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Ameliorative potential of flavonoids and antioxidants on the cell phone and Wifi induced Neuro- degeneration and Oxidative Stress in the Rats.

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Abstract:
Cell phones and wifi have become necessity of life. These are very widely being used worldwide. It is also a very well-known fact that they emit radiation. Radiation affectsnormal functioningof cells including basic anatomical and physiological units of the Nervous system. The damage in brain cells i.e neurons cause early incidence of Dementia/Alzheimer's disease, parkinsonism, epilepsy and even neoplasms.Themain aim of the current study was to observe the destructive effects of Wi-Fi systems and mobile phones released radiofrequency radiation on the Neurons in different areas of the brain. Inthis study cell phone and Wifi emitted radiation harmful effects on the rat brain and oxidative stress were studied and Protective effects of antioxidants were observed on brain of the rats. Brain histo-pathology and oxidative stress parameters were studied .It was observed that Cell phone and Wifi radiation massively damage the neurons .

Keywords
Cell Phone, Wifi, Neuronal damage, Oxidative Stress, Antioxidants, Flavonoids

INTRODUCTION:

Modernization of lifestyle has lead to increased Electromagnetic pollution worldwide due to daily use of wireless communication (Cell phones,Wifi,Personal computers, Tablets, Playing tools, games, Movies etc.). The present situation in routine life has raised wide spread scientific distress on the radiofrequency radiation (RFR) effects of on an individual's health. Available data regarding the effects of cell phones and Wi-Fi, cannot be termed as sufficient but whatever is available ,substantiate the apprehension of harm[1].It has been noticed that Radio frequency-modulated electromagnetic fields (RF-EMFs) are emitted fromMobile phones which are largely absorbed by the head of the user and RF-EMFs affect cerebral carbohydrate biotransformation, and temper with neuronal excitability[2-3].The Entry of RF-EMFs, into the brain bring about detrimental changes. The impact can be correlated with the amount and duration of use and dose in the brain, also their impact can be considerably changed by frequency band, transmission system and position in the brain [4-5].

In many studies, it has been found that radiation exposure, affects different organs/systems negatively and cause, cancer [6], genetic damage [7-8], neurological disease[9-11], reproductive disorders [12-13], immune dysfunction[14-15] , kidney damage[16-17], electromagnetic hypersensitivity [18], cognitive effects [19] ,effects on Pancreas [20].

Oxidative stress has been found to produce harmful effects in the biological systems.Prolonged release of ROS (Reactive Oxygen Species)and imbalance in the antioxidant mechanism, which causes damages the immune mechanism that may induce the development of inflammatory disease, neoplasms etc[21].

The pomegranate is classifiedas a berry ,that belongs to the herbal family, *Punicaceae*. The genus *Punica*, has one principal species called *P. granatum*[22].It has been observed that some components of pomegranate like polyphenols possess antioxidant, anti-inflammatory, and anticarcinogeniceffects,hencemay be possible to use in the prophylaxis and management of many types of neoplasms, cardio vascular disease, bone degenerative disorders, rheumatoid arthritis, and other abnormalities. It also has been found to improve woundhealing[23] .

Reactive oxygen species cause neuronal damage.Vitamin E is a powerful reactive oxygen species (ROS) collector and can promisingly decrease post traumatic brain injury (TBI)oxidative damage .Vitamin E can antagonize the detrimental effects of mild TBI on Nervous system[24].

Materials and Methods:

Animals:

From the animal house, faculty of pharmacy, Northern Border University, fortyWistar Albino (male) rats were acquired and were used in the study. Each rat was of 240-260 g weight and 8 week old at the outof the study.Following the guidelines related to animal research released by the SRD Committee, of the University, the animals were taken care of. For five days they were kept in cages , before use in the research under optimal conditions (25°C temperature, a 12/12-h light/dark cycle, and 22 CO humidity). They were given standard laboratory pellet chow and water *ad libitum*,diet. These animals were divided into 8 groups comprising of 5 rats in each group.

