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Motor Disorders and Impaired Electrical Power of Pallidal EEG Improved by Gallic Acid in Animal Model of Parkinson's Disease

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Abstract: The aim of this study was evaluation the effect of Gallic acid on movement disorders and pallidal electrical power in animal model of Parkinson's Disease (PD). PD is clinically characterized by development of motor disturbances, such as bradykinesia, resting tremors, rigidity and a later loss of postural reflexes. Oxidative stress is a hallmark factor where the oxidation of dopamine generates Reactive Oxygen Species (ROS) and an unbalanced production ROS induces neuronal damage, therefor leading the neuronal death. Gallic Acid (GA) and its derivatives are present in the plant kingdom and acts as a potent antioxidant. Wistar male rats devided into seven groups randomly with 8 in each. Animals in all groups except control received 8 μg/2 μL 6-hydroxydopamine dissolved in normal saline contains 0.01% ascorbate or vehicle in right Medial Forbrain Bundle (MFB) and a bipolar wire electrode was implanted in the left globus pallidus nucleus of all animals under stereotaxic surgery. Two weeks later PD was approved by contralateral rotation signs induced by apomorphine and then movements and electrical power of pallidal were evaluated. Motor functions and pallidal electrical power were impaired and GA could improve motor dysfunctions and gamma wave power in parkinsonian rats' significantly with higher dose of GA (200 mg kg^{-1}). Present result showed that GA may act as a potent antioxidant and free radical scavenger to reverse motor disorders and pallidal gamma wave power after 6-OHDA neurotoxicity in brain.

Key words: Gallic acid, parkinson's disease, 6-hydroxydopamine, motor disorders, electrical power

INTRODUCTION

Parkinson's disease is a progressive neurodegenerative disorder and clinically characterized by both the development of extrapyramidal motor disturbances, such as bradykinesia, resting tremors, rigidity and a later loss of postural reflexes (Soto-Otero *et al*., 2002; Zigmond and Burke, 2002). The symptoms of PD result from selective degeneration of dopaminergic neurons in the Substantia Nigra pars compacta (SNc) (Da Cunha *et al*., 2002; Lu *et al*., 2006). Because of SNc projects predominantly to the striatum, a reduction of the dopamine (DA) levels in the striatum may causes motor and cognition disorders (Da Cunha *et al*., 2002; Lu *et al*., 2006).

Environmental or genetic factors are considered as a factor of pathogenesis of PD. In almost all of these processes, oxidative stress is a hall mark factor where the oxidation of DA generates Reactive Oxygen Species (ROS) and an unbalanced production of ROS induces neuronal damage, therefore leading to neuronal death (Esposito *et al*., 2002; Lu *et al*., 2006).

Polyphenols are a group of chemical substances present in plants, fruits and vegetables. Several studies in the past have shown that polyphenols have *in vitro* and *in vivo* activity in preventing or reducing the effects of Reactive Oxygen Species (ROS) associated with oxidative stress. They have strong antioxidant and metal-chelating properties. Also they are capable to induce intracellular signaling pathways associated with cell survival and gene expression (Jimenez-Del-Rio *et al*., 2010).

Gallic acid (GA, 3,4,5-trihydroxybenzoic acid) and its derivatives are present in the plant kingdom and represent a large family of plant which are secondary polyphenolic metabolites hence natural antioxidants (Lu *et al*., 2006). GA is a strong antioxidant and previous studies have shown that Gallic acid has potent antioxidant property, including superoxide free radical scavenging activity and reducing power (Shahrzad *et al*., 2001, Tung *et al*., 2009).

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So the aim of this study was to evaluate the effect of Gallic acid on motor disorders and local EEG recorded from Pallidum in animal model of Parkinson's disease.

MATERIALS AND METHODS

Animals: Sixty four Male albino rats of Wistar strain (6-7 m; 300±20g) obtained from Ahwaz Jundishapur University of Medical Sciences (AJUMS) laboratory animal center were used in this study. Animals were housed individually in standard cages under controlled room temperature (20±2°C), humidity (55-60%) and light exposure conditions 12:12 h light-dark cycle (lighted on 07:00 am) from 30 Jan-30 Oct, 2010. All experiments carried out during the light phase of the cycle (8:00 a.m. to 6:00 p.m.) in Ahvaz Physiology Research Center (PRC). Access to food and water were *ad libitum* except during the experiments. Animal handling and experimental procedures performed under observance of the University and Institutional legislation, controlled by the Local Ethics Committee for the Purpose of Control and Supervision of Experiments on Laboratory Animals. All efforts were made to minimize animal suffering, to reduce the number of animals used. Prior to the onset of behavioral testing, all rats were gentle handled for 5 days (daily 5 min).

