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Effects of Dietary Taurine and Gamma Aminobutyric Acid on the Steroil CoA Desaturase and Δ6, 5 Desaturase Enzyme Activities in Liver Tissues of Rats

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Abstract: In this study, the effects of dietary taurine (2-amino ethane sulphonic acid) (TAUR) and Gamma Amino Butyric Acid (GABA) on the levels of reduced glutathione (GSH), lipid and fatty acid composition in liver tissues of 3 and 8 months female wistar rats was evaluated. The rats (n = 48) were randomly assigned to 8 treatment groups consisting of 6 rats each. The rats (both 3 and 8 month old) were fed a basal diet (Control) or basal diet plus taurine given by drinking water (500 mg kg^{-1}) (TAUR groups) or basal diet plus GABA given by drinking water (500 mg kg^{-1}) (GABA) or basal diet plus the combinations of GABA and TAUR given by drinking water (500 + 500 mg kg^{-1}) (GABA+TAUR groups). In 3 month old rats, the lipid level in GABA and GABA+TAUR groups was higher than control group ($p<0.01$). GSH level was high in the TAUR group ($p<0.05$). While, the lipid level increased in GABA group of 8 month old rats, its level decreased in TAUR group ($p<0.05$). The level of GSH in GABA, TAUR and GABA+TAUR groups was lower than control group ($p<0.01$). Oleic acid level (18:1, n-9) was high in TAUR group ($p<0.05$) and linoleic acid level (18:2, n-6) GABA and GABA+TAUR groups was higher than control group ($p<0.01$) in 3 month old rats. However, arachidonic acid level (20:4, n-6) in supplemented groups was lower than control group ($p<0.01$). While, the saturated fatty acid level increased in the supplemented groups, unsaturated fatty acid decreased in the same groups ($p<0.05$). In 8 month old rats, palmitic acid level (16:0) increased in supplemented groups ($p\leq 0.05$), but stearic acid level decreased in the same groups. The levels of oleic and linoleic acids were high in GABA and GABA+TAUR groups. Arachidonic and docosahexaenoic acid levels in GABA and GABA+TAUR groups were lower than control group ($p<0.01$). The level of saturated fatty acid level was high in the GABA and TAUR groups, but the unsaturated fatty acid was low in the same groups ($p<0.05$). In conclusion, present study showed that the products of Δ6 desaturation pathway such as arachidonic acid was decreased by the GABA and taurine in 3 and 8 months old of female rats. Conversely, the products of steroil CoA desaturase were increased by dietary taurine treatment.

Key words: Taurine, gamma amino butyric acid, lipid, GSH, cholesterol, fatty acids

INTRODUCTION

Gamma Amino Butyric Acid (GABA) is the principal inhibitory neurotransmitter in the mammalian brain. It has been also demonstrated that GABA present in peripheral tissues and functionally active throughout, the body (Erdo and Wolff, 1990; Mangatt *et al*., 2001). It possesses growth-regulatory properties (Mangatt *et al*., 2001) and also plays an important role in terminating the growth of rapidly developing tissues in uteri (Gilon *et al*., 1987a, b). GABA mediated growth inhibition of the liver following partial hepatectomy and during recovery from various forms of hepatic injury is already reported (Minuk *et al*., 1995; Zhang *et al*., 1996; Kaita *et al*., 1998). Ferenci *et al*. (1983) and Minuk *et al*. (1985) have reported that plasma GABA is elevated in patients with chronic liver diseases, such as liver cirrhosis and may play an important pathogenic role in hepatic encephalopathy. Also, it has been documented that altering GABAergic activity results in altered hepatic regenerative activity

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following partial hepatectomy, as well as following acute and chronic forms of liver diseases (Minuk *et al*., 1991; Minuk and Gauthier, 1993; Minuk *et al*., 1995). Cohen (2002) reported that elevated levels of ammonia in the plasma results in a decrease in GABA synthesis. It is postulated that a link between plasma ammonia and plasma GABA exists where the concentration of GABA in the plasma is directly related to the ammonia plasma concentration.

