Effect of treating lactating rats with lead acetate and its interaction with vitamin E or C on neurobehavior, development and some biochemical parameters in their pups

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Abstract

The current study investigated the effect of administration of vitamin E (600mg/ kg diet) concomitantly with lead acetate (10mg/kg, orally) and vitamin C (100mg/kg, orally) concomitantly with lead acetate (10mg/kg, orally) to the female lactating rats on the neurobehavioral, landmarks development and some biochemical tests in their pups. Administration of lead acetate to the female lactating rats caused a significant increase in open field activity test including (the number of squares crossed and rearing test within 3 minutes), olfactory discrimination test, triglycerides and malondialdehyde brain tissue, with a significant decrease in glutathione brain tissue and high density lipoproteins in their pups. The present study demonstrated that treatment of female lactating rats with vitamin C and lead acetate produced a significant decrease in righting reflex test in their pups. Administration of vitamin E concomitantly with lead acetate to the female lactating rats caused a significant increase in glutathione level accompanied with a significant decrease in malondialdehyde and triglycerides levels in their pups. The present study showed that treatment of female lactating rats with vitamin E or C with lead acetate produced a significant decrease in rearing test, whereas a significant increase in high density lipoproteins in their pups. It is concluded that administration vitamin E or C to the female lactating rats reverse the adverse effects produced by lead acetate on neurobehavioral. Vitamin E had positive effect on the levels of glutathione, malondialdehyde brain tissue, triglyceride and high density lipoproteins in their lactating pups.

Keywords: Vitamin E, Vitamin C, Lead acetate, Neurobehavior, Glutathione, Malondialdehyde, Rat pups.
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تأثير معاملة الجرذان المرضعات بخلات الرصاص وتداخله مع فيتأمين E أوC في السلوك العصبي وعلامات النضج وبعض القياسات الكيميائية الحياتية في صغارها

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الخلاصة

أجريت الدراسة الحاليه لمعرفة تأثير إعطاء فيتامين E (٦٠٠ملغم/كغم علف) سوية مع خلات الرصاص (١٠ملغم/كغم) وفيتامين C (١٠٠ملغم /كغم عن طريق الفم) سوية مع خلات الرصاص (١٠ملغم/كغم) لإناث الجرذان المرضعات على السلوك العصبي وتطور علامات النضج وبعض الاختبارات الكيميائية ألحياتيه في صغارها. أدى إعطاء خلات الرصاص لإناث الجرذان المرضعات إلى زيادة معنوية في اختبار النشاط الحركي داخل الميدان المفتوح والمتضمن (عدد المربعات المقطوعة واختبار عدد مرات الوقوف على القوائم الخلفية لمدة ثلاث دقائق) واختبار التمييز الشمي ومستوى الكليسيريدات الثلاثية والمالونديالديهايد في نسيج الدماغ مع انخفاض معنوي في مستوى الكلوتاثايون في نسيج الدماغ والدهون البروتينية عالية الكثافة في صغارها. أوضحت الدراسة الحالية أن معاملة إناث الجرذان المرضعات بفيتامين C مع خلات الرصاص سبب انخفاضا معنويا في منعكس تصحيح وضع الجسم في

صغارها. أدى إعطاء إناث الجرذان المرضعات لفيتامين E سوية مع خلات الرصاص إلى زيادة معنوية في مستوى الكلوتاثايون رافقه انخفاضا معنويا في مستويات كل من المالونديالديهايد و الكليسيريدات الثلاثية في صغارها. أظهرت الدراسة الحالية أن معاملة إناث الجرذان المرضعات بفيتامين E أو C مع خلات الرصاص سببت انخفاضا معنويا في اختبار عدد مرات الوقوف على قوائم الخلفية بينما حدث زيادة معنوية في مستوى الدهون البروتينية عالية الكثافة في صغارها. ويستنتج من الدراسة أن إعطاء فيتامين E أو C لإناث الجرذان المرضعات عكست التأثيرات السلبية التي أحدثت بخلات الرصاص في السلوك العصبي وأن لفيتأمين E تأثيرا إيجابيا في مستويات كلا من الكلوتاثايون و المالونديالديهايد و الكليسيريدات الثلاثية والدهون البروتينية عالية الكثافة في صغارها الرضيعة.

