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Short Communication

BACOPA MONNEIRA (BRAHMI) MODULATE ALTERED THYROID HORMONES IN ALUMINUM INDUCED ALZHEIMER'S LIKE RAT MODEL

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Abstract: Aluminum (AL) has been recognized play an important role in the development of Alzheimer's disease (AD). In the present study we attempt to explore the protective effect of bacopa moneeira on altered thyroid hormone activity and association with AD in rats. 100 mg /kg body weight of $AlCl_3$ was given orally to rats for 90 days and a group of rats co-administered with 40mg/kg body weight of bacopa monneiri. Time dependent study was carried out on the 30, 60 and 90 days of treatment. The T3, T4 and FT4 were estimated. We observed that the concentration of T3 and T4 levels significantly correlates with the exposure of AL. while the B. monneiri correlates modulate to these changes on 60^{th} and 90^{th} day of treatment. On the basis of results it may conclude that the concentration of T3, T4 and FT4, a marker of AL induced neurodegeneration. B. monneira modulate these changes significantly.

Key**words:** Aluminum; Alzheimer's disease; Thyroid hormone; Bacopa moneiri

INTRODUCTION

Aluminum (Al) is a third most abundant element and potent neurotoxic element. Al has extensively used in our daily life. It is found in food, medicines and drinking water. It is known contributing factor in the etiology of Alzheimer's disease (AD)[1]. It has also been used in dialysis buffer and leads to dialysis dementia. High concentration of Al in serum is responsible for the abnormalities of thyroid hormone (TH) function[2]. Tan and Vasan[3] found that the association of thyroid hormone and amyloid processing leading to risk of AD. TH plays a significant role in brain function, but the precise mechanism is still unknown[4]. It is reported that plasma triiodothyronine (T3) and thyroxine (T4) concentrations were increased in sublethally Al-stressed brown trout[5].

In the recent years, herbal therapy based on traditional knowledge has been increasingly used in world wide. According to the Indian medicinal system "Ayurveda" represent herbal therapeutics interventions in several neurodegenerative disorders. Bacopa monnieri (BM) is one of the potent herbs used as nerve tonic. BM have the mixture of saponin, bacoside a and bacoside which regulate the kinase activity of the brain. On the contrary, it is reported that BM causes mild deterioration in gastrointestinal system and elevated thyroid hormone in phase- I trials[6].

Taking into consideration the above facts, the present study was conducted with an objective to explore the protective effect of B. monneiri on Al induced alteration in thyroid hormone and its correlate them with the time dependent severity of the disease process.

MATERIAL AND METHODS

Animals

Twenty four male albino rats of Wistar strain (220 ± 5.4g) were taking from University animal house and separately housed in polypropylene cages in a room, which was maintained at a temperature of 22 ± 2^0C, relative humidity of 50±10 % and 12h light dark cycles. They were fed a commercial pellet diet (Dayal Industries, Barabanki, UP, India) and allowed access to water ad libitum. The Institutional Animal Ethics Committee approved the study prior to the initiation of the experiment and also approved all experimental protocols.

Bacopa monniera extract

The extract of the *Bacopa monniera* was prepared as per previously described method and extract so prepared contained 40% bacosides estimated as bacoside A by high pressure thin liqid chromatography[7].

Experimental Design

The experimental groups are Group -1 (CT): $AlCl_3$ (100 mg / kg body wt) treated (Al); Group – 2 (BM): 40 mg / kg body weight *Bacopa monniera* extract, Group-3(AL): 100 mg $AlCl_3$ / kg body wt , Group -4(AL + BM): 40 mg / kg body weight *B.monniera* extract with 100 mg $AlCl_3$ / kg body. The dose was directly introduced into the rat pharynx via a feeding cannula for 90 days.

Thyroid estimations

After 30, 60 and 90 days of treatment the blood was collected from the rat tail vein for serum separation. Serum T3 (triiodothyronine), T4 (thyroxine), and FT4 (free tetraiodothyronine) were analysed using commercially

available kit (DPC-USA) through solid phase radioimmuno assay.

RESULT

The results of the present study depicted in figure-2. T3 levels (fig-2A) were found to be significantly ($p<0.01$) increased on the day 60^{th} and 90^{th} as compared with the controls respectively. While the co-administration of B. monerei markedly ($p<0.001$) reduces the elevated concentration of T3 levels when compared with the Al treated rats. The concentration of T4 levels (fig-2 B) were found to be reduced significantly ($p<0.001$) on 60^{th} and 90^{th} day in AL treated rats when compared with the age matched control rats. The co-administration of B. monnerei significantly ($p<0.05$) increased the concentration of T4 near to age matched controls as compared to age matched AL treated rats respectively. On the other hand the level of FT4 (fig-2C) were found to be reduced significantly ($p<0.001$) on the day of 30^{th} and 90^{th} when compared with their respective controls. The co-administration of B. monneiri restore the level of FT4 near to their respective controls as compared with the AL treated rats.