A sulfur-containing amino acid, taurine (2-amino ethane sulfonic acid) is present in mili molar concentrations in many animal tissues especially nervous tissue, retina and neutrophils (Wright *et al*., 1986). Taurine present an in high concentrations in mammalian liver tissues, where its content is in the range of 3.5-60 mmol g^{-1} weight (Sims, 1995). Suggested biological and physiological functions of taurine include cell membrane stabilization, antioxidation, detoxification, osmoregulation, neuromodulation and brain and retinal developments (Sturman, 1986). Also, taurine plays an important role in lipid metabolism to produce the bile acid conjugates in the liver; that is, taurine increases the utilization of bile acid which is the degrading metabolite of cholesterol and participates in fat absorption (Yamanaka *et al*., 1986). Previous studies demonstrated that taurine had a cholesterol-lowering effect in rats and mice (Oda *et al*., 1989; Gandhi *et al*., 1992; Hwang and Wang, 2001; Murakami *et al*., 1999) reported that the taurine reduces serum cholesterol levels, the stimulation of bile acid production via the enhancement of cholesterol 7∝-hydroxylase, a rate-limiting enzyme of bile acid synthesis. They have stated hepatic HMG-CoA reductase activity was not decreased by the taurine and therefore, the hypocholesterolemic effect of taurine is not related to suppression of hepatic cholesterol synthesis.

The levels of oxidized and reduced GSH levels directly in response to chronic dietary taurine manipulation to better understand the antioxidant status under these dietary conditions. Taurine and GSH biosynthesis are closely related because they have the precursor cysteine in common. Changes in taurine levels might also have an effect on GSH levels and vice versa, since, taurine and GSH synthesis are tightly coupled, sharing the same precursor, cysteine (Strolin *et al*., 1991; Stipanuk *et al*., 1992a). Therefore, cysteine sulfinic acid and cysteine sulfinic acid decarboxylase are important enzymes in what is believed to be the most important taurine biosynthetic pathway in mammals and an age-dependent down regulation in either or both of these enzymes could lead to a decline of taurine concentration in body tissues and fluids.

In lipogenic tissues like liver and white adipose tissue, fatty acids can be synthesized de nove from glucose fallowing glycolisis (Duplus and Forest, 2002). In animal cells unsaturated fatty acids are generated by desaturation of fatty acids by microsomal desaturases. The ratio of saturated to unsaturated fatty acids is one of the key factors influencing cell membrane fluidity. Dysfunction or perturbations in these fatty acids that alters the ratio has been reported to be important in various diseases such as aging, cancer, diabetes and neurological and vascular diseases (Kumar *et al*., 1999). Age-related loss of abilities to maintain homeostasis is at least partially responsible for increased morbidity and mortality. Delta-6-desaturase, which is involved in the metabolism of polyunsaturated fatty acids, is shown to be low with aging (Kumar *et al*., 1999). In this research, we aimed to evaluate the improvement effects of dietary taurine, GABA and their combination on the GSH level, lipid and fatty acids compositions (products of fatty acid synthase, steroil CoA desaturase and Δ6 and 5 desaturase enzymes) in liver tissues of 3 and 8 months old female Wistar rats.

MATERIALS AND METHODS

Animal selection and treatment: Twenty four (3 month old) female and 24 (8 month old) female Wistar rats were used in this study. Rats were housed in cages where they had *ad libitum* rat chow (Table 1) and water in an air-condition room with 12h-light/12h-dark cycle. Animals were randomly divided into eight groups as follows:

Group 1: Three months old rats fed basal diet.

Group 2: Eight months old rats fed basal diet.

Table 1: Diet composition for experimental rats

Ingredients	(%)	Fatty acids	(%)
Wheat	10	13:0	0.49
Corn	22	14:0	1.64
Barley	15	15:0	0.21
Wheat bran	8	16:0	22.47
Soybean	26	16:1, n-9	6.69
Fish flour	8	17:0	0.25
Meat-bone flour	5	18:0	2.45
Pelted	5	18:1, n-9	25.32
Salt	0.8	18:1, n-7	4.14
*Vitamin and mineral mix	0.2	18:2, n-9	23.69
		18:3, n-3	1.09
		19:0	0.27
		20:0	0.75
		20:1, n-9	0.27
		22:1, n-9	2.40
		22:6, n-3	0.65

*:Vit. A, D3, E, K, B_1, B_2, B_6, B_{12}, Nicotinamid, Folic acid, Biotin, Cholin chloride, Mn, Fe, Zn, Cu, I, Co, Se, Antioxidant and Ca

Group 3: Three months old rats fed basal diet plus taurine given by drinking water (500 mg kg^{-1}) (TAUR1).