Introduction

Lead is an ubiquitous element in the environment, it is used in many industrial activities including mining, refining and producing lead – acid batteries (1). Although this heavy metal is less widely used today, it remains a significant public health problem. Animals may be exposed to lead via contaminated food or water and fuel additives (2). The alimentary and respiratory tract are the major routes of lead entry into the body (3). Once the lead is in the bloodstream, it is distributed into soft and hard tissues (4). Milk is the most important food source for newborn, however, also be a pathway of maternal excretion of toxic elements such as lead, and these toxins impact most severely on the newborn at a time of rapid development of the central nervous system (5). In the nervous system, all neurons and glial cells form a very large network, integrate all external and internal stimuli and contributes to the elaboration of adequate responses (6). Lead enters the brain and selectively deposited in the hippocampus and cortex, as well as in non-neuronal elements that are important in the maintenance of the blood brain barrier function. Lead exposure causes distractibility inability to maintain physical balance and it affects some complex functions including learning (7). The neuropathlogical effects of lead include nervousness, anxiety and symptomatic encephalopathy at the end (8). Pervious study has shown that the level of lead in milk are thus similar to those in plasma (5). In rodents lead mobilized from the skeleton is transferred to the suckling offspring during lactation (9), and that lactational transfer after current or recent exposure to lead in dams was considerably higher than placental transfer (10). The main targets organ of lead toxicity are the red blood cell, central nervous system, peripheral nerves and the kidney (11).

Recent study reported that lead acetate can be transmitted through mother milk to their offspring. Lead acetate make bad effects on the reproductive systems of both males and females rats. While giving vitamin E as antioxidant found to have no improving effect in the treatment of lead acetate disturbances on the reproductive system of both sexes (12). Lead-induced oxidative stress contributes to the pathogenesis of lead poisoning for disrupting the delicate prooxidant/antioxidant balance that exists within mammalian cells. Production of reactive oxygen species (ROS) is increased after lead treatment in vitro studies, moreover other studies in vivo suggest that lead exposure cause generation of ROS and alteration of antioxidants defense system in animals (13).

The aim of present study is to assess the role of administration of vitamin E & C concomitantly with lead acetate to the dams during lactation period (21days) on the neurobehavioral, landmarks development and some biochemical changes in their pups.

Materials and methods

Adult healthy albino rats were obtained from the animals house of the Veterinary Medical College – University of Mosul at 3-4 months of age weighing 150-200g. The rats were mated (3:1 females to male). Pregnant rats were removed and kept in separated polyproplyne cages under condition of temperature (22-26 C°) and lighting (12hours light /12hours dark). The rats were supplied a standard pellet diet and tap water *ad libitum*. At birth dams were separated with their pups from the first day of parturition.

In this experiment, animals divided into four groups: Group 1: dams (rats during lactation period) received normal saline orally as control group. Group2: dams received lead acetate at (10mg/kg B. Wt.) orally during lactation period, lead acetate dissolved in distalled water and given at 1 ml/kg (12). Group3: dams received lead acetate (10mg/kg B. Wt.) orally with concomitant administration of vitamin E at (600 mg /kg diet) during lactation period (14) (Shang Hang, China). Group 4: dams received lead acetate (10mg/kg B. Wt.) orally with simultaneous administration of vitamin C at (100 mg /kg B. Wt.) orally during lactation period (15) (Chemical Suppl, South Australia).

Twenty pups from each groups were selected randomly for examination. Pups were examined at the 7 day of age for neural behaviour which included righting reflex, cliff avoidance and olfactory discrimination tests (16). Central nervous system activity test were examined at the 21 day which include onset of movement test, open field activity test (17). This test measures the general locomotor activity, exploration which include (the number of squares crossed and rearing test within 3 minutes) and negative geotaxis test

(16). Sensimotor system activity were examined which include approach response, touch response, click response and tail pinch response (18). Landmarks development tests included opening of ear, appearance of hair and teeth, opening of eyes, descending time of testis and appearance time of vaginal opening (16).

Blood was collected from pups at age 21 days for biochemical examination. Total cholesterol, high density lipoproteins, glucose, alanine aminotransfererase, aspartate aminotransfererase, and albumin, were measured using colorimetric assay kit (Syrbio, Syria) and triglyceride was measured using kit (bioMerieux, France), Pups weights monitored at birth and at weaning time. Pups were sacrificed at the end of experiment and the brain was placed in ice normal saline for glutathione (Moron method) (19) and malondialdehyde estimation (Gilbert method) (20).

