11. LIST OF PUBLICATIONS

11.1. Publications from thesis


11.2. Other Publications


11.3. Review articles in journals


11.4. Review articles in books


Assessment of anti-amyloidogenic activity of marine red alga *G. acerosa* against Alzheimer’s beta-amyloid peptide 25–35

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**Objective:** The amyloid hypothesis stimulates the discovery of compounds, which promotes beta-amyloid peptide (Aβ) clearance, thereby altering the underlying pathophysiology of Alzheimer’s disease (AD). Hence, the present study aims at the evaluation of anti-amyloidogenic potential of *Gelidiella acerosa*.

**Methods:** Prevention of Aβ 25–35 aggregate formation and disaggregation of pre-formed fibrils by *G. acerosa* was evaluated in three phases by thioflavin T spectrophotometric assay. The results were further validated by confocal microscopic analysis. The conformational changes in the aggregated and non-aggregated Aβ in the presence of *G. acerosa* were analyzed by Fourier transform infrared (FTIR) spectroscopic analysis.

**Results:** Phase-I study shows that *G. acerosa* reverts (4.56 ± 0.35 AU at 96 hours) the increase in fluorescence intensity of aggregated Aβ (18.76 ± 0.99 AU) significantly (*P*, 0.05) as that of non-aggregated peptides, which suggests that *G. acerosa* prevents the formation of oligomers from monomers. The seaweed also prevents the fibril formation even after the aggregation process was initiated at 20 hours, which was verified by the significant (*P* < 0.05) decrease in the fluorescence intensity (2.94 ± 0.0721 AU) at 36 hours (Phase II). In addition, *G. acerosa* promotes fibrillar destabilization (Phase III), which was further substantiated by confocal microscopic analysis. Fourier transform infrared spectroscopy reveals that alteration in amide I and amide II band spectrum, which occurs due to Aβ 25–35 aggregation was restored upon co-treatment with *G. acerosa* benzene extract.

**Conclusion:** Overall, the results suggest that *G. acerosa* might have direct interaction with the aggregated peptide, thereby preventing oligomerization and fibrillation of Aβ 25–35.

**Keywords:** Alzheimer’s disease, Aβ 25–35, *G. acerosa*, Anti-aggregation, FTIR analysis

**Introduction**

Alzheimer’s disease (AD), an age-related progressive neurodegenerative disorder results in disturbed cognitive functions.1 Extracellular deposition of beta-amyloid peptide (Aβ) surrounded by deteriorating neurons and inflammatory cells, intracellular formation of neurofibrillary tangles, and basal forebrain cholinergic deficit are the major neuropathological hallmarks of AD.2 Short protein fragments of 4 kDa made up of 40 or 42 amino acids (Aβ 1–40 and Aβ 1–42) are the major constituents of Aβ.3 However, Aβ 25–35 fragment containing a stretch of 11 amino acid residues of the full length from position 25–35 (produced as a proteolytic product of full length Aβ 1–40) has been found to be biologically active and confers toxicity to neurons.4 The Aβ aggregation process starts as the self-assemblage of Aβ monomers into low-molecular weight oligomers, which then give rise to high-molecular weight oligomers termed as soluble aggregation intermediates. These high-molecular weight intermediates further aggregate to form fibrils, which along with hyperphosphorylated tau protein deposit as senile plaques in the hippocampal region of the brain.5 Although the deposition of aggregated Aβ is a critical event in AD, the contributing factors for promoting the aggregation and accumulation remains elusive. A recent report suggests that considerable number of environmental factors along with the inherent properties of Aβ together results in the deposition of Aβ aggregates.6 Hence, evaluating the self-assemblage of Aβ in *vitro* would result in the screening and identification of molecules for anti-amyloidogenic properties. Moreover, preventing the formation of oligomers and fibrils from soluble monomers is of significant therapeutic value in the facet of drug discovery against AD.7 Since natural products have successfully served as a source of new AD drugs, the current study...
Research Article

Assessment of Mutagenic Effect of G. acerosa and S. wightii in S. typhimurium (TA 98, TA 100, and TA 1538 strains) and Evaluation of Their Cytotoxic and Genotoxic Effect in Human Mononuclear Cells: A Non-Clinical Study

