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Anti - Demential Effect of EGB 761 on Dementia Induced Wistar Rats

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Abstract:- Dementia is a devastative neurodegenerative disease which needs sufficient examinations on successful treatment choices. Various studies have been carried out to find therapeutic approaches for dementia. Application of therapeutants and other concoction drugs are not fruitful. A large portion of the current drugs not perfect to treat the dementia because of absence of particularity. Be that as it may, the natural medicines are demonstrated as viable with against dementia properties. A large number of plants and plant constituents are being actively pursued for the anti-dementia activity. In the present study biochemical alterations in after induced dementia treated with from EGB761 which is the standard extract of Ginkgo Biloba Leaf Extract in combination with frontline memory enhancing drug Donepezil in different doses were investigated. Animals were randomised and grouped based on the stratified body weight Dementia were induced to all the animals (GII – GVI) by intra peritoneal injection of scopolamine except group I and VII. For group VII, animals were treated with drug for a period of 6 weeks then dementia were induced at the end of the treatment after 6 week to assess the pretreatment effect of drug. Biochemical analysis such as creatinine, cholesterol, sodium, potassium, urea, HDL and LDL were also carried out using standard procedures. The level of urea, Creatinine, sodium, potassium, urea, creatinine, cholesterol, HDL and LDL was observed at after induced dementia with different treatments when compared to scopolamine. EGB 761 could give significant knowledge to development of newer lead compounds against dementia.

Keywords:- *EGB 761, Sodium, Potassium, Urea, Creatinine, Cholesterol, HDL and LDL.*

I. INTRODUCTION

Dementia is alluded to as a gathering of chronic disorders which is described by memory loss, improvement of various cognitive deformities found in instances of adjusted physiological conditions. These adjusted conditions are separate by changes in the character of an individual joined by loss of intellectual function. The modification of the physiological conditions provoking dementia could be because of any medicine or on the other hand numerous etiology prompting social and occupational dysfunction [1]. Memory is the procedure by which creatures can record their encounters and use this so as to adjust their reactions to the nature. Subsequently it is imperative for survival. Impeded subjective capacities are the real highlights of Alzheimer's disease. The ordinary span of survival of AD patients after the start of dementia is 5 to 9.3 years. As a result of absence of a permanent cure, AD has transform into an imperative therapeutic issue, in spite of the way that there are a couple of drugs that may back off its advances. It is assessed that there are 35.6 million people living with dementia worldwide and would have addition to 65.7 million by 2030, whereby an extraordinary piece of the extension will be in developing countries [2-3]. Several factors and conditions provoke dementia. These can be, Alzheimer's disease, dementia with Lewy bodies, vascular illness, heavy drinker dementia, Creutzfeldt– Jakob sickness, Parkinson's ailment, hereditary or a metabolic illness and harmful or an awful infection (4-6). In recent years, several clinical studies have proposed what may be an important key in the progression of AD. The memory is the most imperative elements of the mind. Application of therapeutants and other concoction drugs are not fruitful. A large portion of the current drugs not perfect to handle dementia because of absence of particularity. Be that as it may, the natural medicines are demonstrated as viable with against dementia properties. They improve the memory of dementia induced Wistar rats and incite the regeneration of damaged nerve cells in brain and nerve

tissues. The anti demential effects of a number of compounds were reported [7]. In the present study to develop an effective anti demential compounds from EGB 761 in combination with frontline memory enhancing drug Donepezil in different doses.