Data were analyzed statistically using one way analysis of variance. Group differences were determined using Duncan multiple range test. Data of approach response, touch response, click response and tail pinch response analyzed statistically using Mann _ whitny _ U _ test. Statistical significance was considered at ($P \leq 0.05$) (21).

Results

In the current study Table 1- revealed that administration of lead acetate to the dams during lactation period did not effect the onset of movement and negative geotaxis tests in their pups compared the pups of control group. Treatment with vitamin E to the rats receiving lead acetate during lactation period did not effect significantly the onset of movement and negative geotaxis tests in their pups, but the treatment with vitamin C to the rats receiving lead acetate during lactation period produced a significant increase ($P \leq 0.05$) in the onset of movement test. Treatment with each of vitamin E & C to the rats receiving lead acetate during lactation period did not effect significantly the negative geotaxis test in their pups compared with pups of lead acetate group. Table 1- showed that rats receiving lead acetate during lactation period cause a significant increase ($P \leq 0.05$) in rearing and the number of squares crossed tests within 3 minutes in their pups compared with the pups of the control group. Treatment with vitamin E & C to the rats receiving lead acetate during lactation period caused no significant changes in rearing test in their pups. On the other hand, the number of square crossed test was significantly decrease by vitamin E & C in pups compared with the lead acetate group.

Table 2 shows that administration of lead acetate to the rats during lactation period caused a significant increase in olfactory discrimination ($P \leq 0.05$) in their pups compared with the pups of control group.

Treatment with vitamin E & C to the rats receiving lead acetate during lactation period did not affect significantly in olfactory discrimination test in their pups compared with the pups of lead acetate group. No significant changes between groups in cliff avoidance test. Same Table demonstrated that administration of lead acetate to the rats during lactation period did not effect significantly in righting reflex test in their pups compared with the pups of control values. Treatment with vitamin E of rats receiving lead acetate during lactation period did not affect significantly in righting reflex in their pups compared with the pups of lead acetate group, but treatment with vitamin C of rats receiving lead acetate during lactation period cause a significant decrease ($P \leq 0.05$) in righting reflex test in their pups compared with the pups of lead acetate group.

The data of vitamin E & C revealed no significant differences on sensimotor include (approach, touch, click and tail pinch responses),landmarks development and weighing of pups (at 21 days) from rats receiving lead acetate during lactation period are shown in Table 3,4,5.

Table 1. The onset of movement, open field activity tests and negative geotaxis in suckling pups at(21 days) from dams treated with lead acetate and their interaction with vitamin E or C for 21 consecutive days (lactation period).

Treatment of dams	Onset of movement/ sec	Open field		Negative geotaxis/sec
		Rearing with 3 min	square crossed with 3 mins	
control	ab 2.15±0.13	a 56.75±2.42	a 11.20±0.51	a 4.65±0.41
Lead acetate (10mg/ kg) orally	a 2.05±0.13	b 65.25±3.48	b 14.50±0.48	ab 5.80±0.51
Lead acetate (10mg/ kg) orally + vitamin E (600mg/ kg diet)	ab 2.30±0.14	b 65.20±2.52	a 11.90±0.46	b 6.7±0.64
Lead acetate (10mg/ kg) orally + vitamin C (100mg/kg)	b 2.55±0.18	ab 58.35±1.96	a 12.05±0.65	ab 6.05±0.29

Values were expressed as means ± SE from 20pups per treatment.
Values with different letters are significantly different at ($P \leq 0.05$).

Table 2. The righting reflex,cliff avoidance and olfactory discrimination tests in suckling pups at (7 days) from dams treated with lead acetate and their interaction with vitamin E or C for 21 consecutive days (lactation period).

Treatment of dams	Righting reflex(sec)	Cliff avoidance (sec)	Olfactory discrimination (sec)
Control	b 2.95±0.13	a 9.35±0.57	a 11.75±0.42
Lead acetate (10mg/ kg) orally	b 2.90±0.17	a 8.75±0.89	b 23.85±1.33
Lead acetate (10mg/ kg) orally + vitamin E(600mg/ kg diet)	ab 2.65±0.18	a 10.25±0.95	b 20.70±1.93
Lead acetate (10mg/ kg) orally +vitamin C(100mg/kg)	a 2.30±0.11	a 10.30±0.82	b 20.90±1.48

Values were expressed as means ± SE from 20pups per treatment.
Values with different letters are significantly different at (P≤0.05).

Table 3. The approach, touch, click, tail pinch responses in suckling pups at (21 days) from dams treated with lead acetate and their interaction with vitamin E or C for 21 consecutive days (lactation period).