Group 4 : Eight months old rats fed basal diet plus taurine given by drinking water (500 mg kg^{-1}) (TAUR2).

Group 5: Three months old rats basal diet plus GABA given by drinking water (500 mg kg^{-1}) (GABA1).

Group 6: Eight months old rats fed basal diet plus GABA given by drinking water (500 mg kg^{-1}) (GABA2).

Group 7: Three months old rats fed basal diet plus taurine plus GABA given by drinking water (500 mg kg^{-1}) (TAUR + GABA).

Group 8: Eight months old rats fed basal diet plus taurine plus GABA given by drinking water (500 mg kg^{-1}) (TAUR + GABA).

This administration was done for a period of 4 weeks. At the end of the administration period, each experimental rat was anesthetized with ether. Then, liver tissue samples were collected and stored at -25°C until biochemical analyses.

Methods: The lipids of liver tissues were extracted by the method of Hara and Adin (1978). Liver tissues were homogenized with the mixture of hexane: isopropanol (3:2, v v^{-1}) in MICRA D8 homogenizator. Non-lipid contaminants were removed by washing with 0.88% KCl solution. Aliquots were taken and the total lipid content was determined spectrophotometrically (Strolin *et al*., 1991) and total cholesterol quantified by high performance liquid chromatography (Stipanuk *et al*., 1992b). Aliquots of the lipid extracts were also, the fatty acids esterified with 2% H_2SO_4-methanol (Murakami *et al*., 1999) and the fatty acids composition's determined by gas chromatography (GC).

Total lipid determination: Each lipid extract was taken 10 μL and treated with 500 μL of concentrated sulfuric acid and left at boiling water for 10 min. Then, 5 mL of phosphovanilin reagent was added and the mixture was incubated at 25°C for 20 min. After incubation, the optical densities of samples were read at 540 nm against to blank. In addition, standard solution was prepared in the same condition from USA grade olive oil (Sigma, St. Louis, MO). The total lipid levels were calculated according to the standard curve.

Cholesterol determination: Total cholesterol was analyzed by VP series full automatic high performance liquid chromatography (HPLC) instrument (Shimadzu, Kyoto, Japan). The column used was Supelcosil18 DB column (250×4.6 mm, 5 mm). The mobile phase used was acetonitrile-isopropyl alcohol (70:30 v v^{-1}) at a flow rate of 1 mL min^{-1}. Detection was performed by UV at 202 nm and 40°C column owen. To sample preparation, exactly 1 mL of the hexane extract obtained by direct saponification were dried under nitrogen flow and diluted with a portion of 500 μL of the mobile phase; then samples were injected via Autosampler to HPLC instrument. Quantification was carried out by external standardization by class VP software (Shimadzu, Kyoto, Japan).

Fatty acid composition: Fatty acids in lipid extracts were converted to methyl esters by using 2% sulfuric acid (v v^{-1}) in methanol (Murakami *et al*., 1999). Fatty acid methyl ester forms (FAME) were extracted with n-hexane. Gas chromatography analysis was employed GC-17A intstrument with FID and AOC-20i Autoenjector and Autosampler from Shimadzu (Kyota, Japan). FAMEs were separated by fused silica capiller column, 25 mL and 0.25 mm diameter, Permabond (Machhery-Nagel, Germay). Column temperature was programmed between 130-220, 5°C min^{-1} and the final temperature was hold 15 min. Injector and FID temperatures were 240 and 280°C, respectively. Nitrogen was used as carrier gas under head pressure of 50 kPa (corresponding to 1.2 mL min^{-1}, 43 cm s^{-1} column flow rate). Identification of the individual methyl esters was performed by frequent comparison with authentic external standard mixtures analyzed under the same conditions. Class GC 10 software version 2.01 assited at workup of the data.