Ginkgo Biloba have been used as agents for improving cerebral circulation and exhibits various biological activities such as antioxidant, anti-parasitic, anti-tumor and anti-viral activities. It possessed phytoconstituents such as phenolic acids, proanthocyanidins, flavonoid glycosides, biflavones, as well as alkylphenols and polyprenols [8]. EGB 761 is the standard extract of Ginkgo Biloba Leaf Extract. Biochemical analysis such as sodium, potassium, urea, creatinine, cholesterol, HDL and LDL plays a crucial role in the development of mild cognitive impairment (MCI) and AD. Depressed sodium and potassium levels might lead to a cellular ion imbalance. Renal capacity decreases with age and as per the burden of vascular risk factors, while serum creatinine and proteinuria have been related with late life occurrence all-cause dementia. Both low and high glomerular filtration rates might be valuable markers for mortality and cardiovascular occasions, while hereditary impacts may be essential to interfere those dangers [9-10]. Metabolic syndrome is a multifactorial disorder represented by the co-occurrence of vascular conditions related to impaired glucose metabolism and dyslipidemia. Each individual factor and metabolic syndrome as a whole has been repeatedly correlated with cognitive decline and dementia [11-12]. Keeping in this view the present investigation was undertaken to elucidate the biochemical alterations in after induced dementia treated with from EGB 761 in combination with frontline memory enhancing drug Donepezil in different doses.

II. MATERIALS AND METHODS

A. Experimental design

Animals were randomised and grouped based on the stratified body weight. The weight variation of mouse was minimal and not exceeds ± 20% of the mean body weight. The weights of each mouse were measured before starting the experiment. Prior to the experiments, random sampling was made among the animals to detect any external perceptive symptoms, to ensure that the Wistar rats were free from disease/infections. Group I as Control (Normal saline), Group II as positive control (Scopolamine 1mg/kg + Normal saline), Group III as reference drug (Scopolamine 1mg/kg + Donepezil 10mg/kg), Group IV served as reference drug (scopolamine 1 mg/kg + Donepezil 20mg/kg), Group V served as Test drug (Scopolamine 1 mg/kg + EGB 761 100 mg/kg), Group VI served as Test drug (Scopolamine 1 mg/kg + EGB 761 200 mg/kg) and Group VII served as Test drug (EGB 761 100 mg/kg + Scopolamine 1 mg/kg).

B. Induction of dementia

Dementia was induced to all the animals (GII – GVI) by intra peritoneal injection of scopolamine except group I and VII. For group VII, animals were treated with drug for a period of 6 weeks then dementia was induced at the end of the treatment after 6 week to assess the pretreatment effect of drug. Biochemical analysis such as sodium, potassium, urea, creatinine, cholesterol, HDL and LDL were also carried out using standard procedures.

C. Assay for serum total cholesterol

The level of serum in total cholesterol was measured after enzymatic hydrolysis and oxidation of the sample as depicted by the technique of Stein [13]. Quickly, 1000: l of the reagent was added to all the test sample and standard. This was brooded for 10 minutes at 20-25ºC in the wake of blending and the absorbance of the example (A sample) and standard (A standard) was estimated against the reagent clear inside 30 minutes at 546 nm. The estimation of Total Cholesterol present in serum was expressed in the unit of mg/dL.

D. Assay for serum high density lipoprotein cholesterol

The serum level of high density lipoprotein cholesterol HDL-C was estimated by the method of Wacnic and Alber [14]. Low-density lipoproteins and chylomicron fractions in the sample were precipitated quantitatively by addition of phosphotungstic acid in the presence of magnesium ions. The mixture of the sample was kept for 10 minutes at room temperature and centrifuged at 4000 rpm for 10 minutes. The supernatant described the HDL-C fraction. The cholesterol concentration in the HDL fraction, which remained in the supernatant, was determined. The value of HDL-C was expressed in the unit of mg/dl.

E. Determination of serum low-density lipoprotein

The serum level of (LDL-C) was measured according to protocol of Friedewald et al.[15] The value was expressed in the unit of mg/dL

III. STATISTICAL ANALYSIS

All the results and data were expressed as mean ± standard deviation. Data was analyzed using two way ANOVA by bonferroni test and one way ANOVA tukey's test. ($P< 0.05$ and $P< 0.001$) was considered as statistically significant.

IV. RESULTS AND DISCUSSION

In the present investigation anti demential effect of EGB 761 on biochemical analysis such as sodium, potassium, urea, creatinine, cholesterol, HDL and LDL were studied.