Animals were divided randomly into eight groups, consisting of eight animals in each: 1) control, intact rats, they received no intervention; 2) sham lesion (sham-PD), received two microlitters normal saline containing 0.01% ascorbic acid; 3) PD (lesioned), received 8 μg/2 μL 6-hydroxy dopamine (6-OHDA) (Sigma, St. Louis, MO, USA) dissolved in normal saline with 0.01% ascorbic acid in right medial forebrain bundle (MFB); 4-6) Parkinsonian groups received 50 (PD+GA50), 100 (PD+GA100) and 200 (PD+GA200) mg kg^{-1} Gallic acid (Sigma, St. Louis, MO, USA) by orall gavage (PO) for 10 days, respectively, 7) PD+GA-Veh, lesioned rats received same volume of normal saline; 8) cont+GA100, intact rats, received 100 mg kg^{-1} GA by oral gavages (PO) for 10 days as positive control group.

Medial forebrain bundle lesion: Medial Forebrain Bundle (MFB) in the right brain hemisphere was lesioned with using the Tadaiesky *et al.* (2008) method with a little modifications (Tadaiesky *et al.*, 2008). The stereotaxic surgery was performed under ketamine/xylazine (90/10 mg kg^{-1}, i.p.) anesthesia. Stereotaxic injections were placed 4.0 mm anterior to the interaural line, 1.3 mm lateral to the midline and 8.4 mm ventral to the surface of the skull, according to the atlas of Paxinos and Watson (2006), 8 μg/2 μL 6-hydroxydopamine HBr (Sigma, USA) dissolved in normal saline with 0.01% ascorbic acid injected in right Medial Forebrain Bundle (MFB) using a Hamilton 10 μL syringe with a 26-gauge needle connected to a 30-gauge cannula. Following injection, the cannula was left in place for 5 min before being retracted, to allow complete diffusion of the drug. All animals were treated with intraperitoneal (i.p.) injection of 25 mg kg^{-1} desipramine (Exir Pharmaceutical Co., Iran) 30 min before surgery, in order to prevent noradrenergic terminals depletion by 6-hydroxydopamine (6-OHDA) toxicity. Sham-operated rats followed the same protocol except for the fact that vehicle was injected instead of 6-OHDA.

In order to measurement of rotational behavior, rats were placed in circular cages and the number of complete turns made during each 5 min period was recorded by chronometer. Following two weeks recovery period, rats exhibiting a vigorous rotational response (more than 100 total turns) to apomorphine injection (0.05 mg kg^{-1}, s.c., dissolved in normal saline contains 0.01% ascorbic acid) as parkinsonian rats were selected for further study (Jimenez *et al.*, 1999; Metz *et al.*, 2005). It has previously been demonstrated that rats meeting this criterion have a greater than 95% depletion of striatal dopamine.

Recording electrode implantation: in order to pallidal local EEG recording a bipolar metal wire electrode (stainless steel Teflon, 0.005" bare, 0.008" coated, A-M systems, INC. WA.) was implanted in right globus pallidus nucleus under ketamine/xylazine anesthesia and stereotaxic surgery. Animal passed 7-10 days recovery period.

Stride length: Footprint analysis was used to assess stepping patterns. The animal's forepaws were inked and footprints of paws were made on paper strips covering a narrow runway. A series of at least three sequential steps on six samples was used to determine the mean of base of stride length. Stride length measures refer to the distance between the centers of two consecutive footprints of the same side (Fig. 1) (Metz *et al.*, 2005).

Rotarod test: The rotarod test was performed in order to evaluation the motor coordination two weeks after lesion or after 10 days treatment with GA or vehicle in healthy and lesioned groups. Accelerating rotarod measures fine motor coordination, balance and resistance to fatigue by assessing the duration that a rat can remain standing/walking on a rotating, slowly accelerating rod. After familiar rats with instrument, the rotarod rotating speed was 4 rpm at first 5 min and accelerated up to 40 rpm during remained minutes. Each rat was tested 3 times at one day with 45 min interval (Dekundy *et al.*, 2006).

Catalepsy tests: The catalepsy was assessed by placing one forepaw on a horizontal bar 9 cm above the surface and another forepaw on a podium with 3 cm high. The

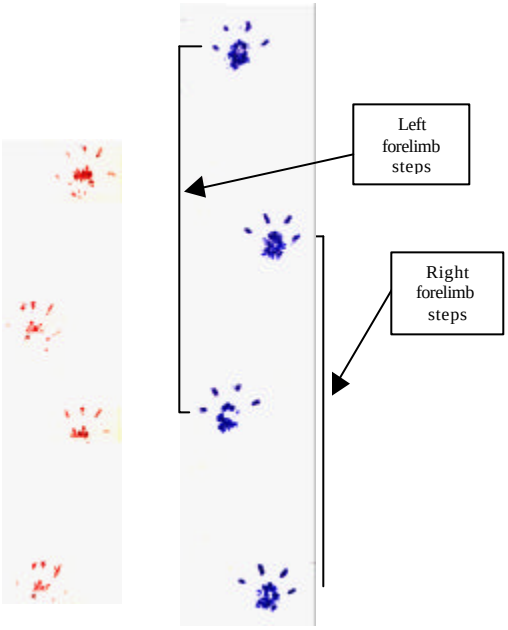

Fig. 1: Illustration of control and rats offered PD forepaw prints in stride length test. Blue ink paw print right recorded from a control (Intact) rat. Red ink paw print left recorded from rat model of PD. There is a longer walks length in control to compare with rats with PD