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The marine red algae (Gelidiella acerosa and Sargassum wightii) possessing excellent antioxidant and anticholinesterase activity were subjected to toxicity evaluation for a deeper understanding of other bioprotective properties of seaweeds. Cytotoxic evaluation was done by trypan blue exclusion, and MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assays using human PBMC (peripheral blood mononuclear cells) and RBC (red blood cells) lysis assay using human erythrocytes. Mutagenicity of the seaweeds was analyzed by Ames salmonella mutagenicity test with the histidine dependent mutant strains TA 98, TA100 and TA 1538. Genotoxic activity was verified in PBMC by comet assay. The results suggest that benzene extract of G. acerosa (BEGA) and dichloromethane extract of S. wightii (DMESW) did not show cytotoxic effect both in PBMC and erythrocytes. Evaluation of mutagenic activity suggests that the seaweeds did not cause any mutagenic effects both in the absence and the presence of S9 microsomal fraction in all the three Salmonella mutant strains. Results of genotoxic study showed that PBMC treated with seaweed extracts (1mg/mL) exhibit less or no damage to cells, thus proving the non-genotoxic effect of the extract. Since these in vitro non-clinical studies clearly demonstrate the non-toxic nature of the seaweeds, they could be exploited for further characterization, which would result in development of novel and safe therapeutic entities.

1. Introduction

The exploitation of plants and other natural products as medicines has been in practice for several decades, since these natural products have excellent therapeutic potentials and serve as leads for the development of novel drugs [1, 2]. More than 80% of the population in the world use botanical preparations as medicines [3]. During the past 20 years, thousands of novel compounds with diverse biological activities ranging from antiviral to anticancer have been isolated from various marine sources [4]. Seaweeds or macroalgae are found to have rich source of secondary metabolites like polysaccharides, sterols, terpenoids, flavonoids, and fatty acids, which acts as excellent drug leads and facilitates the unraveling of novel biosynthetic pathways [5, 6]. However, certain metabolites are toxic in nature, which necessitates the toxicological evaluation of natural products, which includes testing of plants for cytotoxic, genotoxic, and mutagenic potentials [7, 8]. Mutagenicity is the process of induction of permanent transmissible changes in the genetic material of the cells, whereas genotoxicity is a broader term, which is the ability of a compound to interact with the genetic material and also with other cellular apparatus that maintains the fidelity of the genome [9]. Only non-toxic and non-mutagenic plants could be considered for relative safe use and also for detailed study of other pharmacological potentials [8].

The marine macroalgae Gelidiella acerosa and Sargassum wightii belong to the class of Rhodophyceae and Phaeophyceae, respectively. G. acerosa has been recognized as
Original article

Evaluation of *Gelidiella acerosa*, the red algae inhabiting South Indian coastal area for antioxidant and metal chelating potential

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In vitro antioxidant potential and metal chelating activity of various solvent fractions of *Gelidiella acerosa* were evaluated by different antioxidant assays, like ferric reducing antioxidant power (FRAP) assay and scavenging activities for hydrogen peroxide, hydroxyl radical and nitric oxide. Among all the fractions, benzene showed the highest 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical, nitric oxide and hydrogen peroxide scavenging activity when compared to standard BHT with IC\textsubscript{50} values of 308.50 ± 3.04, 328.79 ± 14.25 and 275.43 ± 72.09 µg/ml, respectively. Total antioxidant capacity and reducing power was found to be significantly higher in the dichlormethane fraction. Highest ferrous ion chelating activity was observed in ethyl acetate and benzene fractions. Dimethylsulfoxide fraction exerted the highest hydroxyl radical scavenging effect. Moreover, benzene and dichlormethane fraction showed the highest total polyphenolic content of 18.86 ± 0.27 and 17.69 ± 0.35 µg/g of dry extract, respectively. Preliminary cytotoxic studies suggest that benzene and dichlormethane fraction has no cytotoxic effect, hence, they can be used as effective antioxidant for treating reactive oxygen species (ROS) mediated diseases.