Experimental Design:

The rats were clustered in 8groups ,as follows :

Control (Group 1), EMR(Group 2) , EMR 900 MHz EMR (1hr/Day) + PM (0.4ml/200g)(Group 3).EMR 900MHz EMR (1hr/Day) + PM + 0.8ml/200g) (Group 4), EMR 900MHz EMR + Vit E 50

IU/kg (Group 5), EMR for 56 days) + then PM (0.4ml/200g/day for 28 days (Group 6), EMR for 56 days + PM (0.8ml/200g/day for 28 days (Group 7)), EMR for 56 days + then PM (0.8ml/200g/day) + VitE(50 IU/kg) for 28 days (Group 8).

To observe morbidity and mortality, the animals were checkedtwo times/day during the study period. The cell phone calls were given for two minutes after 2 hours .

Histopathological examination:

From the dissected brain , instantly Sagitalsections (2 m × 2 m) were taken and were kept for twenty four hours in 10% neutral-buffered formalin , for further embedding in paraffin. Histological examination of hematoxylin and eosin (H&E) stained tissuesections [25] was done using a light microscopy provided by a digital camera and photographs were taken.

Results:

In brain tissue homogenate, SOD levels decreased significantly inG2, G3 and G4 compared with G1 but increased significantly in G4, G6 and G8 compared with G2 (Figure 1). In brain tissue homogenate, CAT levels decreased significantly inG2, G3, G6 and G7 compared with G1 but increased significantly in G4, G5, G6, G7 and G8 compared with G2 (Figure 2). In brain tissue homogenate, GSH levels increased significantly inG2, G3, G4, G6, G7 and G8 compared with G1 but decreased significantly in G3, G4, G5, G6, G7 and G8 compared with G2 (Figure 3). In brain tissue homogenate, LPO levels increased significantly inG2, G3, G6, G7 and G8 compared with G1 but decreased significantly in G3, G4, G5, G6, G7 and G8 compared with G2 (Figure 4). In brain tissue homogenate, total protein levels increased significantly inG3 and G7 groups compared with G1 and G2 (Figure 5).

Histopathological Results:

The group 1 sections of the cerebral cortex (Hematoxylin and Eosinstained) disclosedintact normal neuronal pattern with familiar structure of the cerebral cortex. From outside inwards Six layers were visible. Neurons were the commonest cells inside the layers. In addition to neuroglial cells, Pyramidal and granule cells were also found.

As compared to the control group examination of sections (H&E stained) taken from other groups ,displayed implacable multifocal structural changes in all layers of the cortex. **(Fig 6)**

Table (1):Comparison of the oxidative stress markers and total proteins in brain homogenate in different groups.

Parameters	Group 1 (Control)	Group 2	P-Value (Group 2)	Group 3	P-Value (Group 3)	Group 4	P-Value (Group 4)
SOD (U/mg proteins)	0.323 ± 0.001	0.316 ± 0.002	1P = 0.001	0.128 ± 0.002	1P = 0.035, 2P = 0.929	0.322 ± 0.005	1P = 0.996, 2P = 0.010
CAT (µM/g proteins)	0.317 ± 0.006	0.196 ± 0.004	1P < 0.0001	0.233 ± 0.047	1P < 0.0001, 2P = 0.056	0.307 ± 0.015	1P = 0.987, 2P < 0.0001
GSH (nmoles GSH ox/min/mg)	0.654 ± 0.003	0.964 ± 0.006	1P < 0.0001	0.820 ± 0.003	1P < 0.0001, 2P < 0.0001	0.716 ± 0.005	1P < 0.0001, 2P < 0.0001
LPO (µmoles MDA/g protein)	3.878 ± 0.194	5.835 ± 0.179	1P < 0.0001	4.588 ± 0.266	1P < 0.0001, 2P < 0.0001	3.612 ± 0.258	1P = 0.250, 2P < 0.0001

Total Proteins (mg/dl)	0.032 ± 0.046	0.062 ± 0.005	1P = 0.802	0.422 ± 0.031	1P < 0.0001, 2P < 0.0001	0.003 ± 0.001	1P = 0.841, 2P = 0.094