latency to initiate the movement was used as a measure of catalepsy. An ability of a tested substance to decrease the latency in the catalepsy test was considered indicative of its potential antiakinetic effect. After then muscle stiffness (rigidity) induced by 6-OHDA injection in Medial Forebrain Bundle (MFB) of rats was tested. The scoring adopted was based on a three stage model as follows: Stage 1; when the rat was placed on a flat table, if it showed normal movement, the score allocated was zero, if the rat did not move, the allocated score was 0.5. Stage 2; one of the rat forepaws was placed on a 3 cm high wooden podium block, if the rat did not replace its within 10 sec, it received a score of 0.5. Similarly, the second forepaw was placed on the wooden block and scored the same. Stage 3; one of the fore paws was placed on a 9 cm high wooden block and another paw left hanging. A positive sign for full rigidity was gauged by the failure of the animal to correct the imposed position within 10 s and was given a score of 1. A similar procedure was used with another fore paw. Thus if a rat was in full rigidity (muscle stiffness), a total cumulative score of 3.5 was assigned (Dekundy *et al*., 2006; Sarkaki *et al*., 2008).

Histological verification: At the end of the experiments, rats were deeply and irreversible re-anesthetized (with overdose of Ketamine HCl) and sacrificed. Then, rats were perfused transcardially by approximately 100 mL of normal saline to clear the blood, followed by 100 mL of 5% formalin in normal saline. To verify the location of electrode tip and lesion point the direct current (DC, 0.5 μA, 3 sec) was passed via electrodes tip and crystal violet (0.5 μL) injected into MFB, respectively. The brains removed from skull and immersed in 10% formalin solution for at least 5 days. The brains were frozen and cut into coronal sections (50 μm) using a freezing microtome and stained with crystal violet for verification of the point of the electrode tip (Doulah *et al*., 2009). Only experimental data from lesions correctly located in the MFB and correct location of electrode tip in globus pallidus were used for statistical analysis.

Local EEG recording: Electrical field potentials (local EEG) from the right globus pallidus nucleus of freely moving rats were fed to a bio-amplifier (AD Instruments, 4-Channels Power Lab, Australia) with 1 mV amplification, sample recording 400 Hz and 0.3-70 Hz band pass filtration for 5 sec. The local EEG and its gamma, beta, alpha, theta and delta frequency bands electrical power changes during 5 sec were compared between all groups.

Statistical analysis: Data were expressed as Mean±SEM of values for motor activity tests, local EEG and its frequency bands power (μV^2 Hz^{-1}). Statistical analysis was performed by one-way ANOVA followed by LSD post hoc test for motor tests, local EEG and its frequency bands power, the nonparametric Kruskal-Wallis and Mann-Whitney post hoc test for learning and memory data. A p-value less than 0.05 was assumed to denote a significant difference and levels of significance are indicated by symbols: *$p<0.05$, **$p<0.01$, ***$p<0.001$.

RESULTS

Motor functions

Bradykinesia: Data have shown that the grid descent latency (sec) of forepaws on a 9 cm height bar as a valuable parameter for bradykinesia (catalepsy) was increased significantly ($p<0.001$) in untreated lesioned rats to compare with control and sham-PD groups ($p<0.001$). Treatment lesioned rats with GA (doses 50, 100 and 200) decreased could decrease grid descent latency significantly ($p<0.001$ vs. PD and PD+GA.veh groups, Fig. 2a).

Rigidity (muscle stiffness): Data obtained from rigidity test after placing the control and lesioned rats on the table surface for walking and then placing their right and left forepaws on 3 and 9 cm wooden podiums, respectively. Muscle stiffness was increased significantly in PD and PD+GA-veh groups (did not receive GA), they didn't

