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Neuroprotective effect of *Alpinia galanga* (L.) fractions on $A\beta_{(25-35)}$ induced amnesia in mice

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Abstract

Ethnopharmacological relevance

The rhizomes of *Alpinia galanga* (L.) Willd (Zingiberaceae), a ginger substitute for flavouring food was traditionally used as nervine tonic and stimulant.

Aim of the study

This investigation is designed to screen cognitive improvement of *Alpinia galanga* (AG) fractions in Alzheimer's type of amnesia in mice induced by $A\beta_{(25-35)}$.

Materials and methods

Alzheimer's disease induced mice treated with fractions (n-hexane, chloroform and ethyl acetate) of AG in 200 and 400 mg/kg. Neurotoxicity was induced by intracerebroventricular injection of $A\beta_{(25-35)}$ on the 14th day of 21 days drug treatment. Open field and water maze

were carried to determine habituation memory and hippocampal memory. Na^+/K^+-ATPase, acetylcholinesterase (AChE) and antioxidant enzymes (SOD, GPx, catalase and vitamin C) were determined in brain tissue homogenate to estimate the brain biochemical changes and its anti-amnesic potential with intensity of oxidative stress signaling. Further bioactive (chloroform) fraction was eluted through column chromatography to identify the lead molecules.

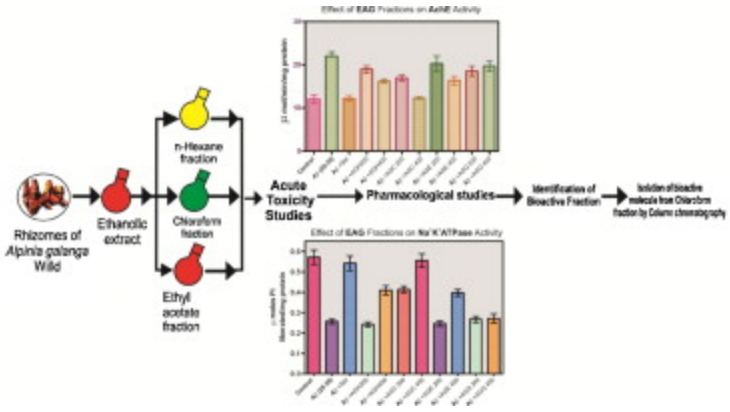
Results

Increased habituation memory and decreased escape latency in behavioral parameter are the indicative of the cognitive enhancement after treatment with *Alpinia galanga* fractions. Increment in Na^+/K^+-ATPase and antioxidant activity depicts brain membrane integrity improvement and free radical scavenging property. AChE level was decreased to improve the cognition by enhancing cholinergic transmission.

Conclusion

Anti-amnesic effect was exerted by various fractions of *Alpinia galanga.* Among all fractions, preeminent neuroprotection was exerted by chloroform fraction, which has compound, 1′δ-1′-acetoxyeugenol acetate and it may be a potential therapeutic agent for Alzheimer's type of amnesia. These results further motivate us to explore the activity of lead compound's anti-amnesic effect on transgenic mice model of AD.