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1. Introduction

Reactive oxygen species (ROS), such as hydroxyl radicals, superoxide, nitric oxide and peroxynitric radicals are formed in human cells by endogenous factors and exogenously result in extensive oxidative damage that in turn leads to geriatric degenerative conditions, like cancer and a wide range of other human diseases [1]. Antioxidants are free radical scavengers, which postpone the oxidation and block the chain initiated by high-energy molecules thereby, protecting the body against oxidative damage [2]. Although many synthetic antioxidants are promising for various human ailments, their pro-oxidant or cytotoxic nature at higher concentration prevents them from long-term use. These findings, together with the consumers’ interests in natural food, have reinforced the efforts for the development of alternative antioxidants of natural origin [3]. Numerous studies have been focused on natural antioxidants in terrestrial plants and their application in food systems to prevent oxidation. Nowadays, aquatic plants are also gaining interest as a potential source of antioxidants. Over the past decades, seaweeds or their extracts have been shown to possess a variety of compounds and some of them have been reported to possess biological activity of potential medicinal value [4,5]. Therefore, new interest has been developed to search natural and safe antioxidants from marine sources. In folk medicine, seaweeds have been used for a variety of remedial purposes, e.g. for the treatment of eczema, gallstone, gout, crofula, cooling agent for fever, menstrual trouble, renal problems and scabies [6]. More recent reports revealed that marine algae possess rich sources of antioxidant compounds with potential free radical scavenging activity as in *Halimeda tuna* [7] and *Acanthophora spicifera* [8]. Some active antioxidant compounds from marine algae were also identified as phylophophephlin in *Eisenia bicyclis* [9], phlorotannins in *Sargassum kielmannianum* [10] and fucoxanthin in *Hijikia fusiformis* [11]. In India, seaweeds are exploited mainly for the industrial production of phycocolloids, such as agar-agar, alginate, carrageenan and not for health aspects. As reports regarding the antioxidant properties of seaweeds are very limited, we attempted to screen for the antioxidant activity of the commonly available seaweeds from Southern coast of India. Preliminary screening for antioxidant activity of seaweeds inhabiting Gulf of Mannar has shown that methanolic extract of *Gelidiella acerosa* exhibited excellent antioxidant activity [12].

*G. acerosa* is a perennial red algae (Rhodophyceae) widely distributed throughout the year along the South coastal region of India i.e., Gulf of Mannar. *G. acerosa* is widely used in agar production and in the treatment of gastrointestinal disorders [13]. S–ACT–1, a sulfono glycolipid of *G. acerosa* showed potent sperm motility stimulating activity under in vitro condition [14]. S–PC–1, a sphingosine derivative was found to act as non-steroidal anti progesterone contraceptives [15]. Reports regarding the pharmacological application of *G. acerosa* are still at its infancy. Since the preliminary work...
Seaweeds as nutritional supplements: Analysis of nutritional profile, physicochemical properties and proximate composition of *G. acerosa* and *S. wightii*

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ABSTRACT

Seaweeds or marine algae are rich in minerals and nutrients that are important for most of the biochemical reactions and non-nutrient components like dietary fibres and polyphenols. The present study aims at elucidating the nutritional composition of the two marine algae *Gelidiella acerosa* (red seaweed) and *Sargassum wightii* (brown seaweed) and the results revealed that the seaweeds possess high fibre content of 13.45 ± 1.076% and 17 ± 1.19% DW and ash content of 0.103 ± 0.049 g/g DW and 0.25 ± 0.02 g/g DW respectively. Nutritional composition analysis showed that the carbohydrate, protein, lipid, proline and chlorophyll contents of the seaweeds were high. Evaluation of mineral content demonstrates that the concentration of potassium was high in *G. acerosa*, whereas *S. wightii* was found to possess high amount of Sodium. Fatty acid profile verified the presence of major fatty acids with high nutritional value including, linolenic acid and α-linolenic acid. Amino acid composition showed that both the seaweeds possess most of the essential amino acids including valine, methionine, lysine and phenyl alanine. Vitamin analysis revealed the presence of high amount of vitamin C (an antioxidant) in the seaweeds. The results suggest that both the seaweeds have greater nutritional value and could be used as excellent nutritional supplements.