F. Sodium and Potassium

It was observed that administration of Scopolamine and normal saline (Group II) increased the level of sodium and potassium and it was found to be 175.83 ± 1.58 and 2.59 ± 0.07. Likewise, EGB 761 and Scopolamine (Group VII) extract also significantly increased the level of sodium and potassium in after induced dementia was found to be 148.45 ± 1.25 and 4.39 ± 0.34 respectively ($P< 0.05$ and $P<$

0.001) (Table 1 and Fig.1). Moderate level of elevation in sodium and potassium was observed at Group III and the decreased level of sodium and potassium was observed at Group IV in after induced dementia. Our results were akin with Ozawa et al [16] who observed that the dietary intake of potassium, magnesium and calcium declined the risk of dementia mainly in vascular dementia. The risk of AD would in general decrease with higher detailed dietary mineral intake, but there was no significant linear progression. Likewise, Cisternas et al.[17] who observed that the increase in the intake of K+ could help to prevent the pathologies such as hypertension, which could possibly prevent or retard the onset of cognitive-related diseases such as AD. The positive effects represented for the K+ diet could be an interesting non-pharmacological treatment at least to some extent, the incidence of cognitive decline and the progression of AD.

G. Urea and Creatinine

A significant variation of urea and creatinine was observed in after induced dementia at all the treatment groups. Maximum level of inhibition was observed at (Group V) Scopolamine + EGB761 on urea and creatinine was found to be 49.88 ± 0.58, 0.88 ± 0.04 and 42.69 ± 0.53, 0.67 ± 0.09. Likewise, Scopolamine + EGB 761 (Group V1) was showed 45.41 ± 0.43, 0.72 ± 0.03 and 41.42 ± 0.36, 0.64 ± 0.08 respectively (P<0.05) (Table 2 and Fig.2). Similar observations was recorded by Chaturvedi et al [18] who reported the significant increased level in the blood urea nitrogen, due to a metabolic cause in dementia. Ferreira de Oliveira [19] additionally considered the impacts of ACE is over creatinine varieties are hereditarily intervened and independent of blood pressure variations in older people with AD. Modifications in urea and creatinine invigorated by scopolamine were altogether prevented by EGB 761.

C.Total cholesterol, HDL and LDL

In the present study, total cholesterol, HDL and LDL in dementia induced Wistar rats was investigated. After induced dementia treatment, total cholesterol level was increased in Group III was found to be 192.43 ± 1.82 and the decreased level of was observed at Group VI and VII was found to be 159.43 ± 1.12 and 180.64 ± 1.43. Likewise, HDL was increased in Group V, VI and VII was found to be 82.21 ± 0.47 and decreased in Group III, II and I was found to be 53.48 ± 0.32, 51.26 ± 0.28 and 66.83 ± 0.32 (P< 0.05 and P< 0.001) respectively (Table3 and Fig.3). Our results were substantiating with Dubey [20] who recorded that the significant lowering of serum cholesterol in EGB 761 treated animals, almost comparable to that of lovastatin B. Similarly, disturbances in cholesterol, HDL and LDL indicate disturbances in protein, carbohydrate and lipid metabolism induced by thioacetamide intoxication was reported by Al-Attar [21]. Ismail et al. [22] also observed the levels of serum cholesterol and LDL were increased, while the level of serum HDL was declined in CCl4 treated rats. Low level of HDL may be a risk factor for loss of memory lead to dementia. EGB 761 has a potential anti dementia activity in Wistar rats compared to Donepezil. These results suggest that EGB 761 can be used as a valuable or effective herbal drug to combat dementia patients.