Determination of Glutathione (GSH): Reduced glutathione (GSH) form in liver was assayed by acting with dithionitrobenzoic acid (DTNB) as described (30). Briefly 0.3 g liver was homogenized in cold 1 mL 20 mM ETDA. After deproteinization with 5% trichloroacetic acid, an aliquot of supernatant was allowed to react with 1 mL 0.4% DTNB solutions. The yellow product was detected and quantified spectrofotometrically at 416 nm. Pure GSH was used as standard for establishing the calibration curve.

Statistical analysis: Experimental results were reported as mean±S.D. Statistical analysis was performed using SPSS Software. The variance analysis (ANOVA) and LSD test were used for comparison between the control and supplemented groups.

RESULTS

Total lipid, cholesterol and GSH levels: in three months old rats, there were no differences between TAUR and control groups lipid levels but GABA and GABA+ TAUR groups levels were high ($p<0.05$, $p<0.01$). Cholesterol level did not differ among the groups. GSH level was no differences among the GABA, GABA+TAUR and control; its level was high in TAUR group ($p<0.05$) (Table 2). In 8 months old rats, the lipid level did not differ between the control and GABA+ TAUR groups, but its level was high in GABA group ($p<0.05$). Conversely, lipid level decreased in TAUR group. However, GSH level in supplemented groups of 8 months old rats were lower than the control group ($p<0.01$) (Table 3).

Fatty acid composition: In 3 month old rats, palmitic acid (16:0) level was high in TAUR and TAUR+GABA groups ($p<0.05$). Stearic acid (18:0) level increased in GABA ($p<0.01$) and TAUR ($p<0.05$) groups, whereas its level did not differ between control and GABA + TAUR. Palmitoleic acid level (16:1, n-9) was low in GABA ($p<0.01$) and TAUR ($p<0.05$) groups, however, there were no differences between control and GABA + TAUR groups. The level of oleic acid (18:1, n-9) in TAUR group was higher than control ($p<0.05$), but there was no differences control and other supplemented groups. Linoeic acid level (18:2, n-6) was high GABA and GABA + TAUR groups ($p<0.01$) and there were no differences between control and TAUR groups. Arachidonic acid level (20:4, n-6) in supplemented groups was lower than control ($p<0.01$) docosahexaenoic acid level (22:6, n-3) did not differ between control and others groups. While, saturated fatty acid level was high in the supplemented groups, unsaturated fatty acid decreased in the same groups ($p<0.05$). In addition PUFA level decreased in the supplemented groups ($p<0.05$) (Table 4).

In 8 months old rats, palmitic acid level in supplemented groups was higher than control group ($p<0.05$). Conversely, stearic acid level decreased ($p<0.01$). Palmitoleic acid level did not differ among the groups. The level of oleic acid (18:1, n-9) in TAUR and GABA+TAUR group was higher than control ($p<0.05$) but there was no differences between control and GABA groups. The level of vaccanic acid (18:1, n-7) in supplemented group was lower than control ($p<0.01$). Linoleic acid level was low GABA group ($p<0.05$), but its level was high in TAUR and GABA + TAUR groups ($p<0.05$). Arachidonic acid level in supplemented groups was lower than control ($p\leq 0.01$). While, docosahexaenoic acid level was low in GABA and GABA+TAUR groups ($p<0.01$), there were no differences between control and GABA. The saturated fatty acid level was high in the GABA and TAUR groups, but unsaturated fatty acid and PUFA levels decreased in the same groups ($p<0.05$) (Table 5).

Table 2: Effects of dietary taurine and gamma aminobutyric acid on the levels of total lipid, cholesterol and GSH of liver in 3 months old rats

Groups	Total lipid mg g^{-1}	Cholesterol mg g^{-1}	GSH μg g^{-1} tissue
Control	36.26±4.33^{b}	1.65±0.15^{c}	480.20±35.19^{a}
GABA	42.26±3.87^{b}	1.56±0.15^{c}	480.11±71.10^{a}
Taurine	37.84±4.52^{b}	1.41±0.27^{c}	529.23±16.99^{b}
Taurine + GABA	47.20±4.10^{b}	1.43±0.19^{c}	484.62±72.77^{a}

Table 3: Effects of dietary taurine and gamma aminobutyric acid on the levels of total lipid, cholesterol and GSH of liver in 8 months old rats