Treatment of dams	Approach response/ score	Touch response/ score	Click response/ score	Tail pinch response/ score
Control	a 1.90±0.02	a 2±0	a 2.60±0.16	a 3±0.1
Lead acetate (10mg/ kg) orally	a 1.90±0.02	a 2.05±0.02	a 2.70±0.14	a 2.90±0.12
Lead acetate (10mg/ kg) orally + vitamin E (600mg/ kg diet)	a 1.90±0.02	a 2.05±0.02	a 2.70±0.14	a 2.95±0.13
Lead acetate (10mg/ kg) orally + vitamin C (100mg/kg)	a 1.95±0.02	a 2±0	a 2.85±0.1	a 3±0.02

Values were expressed as means ± SE from 20 pups per treatment.

Table 4. The landmarks development in suckling pups from dams treated with lead acetate and their interaction with vitamin E or C.

Treatment of dams	Appearance of ear opening	Appearance of hair	Appearance of teeth	Appearance of eye	Descending time of testis	Appearance of vaginal opening
Control	a 2.1±0.12	a 6.4±0.21	a 5.9±0.17	a 16.16±0.2	a 33.5±0.29	a 47.2±0.40
Lead acetate (10mg/ kg)	a 2.15±0.13	a 6.7±0.16	a 5.9±0.17	a 17.15±0.26	a 32.8±0.46	a 47.5±0.36
Lead acetate (10mg/ kg) + vitamin E (600mg/ kg diet)	a 2.15±0.13	a 6.4±.19	a 6±0.16	a 17.3±0.17	a 33.15±0.37	a 47.0±0.24
Lead acetate (10mg/ kg) + vitamin C (100mg/kg)	a 2.1±0.12	a 6.6±0. 2	a 5.9±0.18	a 17.10±0.2	a 33.25±0.33	a 47.4±0.32

Values were expressed as means ± SE from 5 pups per treatment.

In the present study, Table 6 demonstrated that administration of lead acetate to the rats during lactation period cause a significant decrease in glutathione level with increase in malondialdehyde in brain tissue of their pups compared with the control group. Administration of vitamin E to the rats receiving lead acetate during lactation period

produce a significant increased in glutathione and decrease (P≤0.05)in malondialdehyde levels in their pups compared with the pups of lead acetate group. No significant differences in the level of glutathione and malodialdehyde of the pups when their dams treated with vitamin C and lead acetate concomitantly during lactation period compared with the pups of lead acetate group. In same Table the data shows no significant differences in the levels of alanine aminotransferase, aspartate aminotransferase and albumin in the pups of all group.

Table 7 demonstrated that administration of lead acetate alone or concomitantly with vitamin E & C to the rats during lactation period did not effect significantly glucose and cholesterol levels in their pups. Administration of lead acetate to rats during lactation period caused a significant increase (P≤0.05) in triglyceride level and significant decrease in high density lipoproteins in their pups compared with the pups of control value. Treatment with vitamin E to the rats receiving lead acetate during lactation period produced a significant decrease (P≤0.05) in triglyceride and significant increase in high density lipoproteins level in their pups compared with the pups of lead acetate group. Rats administered lead acetate with vitamin C during lactation period did not affect triglyceride level significantly in their pups compared with that of lead acetate group, on the other hand vitamin C caused a significant increase (P≤0.05) in high density lipoproteins in pups compared with the pups of lead acetate group.

Table 5. The body weight in suckling pups from dams treated with lead acetate and their interaction with vitamin E or C for 21 consecutive days (lactation period).

Treatment of dams	Weight(g) at 1 day	Weight (g)at 21 day
Control	a 5.46±0.02	a 25.27±0.19
Lead acetate (10mg/ kg) orally	a 5.44±0.02	a 25.31±0.45
Lead acetate (10mg/ kg) orally + vitamin E (600mg/ kg diet)	a 5.33±0.10	a 25.06±0.15
Lead acetate (10mg/ kg) orally + vitamin C (100mg/kg)	a 5.43±0.02	a 25.13±0.16

Values were expressed as means ± SE from 20 pups per treatment.

Table 6. The glutathione, malondialdehyde brain tissue, alanine amimotraferase, aspartate amimotraferase and albumin in suckling pups from dams treated with lead acetate and their interaction with vitamin E or C for 21 consecutive days (lactation period).

