Exploration of Under Water Medicine Cabinets by Determining the Nutraceutical Potential of *Sargassum Illicifolium* Against Alzheimer's Disease from Karachi Coast, Pakistan

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ABSTRACT

Introduction: Pakistan is a lower-middle income country with an estimated one million people living with dementia. The most common type of dementia includes Alzheimer's disease (AD) which covers 60–70% cases of old age (WHO Report, 2022). AD related dementia is not only the major health issue in Pakistan but due to lack of awareness, its incidence and progression is increasing gradually rapidly. For such dementia-related issues, there is no specific treatment available. The currently available FDA (food and drug administration) approved medications, such as esterase inhibitors and NMDA (N-methyl D-aspartate) receptors, only function on neurons that are still working but cannot stop the ongoing degeneration of neurons in the brain. Despite the fact that these drugs might enhance quality of life and reduce dependency or caregiver support (Avilla, *et al.*, 2020) but they cannot completely treat the disease. Therefore, there is a serious need for the development of treatment approaches that can not only enhance neuronal functions but also prevent the developing neurodegenerative mechanism in brain (Wenk, et al., 2008). Recent studies have been focused on searching for more cost effective, preventive and alternative medications with less or no side effects with greater efficacy. Seaweeds derived bioactive substances shows a variety of nutritional, therapeutic, and nutraceutical properties (Meinita & Harwanto, 2022, Plasek, *et al.*, 2020, Brown *et al.*, 2014) so this study is based on exploration of indigenous marine source including Sargassum *illicifolium (SI)* bioactivity against Alzheimer's disease.

Objectives: The objective of present study is to explore the brain health improving effects of marine algae both *invitro* and *invivo* by investigating the neuroprotective effects against AD-like symptoms induced by co-administration of AlCl3+D-gal in an animal model.

Materials & Methods: Various marine algae mainly brown and green algae surrounding coral reefs were collected from Karachi-Pakistan coast. After species identification of marine algae and related samples, isolated extracts were tested for Acetyl cholinesterase (AChE) and butryl cholinesterase inhibition invitro assays by ELISA technique. After in-vitro analysis and toxicological studies, *Sargassum illicifolium (SI)* was selected for further pre-clinical studies. For above mentioned purpose, 24 healthy male albino-Wistar rats (weighing 100–150 g) were purchased from DUHS, OJHA campus, Karachi, Pakistan. Animal handling and experiments were approved before the start of the study by the Animal Care Committee and Institutional Ethics. After 1-week acclimatization period, animals were randomly divided into four groups (n = 6) and placed into separate cages. Group 1 assigned as a control

group, group 2 assigned as test (model) rats. Group 3 assigned as AD model + treatment group and group 4 assigned as *SI* alone group. Seaweeds was collected from Karachi-coast, and after species identification, seaweeds were carefully washed with water to remove dust and impurities and dried under shade in air at room temperature. The air-dried and coarsely powdered sample was then suspended in tap water and was per oral administered to rats (3 and 4 groups) at a dose of 600mg/kg for a period of two weeks. Sea weeds were freshly suspended in tap water daily before each administration. 24 hours after monitoring the last behavior, rats were sacrificed by decapitation. After decapitation brain samples were removed from skull and immediately rinsed with ice-cold (0.9%) saline. The samples were then directly stored at −70 °C for further biochemical and neurochemical estimations.