Groups	Total lipid mg g^{-1}	Cholesterol mg g^{-1}	GSH μg g^{-1} tissue
Control	46.22±4.92^{b}	1.73±0.12^{c}	582.79±48.21^{a}
GABA	50.20±7.16^{b}	1.71±0.13^{c}	472.63±37.07^{a}
Taurine	40.72±2.47^{b}	1.71±0.13^{c}	462.14±47.26^{a}
Taurine + GABA	45.74±1.99^{b}	1.76±0.18^{c}	450.34±37.19^{a}

$^{a}p>0.05$; $^{b}p<0.05$; $^{c}p<0.01$; $^{d}p<0.001$

Table 4: Effects of dietary taurine and gamma aminobutyric acid on fatty acid compositions of liver in 3 months old rats (%)

Fatty acids	Control	GABA	Taurine	Taurine + GABA
16:0	19.49±0.33^{a}	19.33±0.56^{a}	20.85±0.67^{b}	21.79±0.44^{b}
18:0	20.68±0.18	24.23±0.26^{c}	22.21±0.66^{b}	21.17±0.52^{a}
16:1 n-9	2.93±0.50^{a}	1.60±0.56^{c}	1.99±0.44^{b}	2.32±0.54^{a}
18:1 n-9	9.35±0.65^{a}	9.59±0.29^{a}	11.31±1.00^{b}	10.00±1.63^{a}
18:1 n-7	3.45±0.48^{a}	3.78±0.08^{a}	3.31±0.58^{a}	3.05±0.23^{a}
18:2 n-6	14.64±079^{a}	16.08±0.76^{c}	14.72±0.58^{a}	17.50±0.95^{c}
20:4 n-6	24.32±0.66	20.55±0.38^{c}	20.33±0.42^{c}	18.80±1.00^{d}
22:6 n-3	5.17±0.28^{a}	4.84±0.28^{a}	5.28±0.42^{a}	5.37±0.45^{a}
Σ saturated	39.67±0.54	43.56±0.46^{b}	43.06±0.67^{b}	42.96±0.64^{b}
Σ unsaturated	59.66±0.87	56.44±0.84^{b}	56.43±0.78^{b}	57.04±0.75^{b}
Σ MUFA	15.63±1.63^{a}	14.97±0.93^{b}	16.60±1.02^{a}	15.37±1.40^{a}
Σ PUFA	44.03±0.46	41.47±0.60^{b}	40.84±0.74^{b}	41.67±0.83^{b}
18:1/18:0	0.62	0.54	0.68	0.62
16:1/16:0	0.15	0.08	0.10	0.11
Σ Uns/ΣSat	1.50	1.30	1.31	1.33

$^{a}p>0.05$; $^{b}p<0.05$; $^{c}p<0.01$; $^{d}p<0.001$

Table 5: Effects of dietary taurine and gamma aminobutyric acid on fatty acid compositions of liver in eight months old rats (%)

Fatty acids	Control	GABA	Taurine	Taurine + GABA
16:0	18.88±0.56	22.66±0.66[c]	22.88±0.30[c]	22.13±0.52[b]
18:0	20.68±0.27	19.83±0.97[b]	19.62±0.33[b]	18.74±0.20[c]
16:1 n-9	2.40±0.35[a]	2.78±0.34[a]	2.81±0.49[a]	2.69±0.55[a]
18:1 n-9	11.58±0.60[a]	12.38±0.66[a]	13.96±0.44[b]	13.92±0.82[b]
18:1 n-7	4.22±0.63	3.16±0.42[c]	2.91±0.25[d]	3.18±0.26[c]
18:2 n-6	15.80±0.32	14.94±0.51[b]	16.75±0.49[b]	16.80±0.83[b]
20:4 n-6	19.99±0.44	17.30±0.88[c]	16.57±0.64[d]	17.66±0.82[c]
22:6 n-3	6.37±0.37[a]	6.87±0.44[a]	4.50±0.40[c]	4.78±0.58[c]
Σ saturated	39.64±1.46	42.49±1.66	42.50±1.72	40.97±1.80
Σ unsaturated	60.36±1.75	57.51±1.86	54.40±1.92	59.03±1.66
Σ MUFA	18.20±1.58[a]	18.32±1.42[a]	19.58±1.18[a]	19.79±1.63[a]
Σ PUFA	42.16±1.56	39.19±1.23	37.82±1.16	39.24±132
18:1/18:0	0.76	0.78	0.86	0.91
16:1/16:0	0.13	0.12	0.12	0.12
Σ Uns/ΣSat	1.52	1.35	1.30	1.44