Parameters	**Group 5**	**P-Value (Group 5)**	**Group 6**	**P-Value (Group 6)**	**Group 7**	**P-Value (Group 7)**	**Group 8**	**P-Value (Group 8)**
SOD (U/mg proteins)	0.317 ± 0.001	1P = 0.005, 2P = 1.000	0.317 ± 0.001	1P = 0.005, 2P = 1.000	0.319 ± 0.002	1P = 0.221, 2P = 0.475	0.321 ± 0.002	1P = 0.958, 2P = 0.026
CAT (µM/g proteins)	0.298 ± 0.007	1P = 0.749, 2P < 0.0001	0.254 ± 0.012	1P < 0.0001, 2P < 0.0001	0.276 ± 0.009	1P = 0.027, 2P < 0.0001	0.291 ± 0.023	1P = 0.386, 2P < 0.0001
GSH (nmoles GSH ox/min/mg)	0.654 ± 0.003	1P = 1.000, 2P < 0.0001	0.843 ± 0.031	1P < 0.0001, 2P < 0.0001	0.740 ± 0.044	1P < 0.0001, 2P < 0.0001	0.692 ± 0.011	1P = 0.032, 2P < 0.0001
LPO (µmoles MDA/g protein)	3.846 ± 0.087	1P = 1.000, 2P < 0.0001	4.836 ± 0.122	1P < 0.0001, 2P < 0.0001	5.049 ± 0.076	1P < 0.0001, 2P < 0.0001	5.483 ± 0.223	1P < 0.0001, 2P = 0.046
Total Proteins (mg/dl)	0.064 ± 0.033	1P = 0.747, 2P = 1.000	0.092 ± 0.051	1P = 0.081, 2P = 0.806	0.212 ± 0.055	1P < 0.0001, 2P < 0.0001	0.035 ± 0.004	1P = 1.000, 2P = 0.874

Data are expressed as mean ± standard error, with 1P indicating significance compared to Group 1 (Normal Control) and 2