Results: Results of the present study indicated that pre-treatment with SI significantly protected brain neurodegenerative mechanism and AD associated behavioral disorders in rats. Memory disturbances were not observed in (SI) supplemented rats whereas marked memory decline was observed in AD rats. AD rats showed significant cognitive deterioration as marked from decreased step-through latency whereas such memory deterioration was not observed in rats supplemented with *SI*. Marked increase in step through latency was observed in SI supplemented rats after 60 min of training. Oxidative stress indicated by MDA levels were markedly elevated in AlCl3+D-gal induced AD rats. Antioxidant enzymes activities were also significantly altered in AD model rats but such effects were ameliorated in (SI) ingested rats. *SI* Pre-treatment also significantly decreased AChE activity and acetylcholine levels were significantly increased compared to AD model rats. Marked oxidative stress in terms of reduced SOD, GPx, CAT and GSH and elevated LPO was observed in brain of AD rats while such oxidative damage was not observed in SI supplemented rats

Conclusion: Based on the findings of the present investigation it is suggested that a combination of antioxidant and esterase inhibitor may not only provide symptomatic relief to AD patients but may also protect the brain from neurodegenerative process and to keep brain healthy in normal individuals and prevent from further brain complications in future. SI showed potent antioxidant, AChE inhibitory and memory improving effects against AD animal model in the present investigations. Therefore, it is proposed that Saragassum illicifolium. (SI) may provide a significant role in enhancing cognitive functions and considered as a neuroprotective component for the development of nutraceutical against Alzheimer's disease. It can be used as potential candidate as therapeutic agent in nutraceutical industries for memory boosting effects in aged population.

Keywords: Acetyl cholinesterase, Alzheimer's disease, Butrylcholinesterase, Nutraceutical, *Sargassum Illicifolium*

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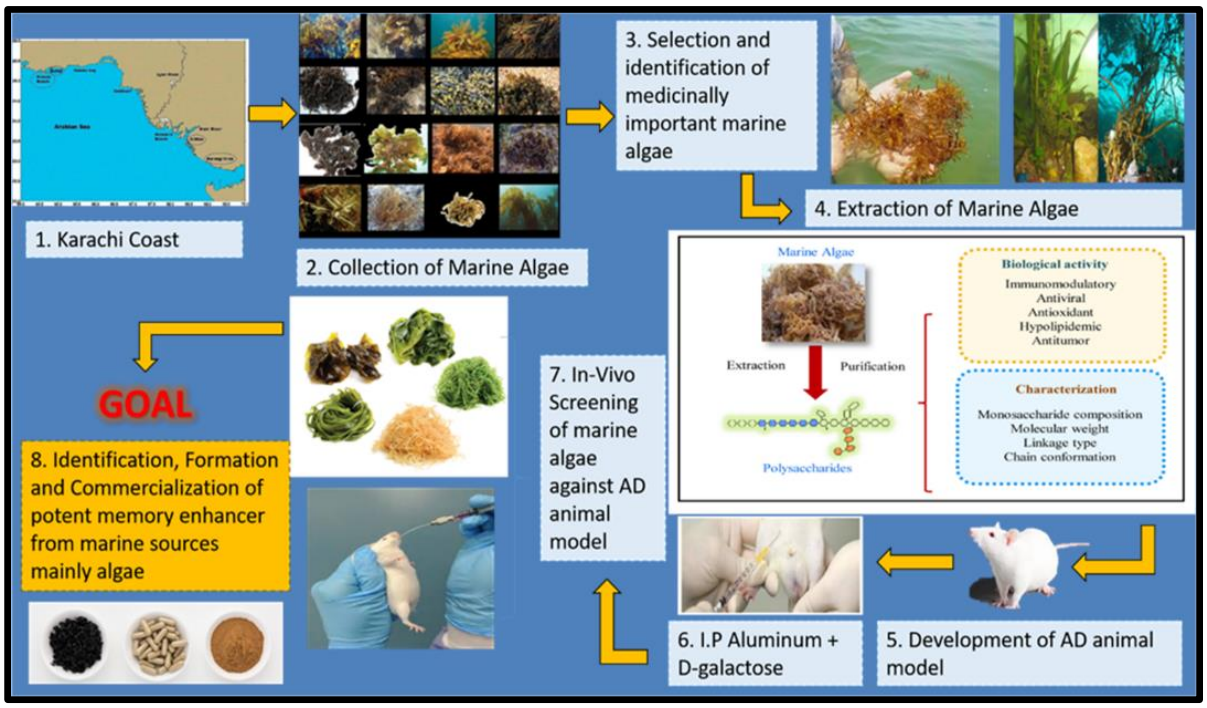