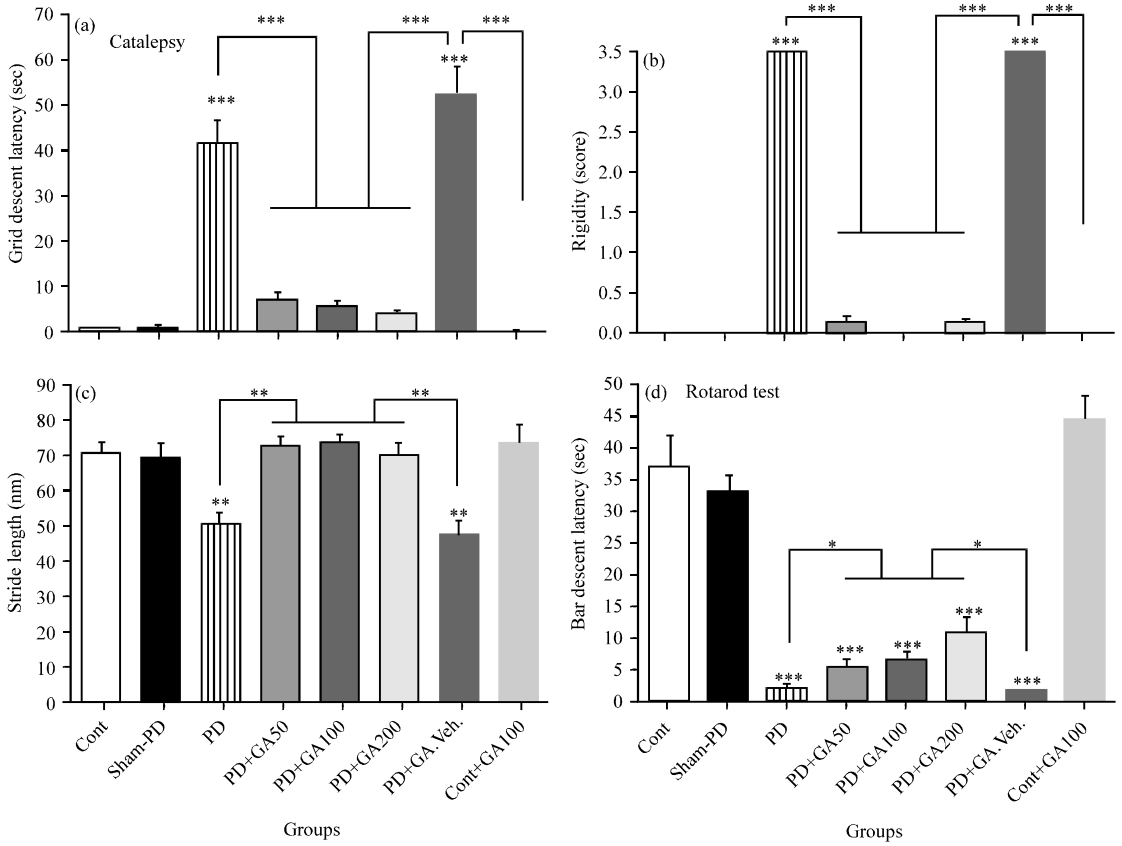

Fig. 2(a-d): (a) Grid descent latency (sec) as a parameter of bradykinsia in lesioned rats (PD), (***p<0.001 for PD and PD+GA-veh. vs. control and sham-PD). In PD+GA groups it was decreased significantly (***p<0.001 for PD+GA vs. PD or PD+GA-veh.,) (b) Rigidity or muscular stiffness score in PD and PD+GA.veh group increased significantly (***p<0.001 for PD and PD+GA-veh. vs. control and sham-PD). In PD+GA groups reduced sore of rigidity significantly (***p<0.001 for PD+GA vs. PD or PD+GA-veh.,). (c) Stride length (mm) in PD and PD+GA-veh. was decreased significantly (**p<0.01 for PD and PD+GA-veh vs. control and sham-PD, n = 10). In groups PD+GA increased significantly (**p<0.01 for PD+GA vs. PD and PD+GA-veh., (d) Bar descent latency (sec) as motor balance was decreased significantly in PD and PD+GA.veh (***p<0.001 for PD , PD+GA-veh, vs. control and sham-PD). In group PD+GA increased it significantly (*p<0.05 for PD+GA groups vs. PD and PD+GA-veh., one way ANOVA followed by LSD post Hoc test)

replace their forepaws from 3 or 9 cm wooden cylinders more than 10 sec duration (p<0.001 as compared with control and sham-PD groups). GA administration decreased it significantly (p<0.001). Treatment with GA could decrease muscle stiffness in PD+GA group significantly (p<0.05). GA may have a potent releasing effect on muscle stiffness induced by 6-OHDA (Fig. 2b).

Stride length: Resulted data from forepaws walk-length measurements (stride-length test) showed that walk length in PD and PD+GA-veh groups was lower than in control and sham- PD groups significantly (p<0.01). Treatment with GA could increase stride length in lesioned (PD+GA) group significantly (p<0.01 vs. PD and PD+GA-veh). Administration of GA to lesioned rats could reverse completely stride length impairment. However, walk length of post-treated lesioned rats was normal (Fig. 2c).

Rotarod: Data obtained from all groups following motor coordination test in rotarod indicated that bar descent latency in untreated lesion groups (PD and PD+GA-veh) was decreased severely when compared with control and sham-PD groups (p<0.001). Treatment with all three doses GA could reverse to normal disrupted motor coordination induced by 6-OHDA (p<0.05, PD+GA vs. PD and PD+GA-veh., Fig. 2d).