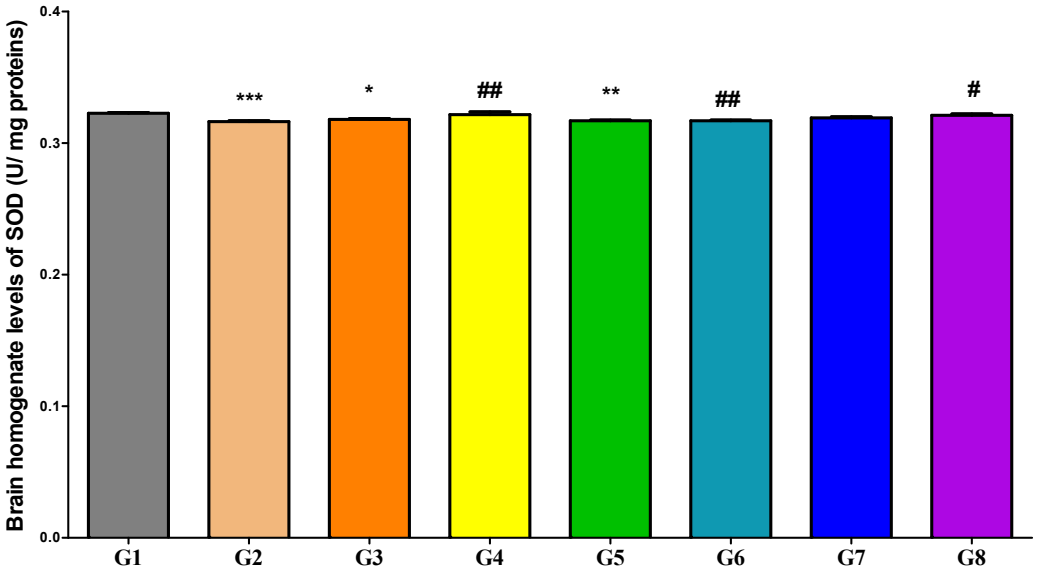

Figure (1): Comparison of the brain homogenate levels of SOD

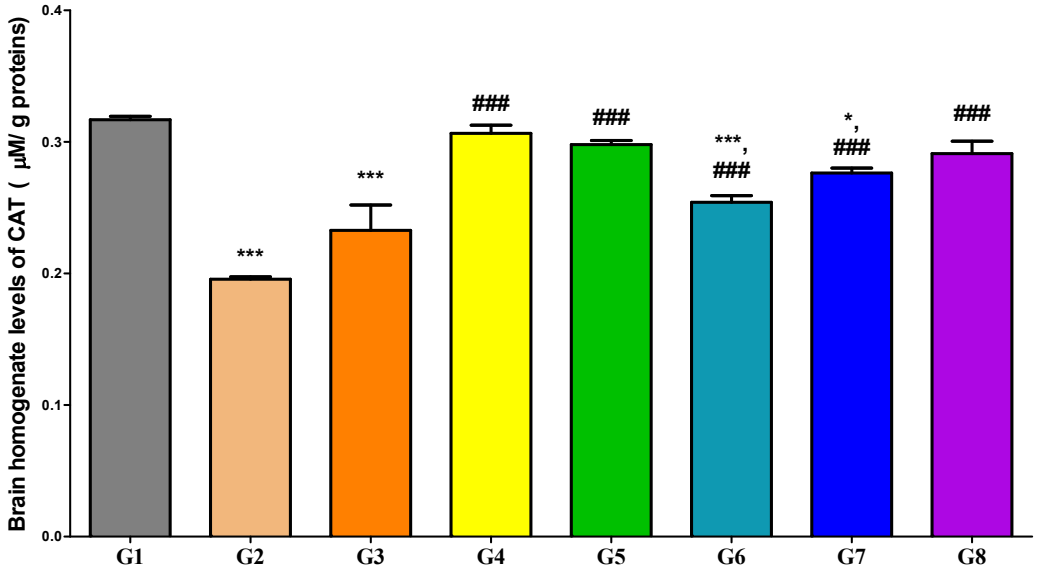

Figure (2): Comparison of the brain homogenate levels of CAT

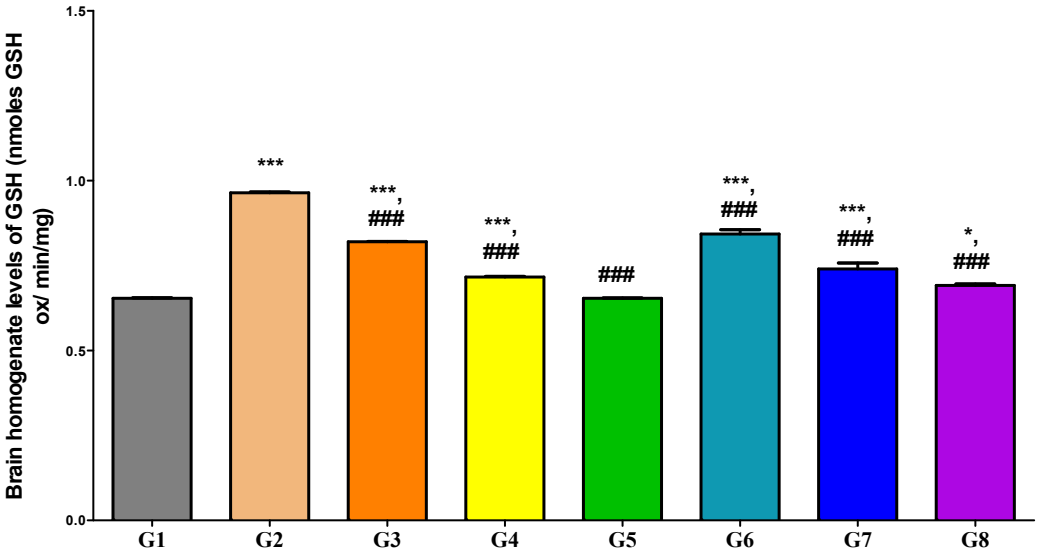

Figure (3): Comparison of the brain homogenate levels of GSH

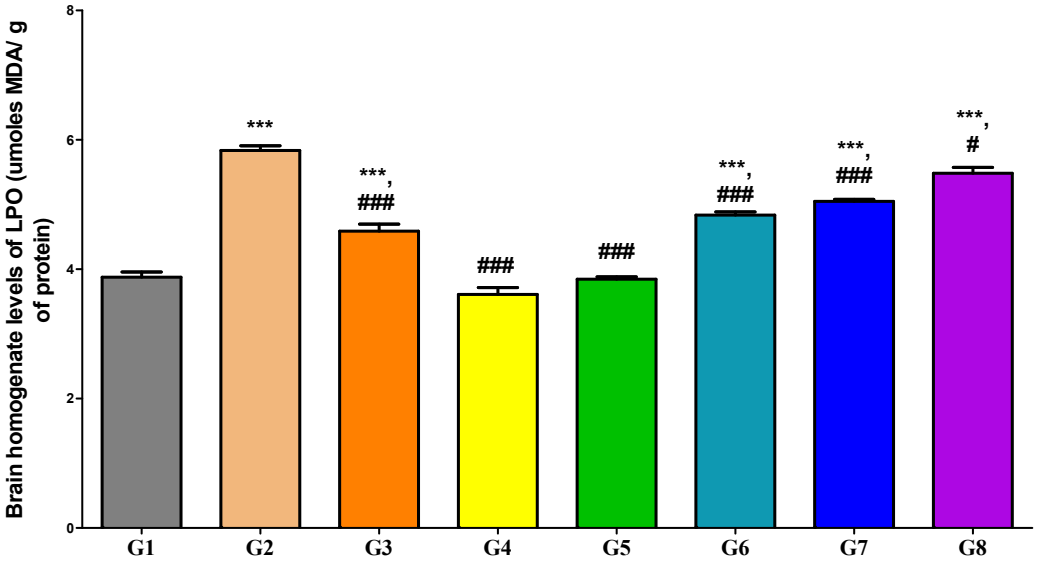

Figure (4): Comparison of the brain homogenate levels of **LPO**

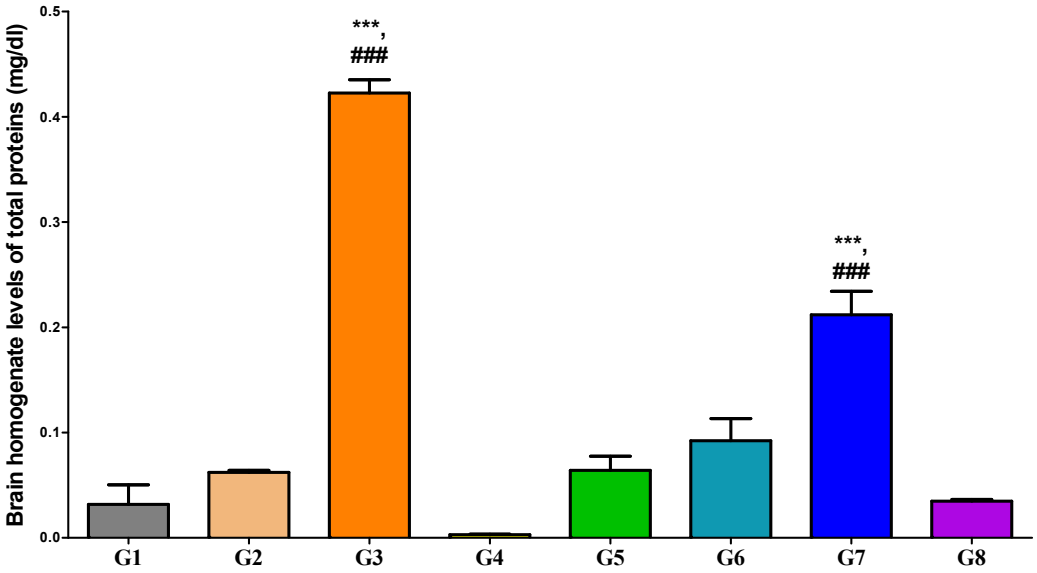

Figure (5): Comparison of the brain homogenate levels of total proteins

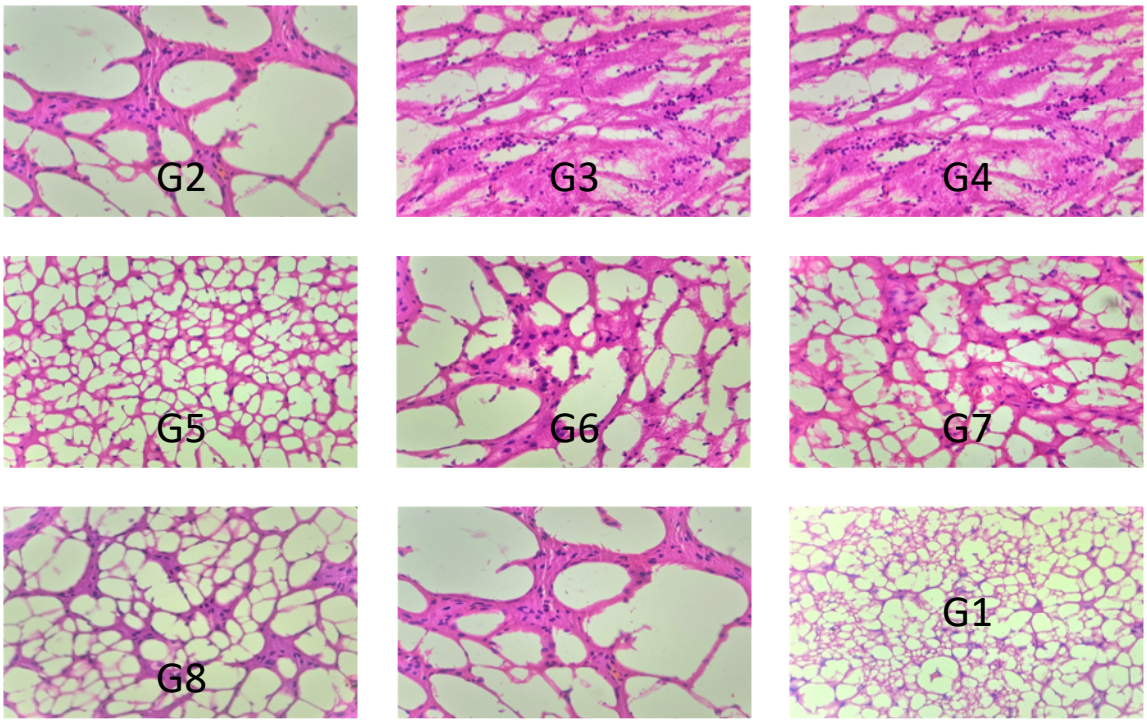

Figure (6) Brain parenchyma sections show intact normal architecture in G1.The G2,G3 and ,G4 pyramidal cells and neuroglial cells appear with inflammatory cell infiltration . The blood vessels appear unremarkable. ,G5,G6,G7 and G8 show scant/improved inflammation.

Discussion:

With modernization of living ,human lifestyles globally have become dependent on the use of technology .Overuse of the modern tools has its detrimental effects on the basic structural and functional units of the body[26], including the Neurons, which control the normal physiological functions .The physiological functions depend on the continuous control directly through the