S. No	Group	Without dementia Treatment		After induced dementia Treatment	
		Sodium	Potassium	Sodium	Potassium
1.	Normal saline	135.74 ± 1.21	3.91 ± 0.12	135.84 ± 1.20	4.36 ± 0.32
2.	Scopolamine + Normal saline	142.82 ± 1.30	3.75 ± 0.10	175.83 ± 1.58	2.59 ± 0.07
3.	Scopolamine + Donepezil	140.02 ± 1.27	4.36 ± 0.32	149.23 ± 1.30	3.64 ± 0.10
4.	Scopolamine + Donepezil	150.19 ± 1.32	4.71 ± 0.38	126.43 ± 1.11	3.89 ± 0.11
5.	Scopolamine + *EGB 761*	140.81 ± 1.25	3.91 ± 0.12	144.18 ± 1.24	4.15 ± 0.18
6.	Scopolamine + *EGB 761*	138.39 ± 1.23	3.91 ± 0.12	142.41 ± 1.23	4.01 ± 0.12
7.	EGB 761 + Scopolamine	136.82 ± 1.19	4.36 ± 0.31	148.45 ± 1.25	4.39 ± 0.34

Table 1:- Sodium and Potassium Level of Dementia in Different Treatment Groups

S. No	Group	Without dementia Treatment		After induced dementia Treatment	
		Urea	Creatinine	Urea	Creatinine
1.	Normal saline	44.31 ± 0.41	0.78 ± 0.03	44.13 ±0.42	0.59 ± 0.07
2.	Scopolamine + Normal saline	44.09 ± 0.41	0.82 ± 0.04	59.43 ± 0.68	1.79 ± 0.4
3.	Scopolamine + Donepezil	47.39 ± 0.50	0.78 ± 0.03	49.64 ± 0.59	1.02 ± 0.1
4.	Scopolamine + Donepezil	48.38 ± 0.54	0.76 ± 0.03	44.39 ± 0.42	0.92 ± 0.1
5.	Scopolamine + *EGB 761*	49.88 ± 0.58	0.88 ± 0.04	42.69 ± 0.53	0.67 ± 0.09
6.	Scopolamine + *EGB 761*	45.41 ± 0.43	0.72 ± 0.03	41.42 ± 0.36	0.64 ± 0.08
7.	EGB 761 + Scopolamine	43.71 ± 0.38	0.65 ± 0.03	44.28 ± 0.41	0.66 ± 0.08

Table 2:- Urea and Creatinine Level of Dementia in Different Treatment Groups

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S. No	Group	Without dementia Treatment			After induced dementia Treatment		
		TC	HDL	LDL	TC	HDL	LDL
1.	Normal saline	180.12 ± 1.68	67.83 ± 0.63	122.39 ± 0.69	179.12 ± 1.52	66.83 ± 0.32	118.17 ± 1.12
2.	Scopolamine + Normal saline	192.34 ± 1.72	55.83 ± 0.48	118.42 ± 0.62	198.27 ± 1.68	51.26 ± 0.28	129.67 ± 1.32
3.	Scopolamine + Donepezil	171.48 ± 1.56	60.46 ± 0.59	110.25 ± 0.57	188.63 ± 1.70	53.48 ± 0.32	139.75 ± 0.98
4.	Scopolamine + Donepezil	187.53 ± 1.70	54.35 ± 0.47	131.28 ± 0.49	192.43 ± 1.82	69.31 ± 0.43	121.31 ± 1.11
5.	Scopolamine + *EGB 761*	165.69 ± 1.43	52.25 ± 0. 43	120.65 ± 0.54	140.23 ± 1.03	74.24 ± 0.53	112.67 ± 1.04
6.	Scopolamine + *EGB 761*	169.78 ± 1.47	68.26 ± 0.32	116.71 ± 0.43	159.43 ± 1.12	82.21 ± 0.47	114.47 ± 1.21
7.	EGB 761 + Scopolamine	185.76 ± 1.73	57.31 ± 0.31	118.43 ± 0.42	180.64 ± 1.43	65.29 ± 0.33	118.64 ± 0.99

Table 3:- Total Cholesterol, HDL and LDL Level of Dementia in Different Treatment Groups