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1. Introduction

Seaweeds are one of the living renewable resources of the marine environment with potential food and therapeutic applications [1]. From the past decades, these marine algae have been consumed widely in Asian countries, whereas they have been used as sources of phycocolloids, thickening and gelling agents in food industries [2]. Seaweeds are also rich in polysaccharides, vitamins and minerals and they have become matchless source of chemical compounds that includes wide variety of biologically active secondary metabolites [3]. These bioactive compounds are molecules obtained from synthetic or natural sources, which are assayed biologically for activities in many therapeutic areas. The activity of these bioactive compounds has been linked to good health for many years, and it appears that bioactive food components can alter the genetic expression of a host of cellular events, thereby influencing health outcomes or providing beneficial antioxidant or enzyme inhibitory activities [4].

The marine red alga *Gelidiella acerosa* is a warm tropical alga, a major source of raw material for the production of superior quality of agar [5]. Agar, the hydrophilic colloid extracted from certain seaweeds of the Rhodophyceae class, has been used as a food ingredient for centuries. It is used as a gelling agent most commonly in icings, sugar confectionery, canned meat and fish products, and dairy products [6]. The other seaweed used in the study is *Sargassum wightii*, brown seaweed, which is a major food source, especially in Japan, where it is added to soups and fermented with the other ingredients in soy sauce to create a specific flavour. *S. wightii* is a major source of alginic acid (acid polysaccharides) which finds wide application in food, pharmaceuticals, cosmetics, paper and textile industries [7]. Though the seaweeds *G. acerosa* and *S. wightii* have been reported to possess excellent food value, detailed analysis of their nutritional composition is not available. Therefore, in the present study the physicochemical properties, proximate composition, mineral content, vitamins, fatty acid and amino acid composition of both *G. acerosa* and *S. wightii* were investigated.

2. Materials and methods

2.1. Collection of seaweed samples

Seaweeds (*G. acerosa* and *S. wightii*) were collected from intertidal region in Gulf of Mannar and identified according to Oza and Zaidu [8] and Krishnamurthy and Joshi [9] and further confirmed...
Research Article

Assessment of Anticholinesterase Activity of Gelidiella acerosa: Implications for Its Therapeutic Potential against Alzheimer’s Disease

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The effect of various solvent extracts of Gelidiella acerosa on acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) activities was investigated. AChE and BuChE inhibitory activities were analyzed by spectrophotometric method. Phytochemical screening of the compounds present in the solvent extracts was done qualitatively. Characterization of the compounds present in the benzene extract of G. acerosa was done by GC-MS analysis. The results showed that, at 487.80 μg/mL, benzene extract showed significant (P<0.05) inhibitory activity against both AChE and BuChE with the percentage of inhibition 54.18±5.65% (IC50 = 434.61 ± 26.53 μg/mL) and 78.43±0% (IC50 = 163.01 ± 85.35 μg/mL), respectively. The mode of inhibition exhibited by benzene extract against the AChE and BuChE was found to be competitive and uncompetitive type of inhibition, respectively. Preliminary phytochemical analysis coupled with GC-MS illustrates that the benzene extract possesses high amount of terpenoids, which could be the reason for potential cholinesterase inhibitory activity.

1. Introduction

Alzheimer’s disease (AD) is the most common neurodegenerative disorder and the prevalent cause of dementia in elderly population [1]. It is clinically characterized by numerous symptoms such as memory and language impairment, cognitive dysfunction, and behavioral disturbances (i.e., depression, agitation, and psychosis), which become progressively more severe [2]. As the aged population grows, the number of individuals worldwide with AD is expected to rise to 34 million in the next three decades, a dramatic increase from 7.3 million today [3]. This is an alarming prospect, particularly in the absence of effective preventive and therapeutic interventions. The most remarkable biochemical change in AD patients is a reduction of acetylcholine (ACh) levels in the hippocampus and cortex of the brain [4]. Therefore, inhibition of acetylcholinesterase (AChE), the enzyme responsible for hydrolysis of ACh at the cholinergic synapse, is currently the most established approach for treating AD [5]. The clinical efficacy of those AChE inhibitors is thought to result from prolonging the half-life of ACh through inhibition of AChE [6]. Currently, five pharmaceutical drugs representing cholinesterase inhibitors (ChEIs), namely, galantamine, rivastigmine, donepezil, and tacrine, are applied clinically. However they can only offer little more than short-term palliative effects, and moreover these inhibitors suffer from pronounced peripheral side effects [7]. Therefore, there is still a great demand in finding new drug candidates for AD treatment.