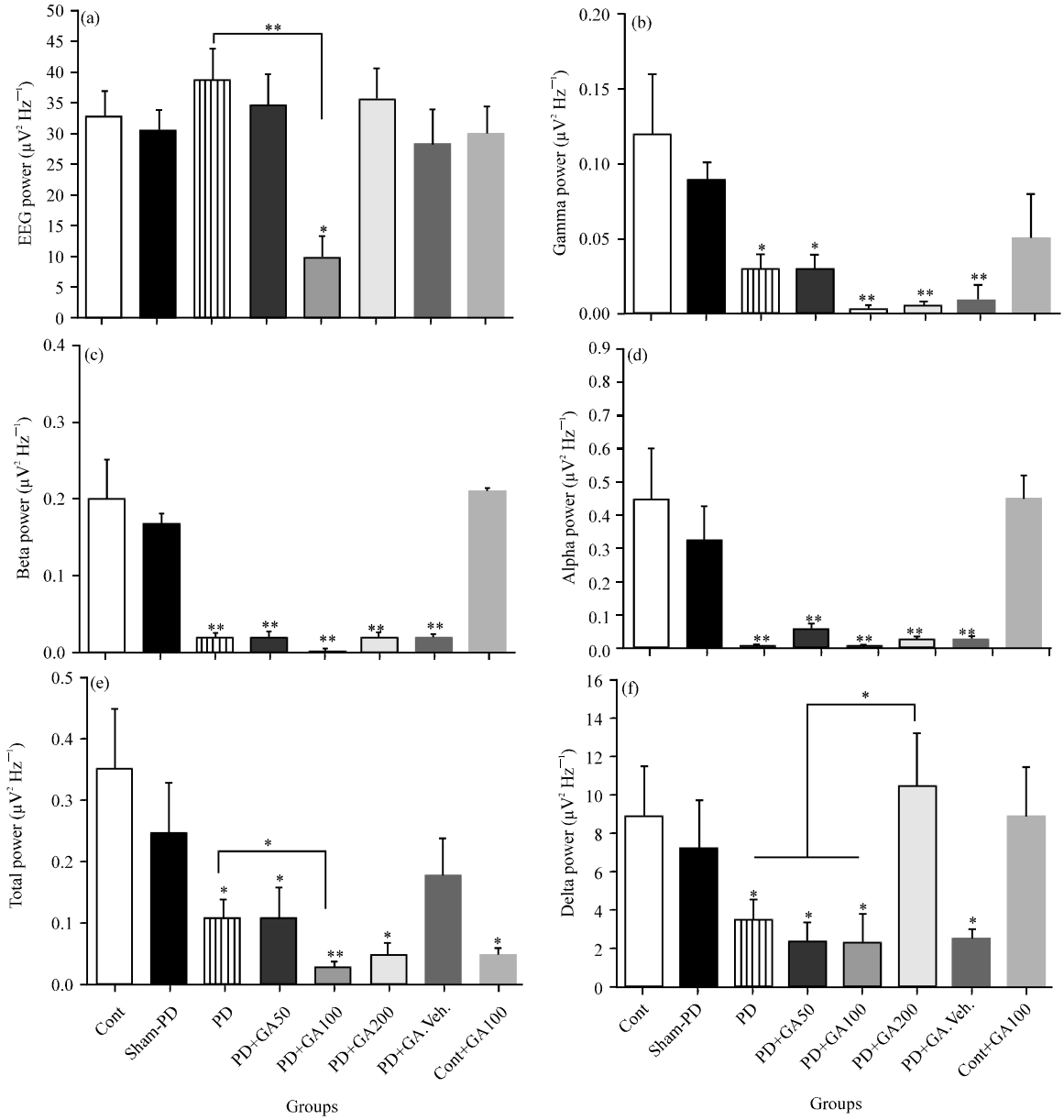

Fig. 3(a-f): Globus Palidus (GP) local EEG and its frequency bands electrical power ($\mu V^2 Hz^{-1}$). Data were analyzed by one-way ANOVA followed by LSD post-hoc test. (a) EEG power (b) Gamma power decreased after MFB lesion in all groups. (**p<0.001, PD+GA100, 200 vs. control and *p<0.05, PD+GA50 and PD vs control (n = 8) (c) Beta power was decreased in all groups vs control and sham-PD. significantly (**p<0.01 for control and sham-PD vs. other groups). (n = 8) (d) Alpha wave power decreased after MFB lesion significantly (**p<0.01, PD vs. control and sham-PD (n = 8) (e) Theta power was decreased in all lesioned groups. significantly (*p<0.05 for PD and PD+GSE-veh. vs. control and PD+GA100) and (f) Delta wave power decreased after MFB lesion while it was increased even more than control by PD+GA200 significantly (*p<0.05, control vs. other groups except PD+GA200, n = 8)