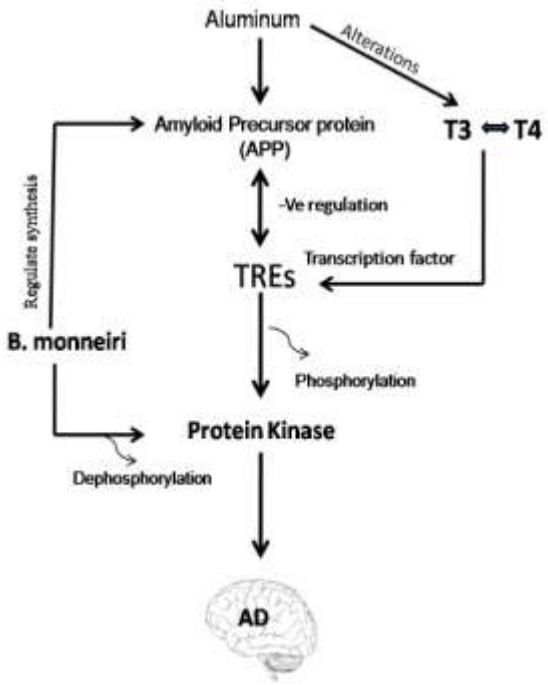

Figure-1. Shows splicing of APP gene leads to formation of aβ protein in AD. Thyroid response elements (TREs) of APP gene bind to transcription factor (TFα &TFβ) of thyroid hormone and negatively regulates the APP transcript which activates the protein kinase and that govern the mRNA turn over in brain. AL alters the level of TH, are responsible for overexpression of APP,Altimates accumulation of aβ protein. BM dephasphorelates the kinase and increase the level of m RNA in brain region and either repair of damaged neuron, neuronal synthesis, restoration of synaptic activity and nerve impulse transmission

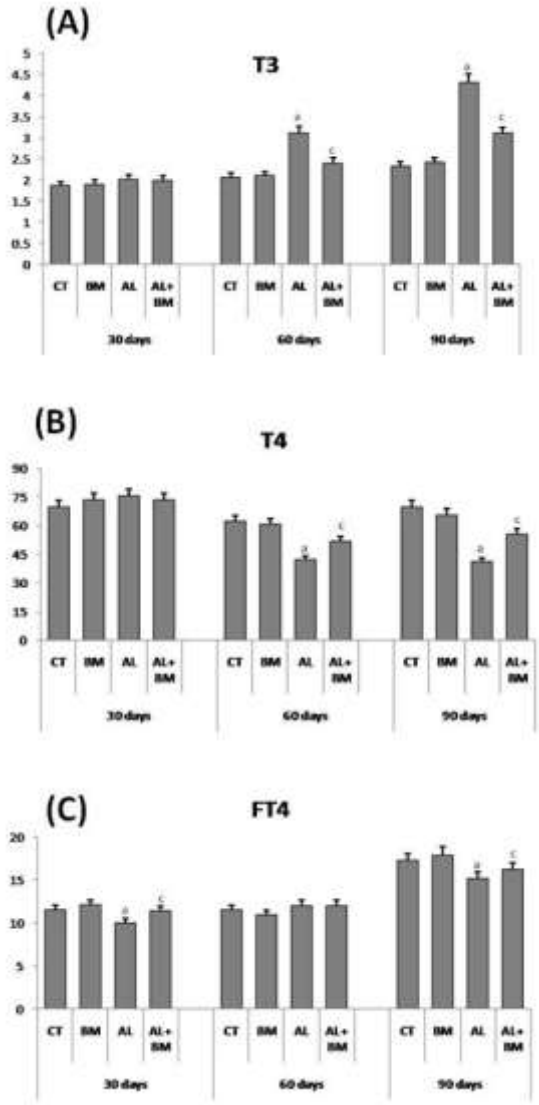

Figure-2. The concentrations of T3, T4 and FT4 (ng/ dl) in control and experimental group on the day 30^{th}, 60^{th} and 90^{th}. The results are expressed as Mean ± SEM in six rat of each group. Superscripts relate significant ($p< 0.05$) comparison with Control (a), Al treated (b) and BM treated (c).

DISCUSSION

In the present study, we evaluated the exploration of BM in thyroid dysfunctioning during long term Al exposure. It is reported that Al is responsible for the deposition of extracellular senile plaques, intracellular neurofibrillary tangles. The major component of NFTs is the phosphorylated tau protein. Senile plaques are largely comprised of β-amyloid protein[8]. Thyroid dysfunction has been implicated as a cause of cognitive impairment and it is used as an indicator of dementia. Recently, several clinical studies demonstrated an association between hypo- or hyperthyroidism and Alzheimer's disease. We observed alterations in altered concentrations of thyroid hormones during different last two intervals for 90 days following Al exposure. Thyroid play an important role to control energy balance and synthesis of proteins. TH secreted into the blood and then carried to every tissue in the body. Alteration in thyroid levels can lead to various ailments like impaired

cognition and anxiety. T3/T4 ratio determined the physiological activity in healthy body but deficiency of thyroid hormone during environmental exposure of brain is associated with profound, and often irreversible morphological defects that may contribute to cognitive impairment[9].The mechanism, BM enhances protein kinase activity in the brain for nootropic action and thus it would aids in repair of damaged neurons by enhancing kinase activity, neuronal synthesis and restoration of synaptic activity and ultimately nerve impulse transmission[10]. It is well established that alteration in thyroid is closely associated with Alzheimer's disease[11], however the mechanism are still unknown[12,13]. Davis and associate[14] aggravate with our finding, they demonstrated a relationship between thyroid disease (i.e., elevated or reduced thyroid stimulating hormone levels with normal T_3 and T_4) and AD. Moreover, T_3 plays an important role in the expression of Aβ[15], which is most characteristic features of the AD[16]. On the other hand, T_3 negatively regulates the gene expression of Amyloid precursor protein at the APP promoter level[17]. The BM extracts enhance nerve impulse transmission It is suggested that bacosides induce membrane dephosphorylation, with a concomitant increase in protein and RNA turnover in specific brain areas[18] in figure 1.

CONCLUSION

On the basis of results it may conclude that Al induced changes in thyroid hormones and protective effect of BMi indicating ameliorating effect Alzheimer's rat model. Time dependent changes may be used as the markers of therapeutic intervention of natural products in neurodegenration.

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