Marine resources are the richest source of fauna and flora with untapped potentials. The southern coast of India bears a luxuriant growth of seaweed, and these have been used in Asia for more than 2000 years as a subsidiary food, fertilizers, and animal feed [8]. Recently, edible seaweeds have been shown to exert many positive physiological effects, including antiviral, antitumor, anticancer, hepatoprotective, and antiviral activity [9, 10]. Seaweeds are considered as marine renewable sources and medicinal food of 21st century. The proposed seaweed G. acerosa is a perennial red algae (Rhodophyceae) widely distributed along the south
Antioxidant compounds in the seaweed *Gelidiella acerosa* protects human Peripheral Blood Mononuclear Cells against TCDD induced toxicity

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**Abstract**

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) is a persistent environmental toxin formed as an unintentional by-product of incomplete combustion. Several therapeutic approaches have evolved to combat its toxicity since it elicits immunotoxicity, neurotoxicity, hepatotoxicity, carcinogenicity and lethality. Search for drugs from natural resources especially from seaweeds has become intense due to their enormous pharmacological potential. Hence, the present study aims at revealing the protective effect of methanolic extract of *G. acerosa* (MEGA) in Peripheral Blood Mononuclear Cells (PBMC) against TCDD induced toxicity, by assessing the antioxidant, anti-apoptotic and cytoprotective activities. The results of antioxidant assays suggests that MEGA reverted TCDD induced toxicity by causing an alteration in the levels of antioxidant enzymes (Catalase [CAT], Superoxide dismutase [SOD], Glutathione peroxidase [GPx], Glutathione-S-transferase [GST]) and Glutathione [GSH]. The results of lipid peroxidation assay and protein carbonyl content reveal that MEGA protects PBMC from TCDD induced macromolecular damage. MEGA was found to exhibit significant \((p<0.05)\) anti-apoptotic activity as verified by evaluation of mitochondrial membrane potential and AO-EtBr dual staining. In addition, PBMC co-treated with MEGA prevented TCDD induced oxidative DNA damage. Levels of phase-I detoxification enzymes determined by EROD assay and semi-quantitative RT-PCR showed that TCDD up-regulates the expression of CYP1A1 and upon co-treatment with MEGA, the expression got slightly decreased suggesting its protective role. Preliminary phytochemical analysis demonstrates that the extract is rich in cardiac glycosides and terpenoids. LC-MS analysis revealed the presence of antioxidants including caffeic acid, phytofl and mannoheptulose in MEGA, which could be attributed for the observed protective effect against TCDD induced toxicity.

**Introduction**

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) a highly toxic ubiquitous environmental contaminant which belongs to the family of polychlorinated dibenzo-p-dioxins (PCDDs) is formed as inadvertent by-product during the manufacture of chlorinated chemicals, pulp and paper industry and incineration and combustion of municipal wastages (Fiedler, 1996). It has been classified by the International Agency for Research on Cancer (IARC, 1997) as a group I carcinogen in humans and animals. This potent toxic substance has generated a great public concern because of its tendency to accumulate in human and animals through intake of food contaminated with TCDD (Fries, 1995; Lensu et al., 2011; WHO, 1998). This colorless and lipophilic compound does not degrade easily and therefore persist in the environment, build-up in the food chain and accumulate in most of the tissues, the highest amount being accumulated in the liver and body fats of animals and human.

Oxidative stress following the production of reactive oxygen species (ROS) has an important role to play in the toxic manifestations of TCDD, which includes lipid peroxidation, DNA damage and other biomarkers of oxidative stress (Ivar do sul et al., 2009). Though liver is the known target organ for the toxic effects of TCDD, the oxidative stress caused by TCDD also affects a variety of other organs like brain, in different species (Bagchi et al., 2002; Hassoun et al., 2000, 2002). The antioxidant enzymes including, superoxide dismutase (SOD), catalase and glutathione peroxidase have been shown to be significantly affected by TCDD (Hassoun et al., 2003). Numerous studies have shown that in vivo exposure to TCDD specifically leads to the suppression of T lymphocyte function including proliferation, differentiation, cytokine production and T cell dependent B cell responses (Kerkvliet et al., 1996; Lundberg et al., 1992; Prell et al., 1995). In recent years various reports suggested that TCDD...
Antioxidant and anti-cholinesterase activity of Sargassum wightii

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Abstract

Context: Sargassum has been used in traditional Chinese medicine since the eighth century AD to treat goiter. Sargassum wightii Greville (Sargassaceae) is a major source of alginic acid used widely in food and drug industries.