[a]p>0.05; [b]p<0.05; [c]p<0.01; [d]p<0.001

DISCUSSION

Taurine plays an important role in lipid metabolism. Many studies have shown the hypolipidemic effect of taurine in various species including rats, guinea pigs, rabbits and cats (Frings *et al*., 1972). GABA is an amino acid neurotransmitter with growth inhibitory properties (Lou *et al*., 1999) and thought to mediate its inhibitory effects via activation of $GABA_A$ receptors present on the surface of hepatocytes that serve to regulate hepatocyte transmebrane potential (Minuk, 2000). Present study results showed that lipid level did not differ in liver tissues of TAUR group, but it increased significantly in those taking GABA group (Table 2). Data derived from models of hepatic regeneration indicate that transient, recipricol changes in polyamines, potent growth promoters and GABA, an amino acid neurotransmitter with growth inhibitory properties, play important roles in enhancing and inhibiting, respectively regulated hepatocyte proliferation (Minuk, 2000). GABA, a major inhibitory neurotransmitter in mammals, is found in a wide range of organisms, from prokaryotes to vertebrates. GABA is widely distributed in no neural tissue including peripheral nervous and endocrine systems (Tillakaratne *et al*., 1995).

Our results showed that total reduced glutathione (GSH) level was high in TAUR group of three months old rats. Conversely, its levels decreased in supplemented groups of eight months age (Table 2 and 3). It has been observed a significant age-dependent decline in taurine concentration in liver, kidney and brain tissues from F344 rats (Eppler and Dawson, 1999). Taurine is not considered to as essential amino acid, since, it can be biochemical synthesized from cysteine in the liver. Its biosynthetic capacities have very high the rat and the mouse. In the biosynthetic pathway for taurine, compounds such as GSH and hypotaurine and their associated enzyme systems can be considered as true antioxidative systems, similar to the superoxide dismutase enzyme system (Tadolini *et al*., 1995). GSH appears to be synthesized all mammalian cells and is normally maintained at milimolar concentrations. However, the synthetic capacity is in sufficient to maintain GSH concentrations when tissues are exposed to certain drugs or their metabolites (Hagen *et al*., 1991). In 8 months age rats, decreasing of the GSH levels may be applied to these drugs. Taurine and glutathione biosynthesis are closely interrelated since, the precursor for both is cysteine (Stipanuk *et al*., 1992a, b). Taurine has also an antioxidants and physiological effects (Michalk *et al*., 1997; Devamanoharan *et al*., 1998).

In fatty acid composition of 3 months old rats, the level of oleic acid (18:1, n-9) in TAUR group and its level in TAUR and GABA+TAUR groups of 8 months old rats was higher than control (Table 4 and 5). Unsaturated fatty acids are generated by desaturation of fatty acids by microsomal desaturases. Of these Stearoyl-CoA desaturase (SCD) is the major enzyme in the biosynthesis of monounsaturated fatty acids (MUFAs) (Kim and Nitambi, 1999). SCD in conjunction with NADPH, cytochrome b_5 reductase and cytochrome b_5 and in the presence of molecular oxygen introduces a single double bond (between carbons 9 and 10) into saturated fatty acyl-CoAs. Many dietary, hormonal and environmental factors regulate SCD expression (Nitambi and Miyazaki, 2004). Lochsen *et al*. (1997) reported that the activity and expression of SCD (Δ9 desaturase, D9) was decreased by dietary fish oil and soybean oil diet Additionally it has been reported to be down regulated in the liver by PUFA. Conversely our results demonstrate that the activity of SCD enzyme is increased by dietary TAUR (Table 4 and 5). Ntambi and Myazaki (2004) have stated that SCD activity was increased by dietary factors such as glucose, fructose, vitamin A and D and cholesterol.