Electrophysiology

GP local EEG frequency bands: The power of GP local EEG of lesioned (PD), post-lesion treated with GA (PD+GA) and PD+GA-veh groups had no differences as compared with control, sham operated EEG electrical power was decreased in PD+GA 100 significantly (p<0.05) (Fig. 3a). Electrical power of gamma band in GP local EEG was decreased in lesioned (PD) and PD+GA-veh.vs

control, sham operated (sham-PD) groups. It decreased even more than control by post lesion oral administration of GA significantly (**p<0.001, PD+GA vs. PD and PD+GA-veh. and other groups). So, GA could not improve post lesion gamma band power of GP local EEG in PD model (Fig. 2a). Electrical power of beta band in G.P local EEG was not different in control, sham operated (sham-PD) while it decreased in PD and PD+GA-veh. and PD+GA groups significantly (*p<0.05 for PD and PD+GA-veh. and PD+GA50 vs. control and sham-PD). Treatment with GA could not affect it (Fig. 3b).

Electrical power alpha band in GP local EEG was decreased after listening to MFB (PD) to compare with control and sham-PD groups (*p<0.01, PD, PD+GA-veh., PD+GA vs. control). So, GA could not change post-lesion alpha band power in PD model (Fig. 3c).

Electrical power of theta band in GP local EEG decreased after listening to MFB (PD) to compare with control, sham-PD, groups (*p<0.05, PD, PD+GA-veh., PD+GA vs. control). So, GA could not increase post-lesion theta band power of G.P local EEG (Fig. 2d).

Electrical power of delta band in GP local EEG decreased after lesion to MFB (PD) to compare with control, sham-PD, groups (*p<0.05). Treatment with doses 50 and 100 mg kg^{-1} GA could not affect its power while high dose of GA (200 mg kg^{-1}) could reverse delta power significantly (*p<0.05, Fig. 3e). Delta wave power decreased after MFB lesion while it was increased even more than control by PD+GA200 significantly (*p<0.05, control vs. other groups except PD+GA200, n = 8, Fig. 3f).

DISCUSSION

In this study we investigated the effect of unilateral injection of 6-OHDA into the rat right Medial Forebrain Bundle (MFB) as an animal model of PD and following motor disorders and Globus pallidus nucleus (GP) local EEG after listening and after two weeks treatment with 50, 100 and 200 mg kg^{-1} GA. We found that 10 days oral administration of 50, 100, 200 mg kg^{-1} GA to rat model of PD causes extensive improving the motor disorders significantly while pallidal delta wave power was reversed with 200 mg kg^{-1} GA.

The neuronal degeneration that occurs in PD has been lead to hypothesis for its pathogenesis. The free radical theory has been subjected of many excellent reviews (Zigmond and Burke, 2002). In addition to the possible involvement in aging, mitochondrial dysfunction and oxidative damage may play important roles in the slowly progressive neuronal death that is characteristic of several different neurodegenerative disorders including PD (Hsiao *et al*., 2001). The possibility that DA neurons may undergo free radical-mediated injury in PD has received support from experiments on animal. There is substantial evidence that the brain which consumes large amounts of oxygen, is particularly vulnerable to oxidative damage (Hsiao *et al*., 2001, Jadon *et al*., 2007). Features of the human pathological condition of PD can be mimicked in rats by injection of the neurotoxin 6-hydroxydopamine (6-OHDA) to induce striatal dopamine depletion. The injections are usually made unilaterally and so affect motor performance on the contralateral side of the body, including skilled fore- and hindlimb use and sensorimotor functions (Metz *et al*., 2005).

6-OHDA induces dopaminergic dysfunction due to caspase activations by increase in oxidative stress in the striatum. Several reports have suggested that the excessive ROS generated by 6-OHDA leads to oxidative stress which injures the cells and induces cell death via apoptosis (Tiffani-Castiglioni *et al*., 1982, Soto-Otero *et al*., 2000, 2002; Tanaka *et al*., 2006). Reactive oxygen species, such as superoxide radical anion, hydroperoxyl radical, hydrogen peroxide and hydroxyl radical, are constantly generated in cells as unwanted by products of aerobic metabolism (Yeh *et al*., 2009). 6-OHDA reacts with oxygen to produce superoxide anion radical, H_2O_2 and hydroxyl radical (Zigmond and Burke, 2002; Tanaka *et al*., 2006). Oxidation of polyunsaturated fatty acids (PUFA) results in the production of multiple aldehydes with different carbon chain lengths. The malondialdehyde (MDA) levels may be predominantly dependent on oxygen reactive species (ROS) levels, including hydroxyl radicals (Sultana *et al*., 2006).