Objective: To evaluate the anti-Alzheimer potential of S. wightii through evaluation of antioxidant and cholinesterase inhibitory activities.

Materials and methods: Successive extraction was done using solvents of varying polarity. Solvent extracts (100–500 ng/mL) were employed for all the antioxidant assays. Free radical scavenging activity was evaluated by 2,2-diphenyl-1-picrylhydrazyl, OH", H2O2 radical scavenging assay. The reducing power of the seaweed was evaluated by ferric reducing antioxidant power and reducing power assay. Cholinesterase (ChE) inhibitory activity was evaluated and the Km, Vmax and Ki were calculated. Further, compound characterization was done by GC-MS analysis.

Results: The non-polar extracts were found to possess significant antioxidant activity. At 100 ng/mL, petroleum ether, hexane, benzene and dichloromethane extracts showed significant ChE inhibitory activity with IC50 values of 19.33 ± 0.56, 46.81 ± 1.62, 27.24 ± 0.90, 50.56 ± 0.90 µg/mL, respectively, for AChE, and 17.91 ± 0.65, 32.75 ± 1.00, 12.98 ± 0.31, 36.16 ± 0.64 µg/mL, respectively, for BuChE. GC-MS reveals that 1,2-benzenedicarboxylic acid, disoactyl ester is the major compound present in dichloromethane extract of S. wightii. The mode of inhibition exhibited by dichloromethane extract against the cholinesterases was found to be competitive type.

Discussion and conclusion: The presence of high amount of terpenoids could be the possible reason for its potential antioxidant and ChE inhibitory activity.

Introduction

Neurodegenerative disorders are chronic and progressive, characterized by selective and symmetric loss of neurons in motor, sensory, or cognitive systems. Most of them have common cellular and molecular pathological mechanisms such as oxidative stress, protein aggregation and formation of inclusion bodies (Ross & Poirier, 2004). The central nervous system (CNS), due to high consumption rate of oxygen, abundant lipid content and relative scarcity of antioxidant enzymes, is highly vulnerable to free radical damage when compared to other tissues (Markesbery, 1997). The free radicals generated in the cells, upon accumulation, react with macromolecules like lipids, proteins and nucleic acids and damage cellular functions. Moreover, oxidative damage to the cellular components results in alteration of the membrane properties such as fluidity, ion transport, enzyme activities and protein cross-linking eventually resulting in cell death (Chauhan & Chauhan, 2006). It is believed that oxidative stress plays a significant role in Alzheimer’s disease (AD) pathogenesis and it has been demonstrated that the increased load of reactive oxygen species in the brain is specifically associated with neuritic plaques (Pereira et al., 2005).

AD is a multineurotransmitter deficiency disease, as it involves loss of cholinergic markers like choline acetyltransferase and AChE in the cerebral cortex region. Several studies have demonstrated that the activity of AChE is high around the amyloid plaques and in neurofibrillar tangles bearing neurons. This increase in activity may be caused by the direct effect of Aβ on this enzyme. Furthermore, it has been previously demonstrated that AChE promotes Aβ aggregation. It has also been demonstrated that a remarkable increase in the cortical levels of BuChE is associated with neuritic plaques and neurofibrillary tangles, which are the major neuropathological features of AD (Darvesh et al., 2003). Hence, in the current senario, inhibitors of AChE and BuChE have become a major target for the development of therapeutic strategies for AD. The ChE inhibitors directly block the ACh and BuCh hydrolysis thereby promoting the cholinergic functions, which ultimately results in the improvement of cognitive deficit (Rhee et al., 2004). There are a few synthetic medicines, like tacrine, donepezil and rivastigmine, for treatment of cognitive dysfunction and memory loss associated with AD. These compounds have been reported to have...
Eugenol alters the integrity of cell membrane and acts against the nosocomial pathogen Proteus mirabilis


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Eugenol (an essential oil of clove) acts as an antibacterial agent against *Salmonella typhi* by disrupting the cellular membrane

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**Abstract**

Aim of the study: To evaluate the antibacterial activity of eugenol and its mechanism of bactericidal action against *Salmonella typhi*.