Treatment of dams	Glutathione µmlg	Malodialdehyde nm/g	Alanine Amimotraferase Unit/ L	aspartate amimotraferase Unit/ L	Albumin g/dl
Control	a 2.73±0.2	b 107±4.19	a 11.54±0.62	a 23.34±1.61	a 3.06±0.17
Lead acetate (10mg/ kg) orally	c 1.19±0.17	a 181.8±8.39	a 11.16±0.99	a 22.12±0.99	a 2.97±0.11
Lead acetate (10mg/ kg) orally + vitamin E (600mg/ kg diet)	b 1.8±0.15	b 112±6.71	a 10.56±0.54	a 24.92±0.8	a 3.2±0.38
Lead acetate (10mg/ kg) orally + vitamin C (100mg/kg)	c 0.99±0.002	a 167.4±9.9	a 11.08±0.47	a 22.6±1.28	a 3.42±0.48

Values were expressed as means ± SE from 5pups per treatment.
Values with different letters are significantly different at (P≤0.05).

Discussion

The present study showed that administration of lead acetate to rats during lactation period caused a significant increase in the open field activity test including (rearing and the number of squares crossed tests within 3 minutes) and olfactory discrimination test in their pups compared to pups of the control group.

The nervous system is the most sensitive target of lead exposure. Fetuses and young animals are especially vulnerable to the neurologic effects of lead because their brains and nervous system are still developing and blood brain barrier is incomplete (22). Lead neurotoxicity results in behavioral and neurochemical alteration in neurons as a result of changes and disruption of main structural components of the blood brain barrier, through primary injury to astrocytes and to secondary damage of the endothelial microvasculature (3). There are numerous studies utilizing experimental animal models on the central nervous system, These studies have mainly been concerned with possible effects of lead on certain performance tasks that might reflects a cognitive function (learning and memory) or sensorimotor function in the infant animal exposed to lead very early in life or in utero (23). Some investigators studied effects of lead on the action of neurotransmitters using isolated peripheral nerve preparation, both cholinergic and adrenergic synaptic evoked transmitter released is inhibited by lead, and this effect is prevented by calcium (23). Lead affects primarily the metabolism of calcium (24), and inhibits the action of calcium as a result lead can affect calcium-dependent processes and interact with proteins including sulfhydryl, amine, phosphate, and carboxyl groups (21).

Table 7. The glucose, cholesterol, triglyceride and high density lipoproteins in suckling pups from dams treated with lead acetate and their interaction with vitamin E or C for 21 consecutive days (lactation period).

Treatment of dams	glucose mg/dl	Cholesterol mg/dl	Triglyceride mg/dl	High density Lipoprotein mg/dl
Control	a 102±6.5	a 71.3±4.8	b 121±4.8	a 44.1±3.9
Lead acetate (10mg/ kg) orally	a 106±3.7	a 91.9±10.4	a 186.8±5.8	b 29.2±3.4
Lead acetate (10mg/ kg) orally + vitamin E (600mg/ kg diet)	a 104±4.3	a 71.6±5.9	b 118.2±6.3	a 42.1±2.3
Lead acetate (10mg/ kg) orally + vitamin C (100mg/kg)	a 106±3	a 80.5±7.8	a 196±4.8	a 40.9±4.7

Values were expressed as means ± SE from 5pups per treatment.
Values with different letters are significantly different at ($P \leq 0.05$).

The nervous system is the most sensitive target of lead exposure. Fetuses and young animals are especially vulnerable to the neurologic effects of lead because their brains and nervous system are still developing and blood brain barrier is incomplete (22). Lead neurotoxicity results in behavioral and neurochemical alteration in neurons as a result of changes and disruption of main structural components of the blood brain barrier, through primary injury to astrocytes and to secondary damage of the endothelial microvasculature (3). There are numerous studies utilizing experimental animal models on the central nervous system, These studies have mainly been concerned with possible effects of lead on certain performance tasks that might reflects a cognitive function (learning and memory) or sensorimotor function in the infant animal exposed to lead very early in life or in utero (23). Some investigators studied effects of lead on the action of neurotransmitters using isolated peripheral nerve preparation, both cholinergic and adrenergic synaptic evoked transmitter released is inhibited by lead, and this effect is prevented by calcium (23). Lead affects primarily the metabolism of calcium (24), and inhibits the action of calcium as a result lead can affect calcium-dependent processes and interact with proteins including sulfhydryl, amine, phosphate, and carboxyl groups (21).