Ratio of 18:0/18:1 has been implicated in the regulation of cell growth and differentiation through

effects on membrane fluidity and signal transduction. MUFAs influence apoptosis and may have some role in mutagenesis of some tumors (Dobrzyn and Nitambi, 2004). Overall, SCD expression affects the fatty acid composition of membrane phospholipids, triglyceride and cholesterol ester, resulting in changes in membrane fluidity, lipid metabolism and obesity. MUFAs also serve as mediators of signal transduction and cellular differentiation, including neuronal differentiation. Present study results showed that dietary taurine promoted the activity of fatty acid synthase, because the levels of palmitic and stearic acids were high in the fatty acid composition (Table 4 and 5).

In liver fatty acid composition arachidonic acid level decreased in both three and eight months age rats, whereas, docosahexaenoic acid decreased in just 8 month age rats (Table 4 and 5). Arachidonic acid (20:4, n-6) and docosahexaenoic acid (22:6, n-3) have a variety of physiological functions that include being the major component of membrane phospholipid in brain and retina, substrates for eicosanoid production and regulators of nuclear transcription factors. The rate-limiting step in the production of 20:4 and 22:6 is the desaturation of 18:2 (n-6) and 18:3 (n-3) by $\Delta 6$ and $\Delta 5$ desaturases (Kuresh *et al*., 2000). Both linolenic acid (18:3, n-3) and linoleic acid (18:2, n-6) are metabolized to longer-chain fatty acids, largely in the liver; 18:3 is converted to eicosapentaenoic acid and thence to docosahexaenoic acid, while, 18:2 is the metabolic precursor of arachidonic acid (AA). Many studies reported that $\Delta 5$ desaturase (D5D) activity is highly regulated by the large number of exogenous factors including specific components of the diet, hormonal status, circadian rithm, age and genetic background and diseases (Zolfaghari and Ross, 2003).

Cho *et al*. (1999) reported that when mice were fed a diet containing 10% fat, hepatic enzymatic activity and mRNA abundance for hepatic $\Delta 6$ desaturase in mice fed corn oil were 70 and 50% lower than in mice fed triolein. Azavache *et al*. (1998) found that the rat neonate has a very low $\Delta 6$ desaturase activity in liver microsomes as compared with the adult. Dinh *et al*. (1995) reported that hepatic $\Delta 6$ desaturase (D6D) activity was analyzed 3 and 7 days after the change in diet when rats were fed the diet containing 10% fish oil, D6D activity was lower than in those fed the diet deficient in α-linolenic acid. Umeda-Sawada *et al*. (2003) suggested that sesamin reduced the $\Delta 5$ desaturation index without the changing of the D5D mRNA level. As above studies results, present study indicated that the levels of D6 and D5 desaturase enzymes products such as arachidonic and docosahexaenoic acids decreased in fatty acid composition of liver. Therefore, it could be result that the activity of these enzymes was affected these dietary factors such as GABA and taurine. Increased of linoleic acid level in TAUR and TAUR+GABA groups (Table 4 and 5) support the sight.

It has been determined that the activities of both D5D and D6D change according to stage of development and age, these differences may be a factor in age-dependent differences reported membrane fatty acid composition (Zolfaghari and Ross, 2003). Maniongui *et al*. (1993) studied age-related changes in the liver's capacity for D6D and D5D fatty acid desaturation using microsomes from Wistar rats ranging in age from 1.5 and 24 months. They reported that the capacity for D6 desaturation increased 1.5 and 3 months of age, when it reached its highest level and then declined when rats were 24 months age. It has been shown that in aged rodents the deasturase activity of the rat liver and mouse liver decreases with age (Kuresh *et al*., 2000). Although, there are a number of conflicting results reported, it is generally though, that D6 and D5D activities decline during aging. Bordoni *et al*. (1997) reported that arachidonic acid level decreased as a function of age in all the phosphoinosities.

CONCLUSION

In conclusion, many studies reported that D5 and D6 desaturation enzyme activities and their products varied with aging. In present study showed that the D6 desaturation enzyme products level declined in the young rats of GABA and TAUR group. The reason of this may be due to inhibitor effect of taurine and GABA. Conversely, the products of steroil CoA desaturase (D9) were increased by dietary taurine treatment.

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