**Materials and methods:** The antibacterial activity was checked by disc-diffusion method, MIC, MBC, time course assay and pH sensitivity assay. The chemo-attractant property of eugenol was verified by chemotaxis assay. The mode of action of eugenol was determined by crystal violet assay, measurement of release of 260 nm absorbing intracellular materials, SDS-PAGE, SEM and AFM analysis confirmed the disruptive action of eugenol on cytoplasmic membrane. The deformation of macromolecules in the membrane resulted in complete inhibition of the organism. Eugenol inactivated *Salmonella typhi* within 60 min exposure. The chemo-attractant property of eugenol combined with the observed high antibacterial activity at alkaline pH favors the fact that the compound can work more efficiently when given in vivo.

**Conclusion:** The results suggest that the antibacterial activity of eugenol against *Salmonella typhi* is due to the interaction of eugenol on bacterial cell membrane.

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**1. Introduction**

*Salmonella typhi* (*Salmonella enterica* subsp. *enterica* ser. *typhi*) is a human restricted pathogen that causes 21 million cases of typhoid fever and 200,000 deaths each year. The disease is endemic in many developing countries particularly the Indian subcontinent, Southeast Asia, Africa and Central America. Infection with *Salmonella typhi* usually results from ingestion of contaminated food and water (Stearns and Koella, 2008). *Salmonella* are Gram-negative motile rods and belongs to the family Enterobacteriaceae. Based on the serology *Salmonella* is classified into more than 2200 serovars. Fundamental for *Salmonella typhi* infectivity is its capacity to cross the mucosa of the distal ileum, as well as to survive and multiply within macrophages (Contreras et al., 1997). It makes the innate immune system ineffective by inhibiting the oxidative burst of leukocytes. Once the bacterium invades the blood stream, it causes severe damage in gut epithelial cells, which leads to gastroenteritis and salmonellosis (typhoid). Many antibiotics and drugs like ampicillin, chloramphenicol and fluoroquinolones like ciprofloxacin are active against *Salmonella*, but the strain has developed multiple resistance to the first-line antibiotics in many developing countries (Finch, 2003). There are reports from India that ciprofloxacin has begun to produce delayed clinical responses in enteric fever with gradual increase in MICs of ciprofloxacin and clinically quinolone-resistant typhoid fever (Nath et al., 2000).

The pathogenic role of *Salmonella* infection in the development of human diseases and the impact of resistance on the clinical outcome stimulated the search for newer treatments and natural products could provide alternative therapies against salmonellosis. Natural compounds possess an excellent therapeutic potential without developing resistance in the causative organisms (Culafic et al., 2005).

Research in the past decade has focused on the antimicrobial activity of various plant oil extracts and their components in the field of medicine and therapeutics (Gill and Holly, 2006). More specifically, essential oils derived from aromatic medicinal plants have been reported to exhibit exceptionally good antimicrobial

**Abbreviations:** AFM, atomic force microscope; ATR, attenuated total reflection; CFU, colony forming unit; CGMA, Chemical Gradient Motility Agar; EDTA, ethylenediaminetetraacetic acid; FT-IR, Fourier transform infrared spectroscopy; MAM, monoamine oxidase; MBC, minimum bactericidal concentration; MHA, Mueller Hinton Agar; MIC, minimum inhibitory concentration; MTCC, microbial type culture collection; PBS, phosphate buffer saline; SDS-PAGE, sodium dodecyl sulphate-polyacrylamide gel electrophoresis; SEM, scanning electron microscope; TNTC, too numerous to count.

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Botanics: a potential source of new therapies for Alzheimer’s disease?