MDA is derived from lipid peroxides of polyunsaturated fatty acids with three or more double bonds (Niki, 2009). Therefore, the non-radical products, including MDA which have cytotoxic properties themselves from lipid peroxidase (LPO), may play a key role in the progressive alterations induced by 6-OHDA unilateral injection (Tanaka *et al*., 2006). It has been shown that LPO products exert various biological effects either directly by reacting with proteins, enzymes and nucleic acids or indirectly through receptor-mediated pathways (Niki, 2009). Under physiological conditions, a low level of ROS is scavenged effectively by the cellular antioxidant defense system (Yeh *et al*., 2009). Cells normally have a number of mechanisms to resist against damage induced by free radicals. The major antioxidant defenses consist of antioxidant scavengers such as glutathione (GSH), vitamin C (ascorbic acid), vitamin E (alpha-tocopherol), carotenoids, flavonoids, polyphenols

and antioxidant enzymes (Esposito *et al*., 2002; Yeh *et al*., 2009). Therefore, a compound with anti-peroxidative activity seems to exert a pharmacological benefit in the protective and therapeutic implications of radical-induced pathological events (Hsiao *et al*., 2001). GA is a strong antioxidant that possesses antimutagenic and anticarcinogenic activities (Shahrzad *et al*., 2001). Gallic acid may directly combine with free radicals and lead to inactivate them which may suppress the intracellular concentration of free radicals (Jadon *et al*., 2007).

Tanaka *et al*. (2006) investigated to clarify the possible role of *in vivo* toxic effects of 6-hydroxydopamine (6-OHDA), especially caspase activations. He examined its effects on striatal lipid peroxidation (LPO) and caspase activations in 6-OHDA-lesioned mice. An increase in lipid peroxidation (LPO) in the striatum was recognized at 1, 3 and 14 days after 6- OHDA injection. Furthermore, the striatal GSH content was decreased in comparison with the pre-injection level at 3 and 14 days after the injection, thus indicating that LPO is transiently increased due to the production of intracellular oxidative stress (Tanaka *et al*., 2006). Among various antioxidants in the brain, the GSH system is particularly important in controlling cellular redox states and is the primary defense mechanism for peroxide removing from the brain. GSH system has a rapid and high capacity for the prevention of ROS-induced cell damage (Tanaka *et al*., 2006).

Yeh *et al*. (2009) evaluated the role of phenolic acids on the expression of antioxidant enzymes in the heart of male Sprague-Dawley rats. Rats that received 100 mg kg^{-1} of gallic acid significantly elevated glutathione peroxidase (GPx) activity compared to the control group. The activity of GPx in rats treated with gallic acid was significantly higher than in rats with coumaric acid. Regarding cardiac catalase (CAT) activity, administrations of gallic acid to rats also resulted in higher enzyme activity as compared to the control rats. Gallic acid supplementation significantly elevated the total antioxidant capacity in the heart as compared to the control group. Dietary phenolic acids may also have physiological antioxidant properties (Yeh *et al*., 2009).

Li *et al*. (2005) investigated the activities of the antioxidant enzymes catalase (CAT) and glutathione peroxidase (GPx) in the blood and liver of the aging model induced by injection of different doses of D-gal into normal mice and in senescence accelerated mice (SAM) of different ages. When gallic acid purified from rose flowers was used to treat the 9-month-old male rats it not only reinstated the activities of CAT and GPx but also significantly reduced the amount of malondialdehyde (MDA) in the liver, brain and kidney (Li *et al*., 2005).

CONCLUSIONS

Ten days oral administration of GA could reverse motor disorders significantly after MFB lesion by 6-OHDA in rats, but could not reverse decreased electrical power of globus pallidus nucleus local EEG frequency bands except delta wave power with high dose of GA. We believed to reverse the PD local EEG power to normal may need longer treatment with GA.

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REFERENCES

Da Cunha, C., M.E.M. Angelucci, N.S. Canteras, S. Wonnacott, R.N. Takahashi, 2002. The lesion of the rat substantia nigra pars compacta dopaminergic neurons as a model for parkinson's disease memory disabilities. Cell. Mol. Neurobiol., 22: 227-237.

Dekundy, A., M. Pietraszek, D. Schaefer, M.A. Cenci and W. Danysz, 2006. Effects of group I metabotropic glutamate receptors blockade in experimental models of parkinson's disease. Brain Res. Bull., 69: 318-326.

Doulah, A.H., A.H. Rohami, H.M. Khaksari, F. Motamedi and Y. Farbood *et al*., 2009. The effect of peripheral administration of growth hormone on AD-like cognitive deficiency in NBM-lesioned rats. Neurosci. Lett., 466: 47-51.

Esposito, E., D. Rotilio, V. Di Matteo, C. Di Giulio, M. Cacchio and S. Algeri, 2002. A review of specific dietary antioxidants and the effects on biochemical mechanisms related to neurodegenerative processes. Neurobiol. Aging, 23: 719-735.

Hsiao, G., C.M. Teng, J.R. Sheu, Y.W. Cheng and K.K. Lam *et al*., 2001. Cinnamophilin as a novel antiperoxidative cytoprotectant and free radical scavenger. Biochim. Biophy. Acta (BBA)-Gen. Subj., 1525: 77-88.

Jadon, A., M. Bhadauria and S. Shukla, 2007. Protective effect of *Terminalia belerica* Roxb. and gallic acid against carbon tetrachloride induced damage in albino rats. J. Ethnopharm., 109: 214-218.