Neurotoxicity may be a consequence of alterations in cholinergic function mediated by the enzyme acetylcholinesterase (AchE) (25).

Maged recorded that lead caused a progressive decrease in the activity of acetylcholinesterase in different brain regions and spinal cord (26).

The enzyme inhibition is generally reached its significance after 10 to 20 days of lead acetate intake orally to the rabbits, such alteration in cholinergic transmission suggests that lead is able to reach the CNS and exerts its neurotoxic effect (26). It was supposed that oxidative stress was one possible mechanism for lead neurotoxicity. lead–induced oxidative stress might result from accumulation of 5-aminolevulinic acid (ALA), a potential endogenous source of free radical, induced by inhibition of lead to ALA dehydratase, overload of ALA seemed to be involved in the neurological disturbances, which leads to inhibition γ-aminobutyric acid (GABA) release from synaptosomes and blocking GABA receptor (27). Nihei et al (28) have

reported ALA can cause oxidative stress to rats brain. Additionally, direct interaction of lead to biological membranes was to induce lipid peroxidation. Lead-exposure might also induce decrease in activities of free radical scavenging enzymes. This mainly attributed to high affinity of lead to sulfhydryl-groups in these enzymes (29).

The result of the current study showed that administration of lead acetate to the rats during lactation period caused a significant increase in malondialdehyde and triglyceride with a significant decrease in glutathione in their pups compared with the control group. Numerous reports have documented increased lipid peroxidation (LPO) and decreased glutathione (GsH) and superoxide dismutase (SOD) activity in the brain homogenates of lead treated rats (30). Furthermore, lead exposure led to depletion of brain glutathione content, superoxide dismutase activity, and increase in thiobarbituric acid reactive substances (TBARS), and the activity of glutathione S-transferase bound enzyme (31). Oxidative damage associated with lead in the brain has been proposed as a possible mechanism of lead toxicity (31). Some investigators revealed that lead –treated cultured aortic endothelial cells caused increase in the production of the lipid peroxidation products malondialdehyde and enhanced generation of hydroxyl radical compared with control cells which is considered as a direct cause of oxidative stress (33). It should be noted that hydroxyl radicals are primarily produced from sequential reduction of superoxide radical and hydrogen peroxide radical (33). Lead-induced oxidative stress associated with hyperglycemia suggested to contribute in the overproduction of very low density lipoprotein (VLDL), increasing the burden of triglyceride-rich lipoproteins on the common lipolytic pathway at the level of lipoprotein in lipase (34).

In the current study administration vitamin E &C to the rats receiving lead acetate during the lactation period ameliorating the effect of lead acetate in their lactating pups. Recent study carried out effects of lead actate at 600 p.p.m. in drinking water during pregnancy and lactation caused significant decrease in activities of superoxide dismutase, glutathione peroxidaes and glutathione reductase in hypothalamus, corpora quadrigemina and corpus striatum in weaned pups (mouse) (27).

Vitamin E is necessary for the maintenance of normal neurological structures and function, and play a role in protecting lipid rich structures such as the brain from free radical (35). Antioxidant /chelating action represented by vitamin E improved the enzyme activity in the central nervous system (25). A major contributor to non-enzymatic protection of polyunsaturated fatty acid and low density lipoprotein from oxidation by free radicals against lipid peroxidation is vitamin E (35). Vitamin E as a lipid soluble, chain breaking antioxidant (37), plays a major protective role against oxidative stress (38), and prevents the production of lipid peroxide by scavenging free radicals in biological membrane (39).

Previous studies have revealed that vitamin E possesses an antioxidant activity in protecting cells from damage by highly reactive superoxide free radicals production (35). In the tissue of vitamin E deficient animals, it is reported that lipid peroxidation is enhanced suggesting that vitamin E plays a role as physiological antioxidant on its chemical properties, and prevent oxidation of low density lipoprotein (40). While vitamin C the most abundant water- soluble antioxidant in the body acts primarily in cellular fluid of particular in combating free radical for caused by pollution furthermore vitamin C help vitamin E to return to its active form (40). Moreover, Frei (41) found that only ascorbic acid is protectively enough to intercept oxidant in the aqueous phase before they can attack and cause detectable oxidative damage to lipids, as compared to many other lipophilic and hydrophilic antioxidants. (42) revealed that administration of vitamin E to rats during lactation period caused a positive effects on lipid profile, glutathione and malondialdehyde in brain tissue, of their offspring.

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