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Abstract: Alzheimer’s disease is an age-related, complex neurodegenerative disorder characterized by loss of memory and impairment of multiple cognitive functions. Several factors contribute to the progression and development of the disease including amyloid beta accumulation, neurofibrillary tangle formation, cholinergic deficit, oxidative stress, neuroinflammation, and apoptosis. Numerous traditional and herbal medicinal plants have been used to treat several cognitive disorders including Alzheimer’s disease. They act as excellent antioxidants, anti-inflammatory mediators, and cholinesterase and β-secretase inhibitors. In addition, these natural compounds also prevent the accumulation of amyloid beta and its fibril formation. Besides acting as core-molecules, these natural compounds act as a template for the production and synthesis of several drug leads with improved pharmacokinetic potentials and greater efficacies. Hence, herbal medicines that have interesting pharmacological effects with noticeable anti-Alzheimer’s potential deserve increased attention for further development to drug entities. The present article reviews the botanical pharmacology with special reference to anti-Alzheimer activity of plants and plant-derived compounds.

Keywords: neurodegeneration, medicinal plants, antioxidants, Aβ peptide, neuroprotective, clinical trials

Introduction

Alzheimer’s disease (AD) is a progressive age-related neurodegenerative disorder characterized by progressive cognitive deficits and behavioral disturbances. Several complex pathogenic pathways have been found to be involved in the disease development and progression, including plaque formation, inflammatory cascade, cholinergic deficit, oxidative stress, etc. Formation of senile plaques and neurofibrillary tangles remain the most important neuropathological hallmarks of AD. Senile plaques are the major constituent of toxic amyloid beta (Aβ) peptide, which is surrounded by dystrophic neurites and activated microglia. Aβ accumulates as a result of altered proteolytic processing of amyloid precursor protein (APP) by β-secretase and γ-secretase. An increased amount of Aβ (soluble monomeric form) self-aggregation into Aβ oligomers is found to be present in the brain of AD patients. These oligomers are highly toxic in nature and cause synaptic dysfunction due to oxidative stress and inflammation. It has been demonstrated that at least two intermediate processes are involved in the process of fibrillogenesis. The small oligomers undergo noncovalent interactions and form protofibrils, which are less structured than mature fibrils. The protofibrils, upon maturation, result in the formation of mature amyloid-like fibrils (Figure 1).
11

Natural Bioactive Compound from Marine Plants with Anticancer Potential: A Review

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ABSTRACT

Cancer is a multifactorial disease, which affects people of all ages. Chemotherapy and radiation therapy remains the most widely adopted approach against a large variety of cancers. These therapeutic methods often cause negative consequences like chemotoxicity and radiation toxicity, which ultimately results in the severe damage of vital organs. Therefore identification of natural compounds with lesser side effects and with greater therapeutic potentials is crucial. In recent years, marine natural products have become a boon to the field of cancer therapy with enormous bioactive potentials. The current research in cancer therapeutics is mainly focused on developing drugs or vaccines to target key molecules for combating tumor cell growth, metastasis and proliferation. Studies on a large spectrum of marine natural products show that these marine sources can act as potent anti-inflammatory, antioxidant and anticancer agents. Moreover, a vast structural diversity of marine natural compounds has been extensively studied and it serves as lead compounds for the improvement of therapeutic potential against cancer. Additionally, semi-synthesis processes of new compounds, obtained by molecular modification of the functional groups of lead compounds, are able to generate structural analogues with greater pharmacological properties. Recent technological advances in structure elucidation, organic synthesis, and biological assay have resulted in the rapid isolation and evaluation of prospective and novel anticancer agents from marine flora. This

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Neuropharmacology of Essential Oils

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ABSTRACT

Neurodegenerative disorders are chronic and progressive, characterized by selective and symmetric loss of neurons in motor, sensory, or cognitive systems. Over the last several decades there has been a great progress in understanding the mechanism of these disorders. Several synthetic drugs are currently being employed for treating a wide range of neurological disorders. However they can only offer little more than short-term palliative effects and they suffer from pronounced peripheral side effects, which necessitate the interest in finding better drugs from natural resources. Natural products provide important clues for identifying and developing synergistic drugs that has been largely neglected. From the ancient period, the essential oils were recognized as powerful natural products with interesting medicinal values. Recently, the neuroprotective effects of essential oils from various aromatic plants have been investigated. Since these essential oils hold promising neuroprotective effects, this review mainly focuses on pharmacological effects of essential oils against various neurodegenerative disorders.

Key words: Neurodegenerative disorder, Essential oil, Natural products, Synergistic drugs, Aromatic plants