Figure 1. Flow Chart followed for the Study

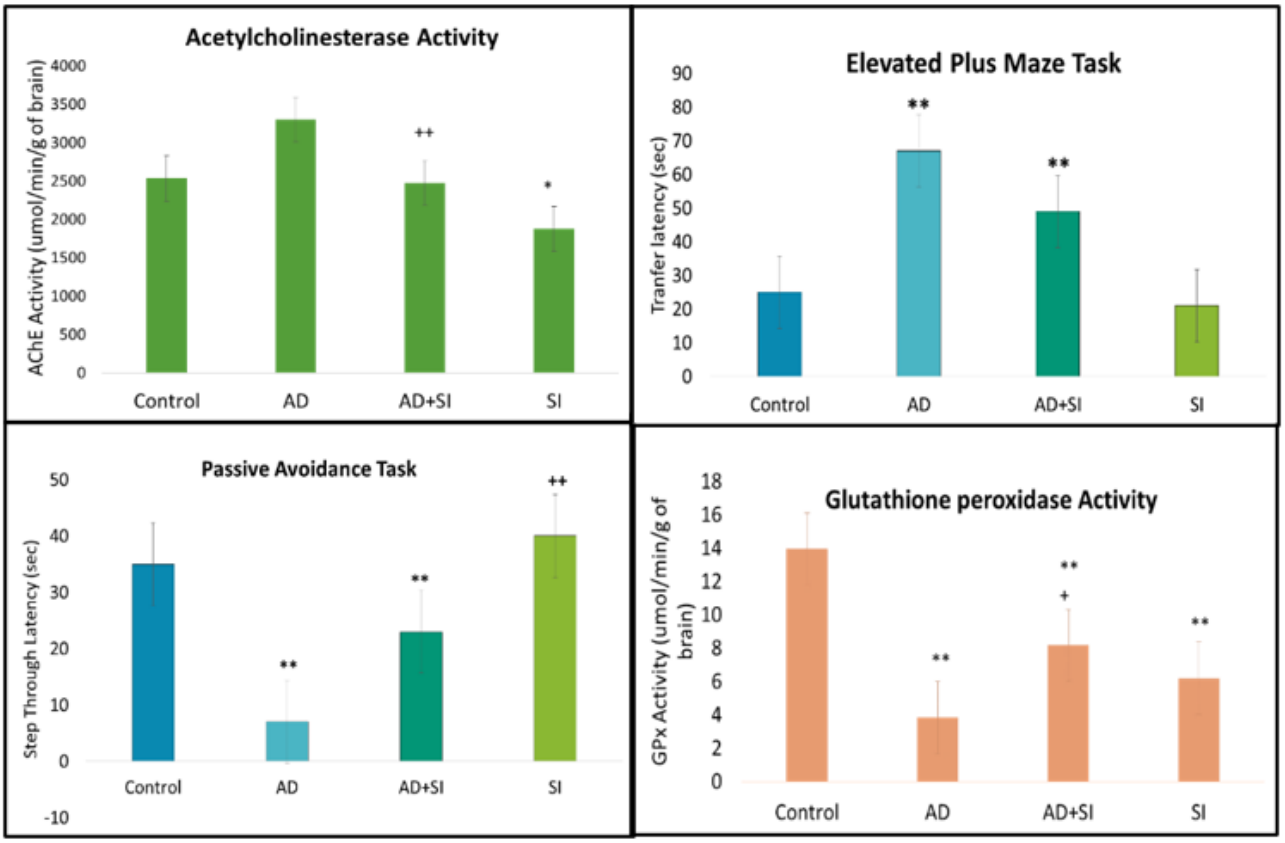

Figure 2, Effect of SI administration on behaviors in AD animal model for Memory assessment.

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