Jimenez, A., C. Marin, M. Bonastre and E. Tolosa, 1999. Narrow beneficial effect of dextromethorphan on levodopa-induced motor response alterations in an experimental model of parkinsonism. Brain Res., 839: 190-193.

Jimenez-Del-Rio, M., C. Guzman-Martinez and C. Velez-Pardo, 2010. The effects of polyphenols on survival and locomotor activity in *Drosophila melanogaster* exposed to iron and paraquat. Neurochem. Res., 35: 227-238.

Li, L., T.B. Ng, W. Gao, W. Li and M. Fu *et al.*, 2005. Antioxidant activity of gallic acid from rose flowers in senescence accelerated mice. Life Sci., 77: 230-240.

Lu, Z., G. Nie, P.S. Belton, H. Tang and B. Zhao, 2006. Structure-activity relationship analysis of antioxidant ability and neuroprotective effect of gallic acid derivatives. Neurochem. Int., 48: 263-274.

Metz, G.A., A. Tse, M. Ballermann, L.K. Smith and K. Fouad, 2005. The unilateral 6-OHDA rat model of Parkinson's disease revisited: An electromyographic and behavioural analysis. Eur. J. Neurosci., 22: 735-744.

Niki, E., 2009. Lipid peroxidation: Physiological levels and dual biological effects. Free Radical Biol. Med., 47: 469-484.

Paxinos, G. and C. Watson, 2006. The Rat Brain in Stereotaxic Coordinates. 6th Edn., Academic Press, San Diego, ISBN: 978-0-12-374121-9.

Sarkaki, A., M. Badavi, N. Hoseiny, M.K. Gharibnaseri and F. Rahim, 2008. Postmenopausal effects of intrastriatal estrogen on catalepsy and pallidal electroencephalogram in an animal model of parkinsons disease. Neuroscience, 154: 940-945.

Shahrzad, S., K. Aoyagi, A. Winter, A. Koyama and I. Bitsch, 2001. Pharmacokinetics of gallic acid and its relative bioavailability from tea in healthy humans. J. Nutr., 131: 1207-1210.

Soto-Otero R., E. Mendez-Alvarez, A. Hermida-Ameijeiras, A.M. Munoz-Patino and J.L. Labandeira-Garcia, 2000. Autoxidation and neurotoxicity of 6-hydroxydopamine in the presence of some antioxidants: Potential implication in relation to the pathogenesis of Parkinson's disease. J. Neurochem., 74: 1605-1612.

Soto-Otero, R., E. Mendez-Alvarez, A. Hermida-Ameijeiras, A.M. Munoz-Patino, A.M. Lopez-Real and J.L. Labandeira-Garcia, 2002. Effects of (-)-nicotine and (-)-cotinine on 6-hydroxydopamine-induced oxidative stress and neurotoxicity: relevance for Parkinson's disease. Biochem. Pharmacol., 64: 125-135.

Sultana, R., M. Perluigi, D.A. Butterfield, 2006. Protein oxidation and lipidperoxidation in brain of subjects with Alzheimer's disease: Insights into mechanism of neurodegeneration from redox proteomics. Antioxid. Redox Signal, 8: 2021-2037.

Tadaiesky, M.T., P.A. Dombrowski, C.P. Figueiredo, E. Cargnin-Ferreira, C.C. Da and R.N. Takahashi, 2008. Emotional, cognitive and neurochemical alterations in a premotor stage model of parkinson's disease. Neuroscience, 156: 830-840.

Tanaka, K., N. Ogawa and M. Asanumab, 2006. Molecular basis of 6-hydroxydopamine-induced caspase activations due to increases in oxidative stress in the mouse striatum Neurosci. Lett., 410: 85-89.

Tiffani-Castiglioni, E., R.P. Saneto, P.H. Proctor, J.R. Perez-Polo, 1982. Participation of active oxygen species in 6-hydroxydopamine toxicity to a human neuroblastoma cell line. Biochem. Pharmacol., 31: 181-188.

Tung, Y.T., J.H. Wu, C.C. Huang, H.C. Peng, Y.L. Chen, S.C. Yang and S.T. Chang, 2009. Protective effect of Acacia confusa bark extract and its active compound gallic acid against carbon tetrachloride-induced chronic liver injury in rats. Food Chem. Toxicol., 47: 1385-1392.

Yeh, C.T., L.C. Ching and G.C. Yen, 2009. Inducing gene expression of cardiac antioxidant enzymes by dietary phenolic acids in rats. J. Nutr. Biochem., 20: 163-171.

Zigmond, M.J. and R.E. Burke, 2002. Pathophysiology of Parkinson's Disease. In: Neuropsychopharmacology: The Fifth Generation of Progress, Davis, K.L., D.S. Charney, J.T. Coyle and C.B. Nemeroff (Eds.), Lippincott, Williams and Wilkens, Philadelphia, pp: 1881-1884.