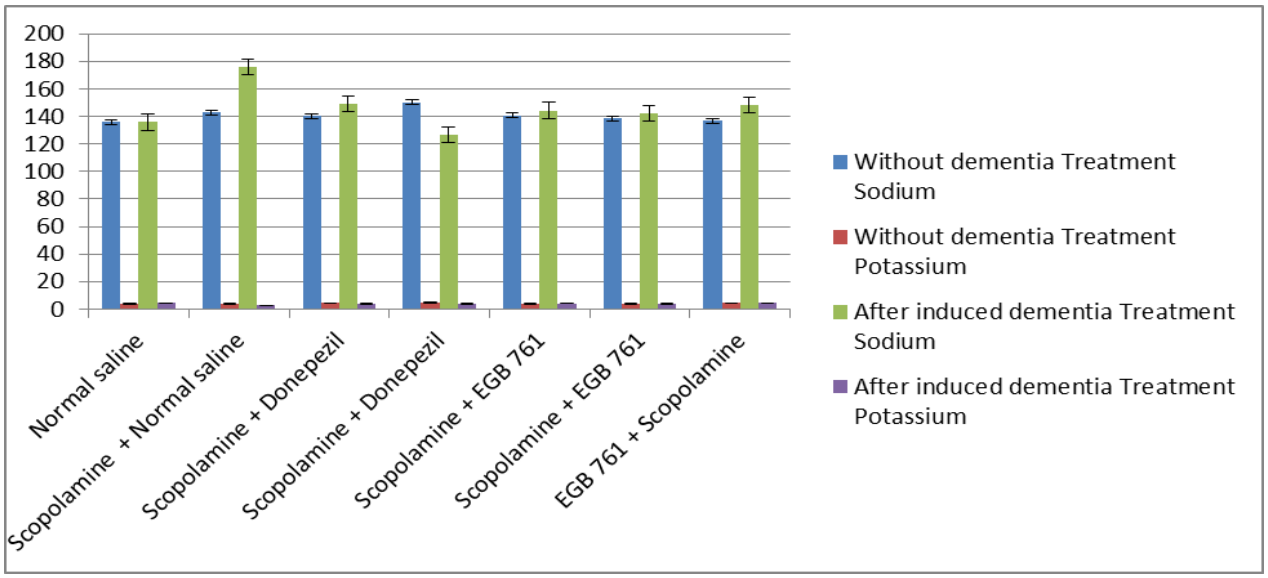

Fig 1:- Sodium and Potassium Level of Dementia in Different Treatment Groups

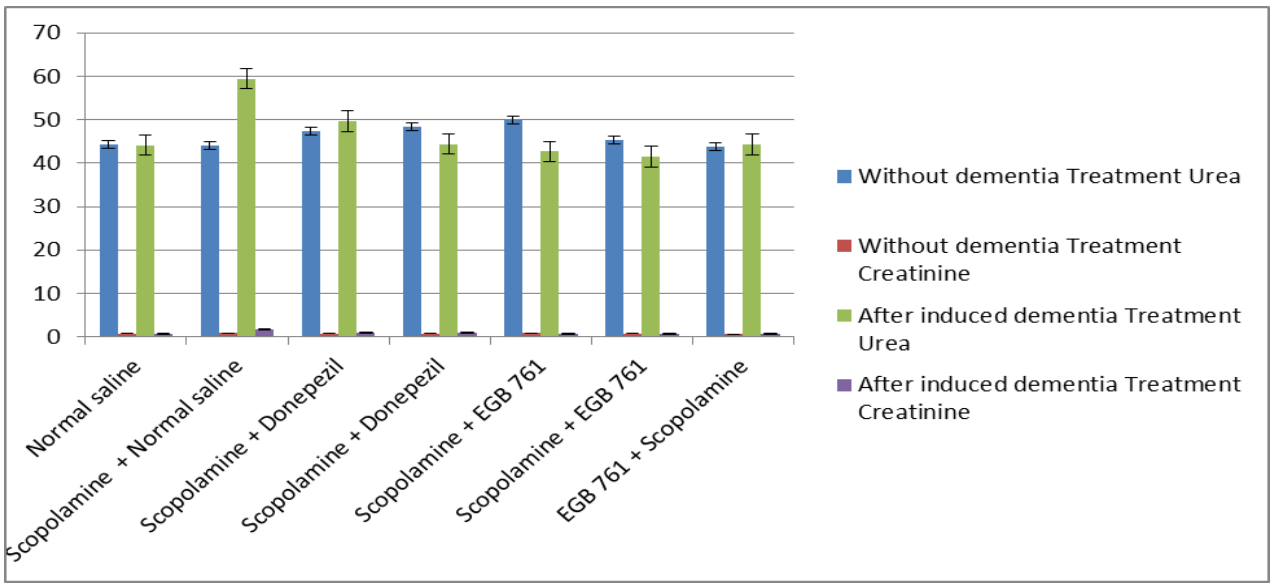

Fig 2:- Urea and Creatinine Level of Dementia in Different Treatment Groups

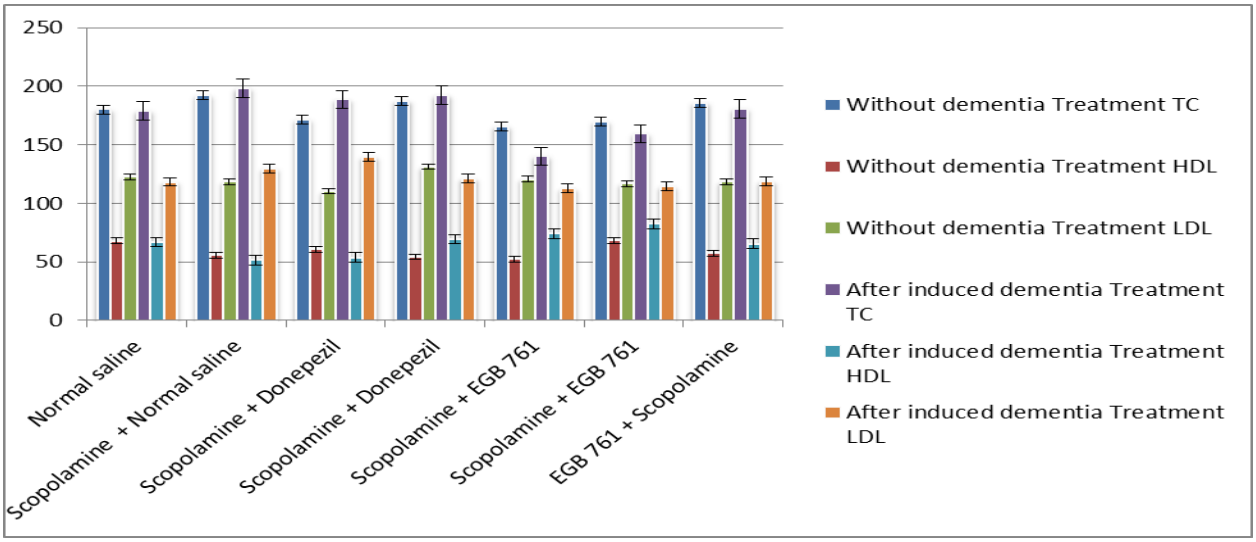

Fig 3:- Cholestrol, HDL and LDL Level of Dementia in Different Treatment Groups

V. CONCLUSION

Anti-demential effect of EGB 761 on biochemical analysis such as sodium, potassium, urea, creatinine, cholesterol, HDL and LDL were studied. EGb761 affects the mechanisms associated with proper brain functions. A major chemical constituent occurs in Gingko Biloba is gingkolides and it is a pertinent antioxidant, with neuroprotective and cholinergic activities that works in the management of AD. EGb761 altered the biochemical parameters in dementia treated rats when compared to Donepezil. EGB 761 also protected rodent neurons and glial cells against cerebral ischemia or scopolamine induced toxicity.

EGB 761 can be used as an efficacious herbal treatment to prevent and might be a promising therapeutic agent for anti-demential properties and speculate that Ginkgo Biloba extract may reach the market in near future.

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