network of nerves and indirectly via increase and decrease in the levels of neurotransmitters and hormones. All the homeostatic factors in the body are interdependent ,therefore pathology in one functional area ultimately leads to produce dysfunction in other[27].In the current study ,modern tool of the life cell phone and Wifi emitted Radio frequency effects, were observed on the Neurons in different areas of brain and their damaging pathway association with Oxidative stress, also the protective effects of flavonoids present in Punicagranatum and Vitamin Ewere observed. In the past, some studies were performed to observe the consequences of radio frequencyexposure ,on the genes [28](co related with development of cancers), enzyme changes leading to development of Oxidative stress[29], membrane effects ,effects on number of cells in different systems. It is observed in the current invitro and histopatholological study that Cell phones and Wifi emitted radiation causes increase in oxidative stress leading degeneration of neurons as well changes in morphology of the cells[30]. At the same time it was also seen the use of Vit E and Flavonoids rich Punicagranatum extract reduces ROS induced neuronal damage.Classically ,causes of Neuronal damage are classified in two main broad categories , like Traumatic Brain Injuries (TBI) and Acquired Brain Injuries (ABI) [31], unfortunately little work has been done on newly emerging causes of Brain/Neuronal damage and its prevention and treatment .In the previous studies conducted ,it has been found that Antioxidants and Falvonoids reduce the cell injury ,cardiovascular disorders, inflammation, Cancer and Alzhiemer,disease etc. Results of our study are in conformity regarding reduction in oxidative stress and prevention of neuronal damage and inflammation , with the previously conducted studies .

Conflict of intrest: There is no conflict of interest related to the study.

Conclusion:

It can be concluded from the results of this study that Cell Phones and Wi-Fi exposure, leads to oxidative stress causing inflammation and damage /injury to the Neurons in almost all the parts of the brain . Concomitant use of Antioxidants and Flavonoids prevent/reduce this damage .It is suggested that further studies ,with different methodologies should be conducted to establish role of Antioxidants and Flavonoids in prevention of Neuronal damage .

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