wi Fi** on human health.

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