Graphical abstract



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Introduction

Neuropathology of Alzheimer's disease (AD) implicates the deposition of extracellular amyloid plaques in the brain, composed of amyloid beta-protein (Aβ). Aβ is derived from the amyloid precursor protein (APP) by proteolysis, and is concealed into the extracellular fluid. Of the multifactorial implications for AD type of neurodegeneration, Aβ is one of the underlying mechanism for AD (Price and Sisodia, 1994). The risk factor for AD is ageing and the ageing based neurodegeneration are distinguished in two forms: late onset Alzheimer's disease (LOAD) which onsets the pathological symptoms onwards the age of 65 and early-onset Alzheimer's disease (EOAD) before 65 years of age. AD also detected to be as by autosomal dominant trait indicates the involvement of genetic transmission (Hendrie, 1997). All multifactorial pathological conditions of AD are evidenced to link with oxidative stress (Butterfield and Stadtman, 1997, Markesbery, 1997). $A\beta_{(1-42)}$ has been shown to induce oxidative stress in both *in vitro* and *in vivo* studies. Among the existing forms of $A\beta_{(1-42)}$ such as monomers, oligomers, protofibrils, and fibrils, oligomeric nature induces extreme toxicity. The neuronal membrane integrity is maintained by Na^+/K^+-ATPase activity and is vital for a wide variety of neuronal functions; regulates cell volume, restores Na^+ and K^+ gradients after neuronal excitation, and provides energy (via Na^+ gradient) for other transport mechanisms (Na^+/Ca_2^+ exchange and uptake of neurotransmitters) (Lees, 1991). In AD a considerable reduction in activity of Na^+/K^+-ATPase especially in thalamus and nucleus basalis was reported (Liguri et al., 1990). Primary hippocampal and cortical neurons from rat brain exposed to 20–50mM of $A\beta_{(1-40)}$ and $A\beta_{(25-35)}$ for 2–6 days had decreased Na^+/K^+-ATPase activity (Mark and Mattson, 1994, Mark et al., 1995). One of the characteristic changes that occur in AD is the loss of acetylcholinesterase (AChE) activity, the enzyme responsible for acetylcholine hydrolysis, from both cholinergic and non-cholinergic neurons of the brain (Atack et al., 1983). However, AChE activity has been shown to be increased within and around amyloid plaques to promote the assembly of amyloid beta-peptides into fibrils (Inestrosa et al., 1996) and increase the cytotoxicity of these peptides (Alvarez et al., 1998).

Alpinia galanga (L.) Willd (Zingiberaceae) is widely distributed in India. It is a perennial, aromatic, rhizomatous herb. In India it is traditionally used as nervine tonic and stimulant effect. It is also used as revulsive, carminative, stomachic, disinfectant, aphrodisiac and for inflammation (Warrier, 1994). It is a ginger substitute for flavouring food. Various compounds are isolated and screened for biological activities such as terpenyl ester (2-endo-hydroxy-1,8-cineole) for antimicrobial and antibacterial activity (Miyazawa and Hashimoto, 2002), essential oils for antifungal activity (Jantan et al., 2003), hypoglycemic activity (Akhtar et al., 2002) and *in vitro* cholinesterase enzyme inhibition (Khattak et al., 2005). Bioassay guided separation, yielded three new 8–9 linked neolignans, galanganal, galanganols screened for nitric oxide (NO) production inhibitory action (Morikawa et al.,

2005), and Nuclear factor-kappa B activation was suppressed by 1′-acetoxychavicol acetate (Ichikawa et al., 2006). Recent studies indicated the anti-amnesic activity of crude ethanolic extract in $A\beta_{(25-35)}$ induced neurodegeneration in mice. It also reported the improvement in cognitive function through decreasing the level of neurotransmitter metabolic enzyme AChE in relation to biochemical change. Behavioral studies with step down inhibitory avoidance indicated the improvement in short term and long term memory (Hanish et al., 2011).

The present investigation was designed with the above background to identify the potential activities and bioactive molecule from various fractions of ethanolic extract of Alpinia galanga (EAG) on Aβ induced neurotoxicity in mice. Screening was carried out by estimating the behavioral and biochemical parameters. Open field exploration and water maze were carried to determine the behavioral activity. The biochemical changes in brain were determined by estimating the memberane bound Na^+/K^+-ATPase level, neurotransmitter metabolic enzyme AChE and antioxidant enzymes after the treatment with fractions of EAG.

Section snippets

Chemicals and drugs

Acetylthiocholine iodide, β-amyloid, reduced glutathione, oxidized glutathione and dithiobisnitro benzoic acid, were purchased from Sigma Aldrich, USA. All other reagents were analytical grade and from SD Fine Chemicals, Mumbai, India

Plant material and extraction

The rhizomes of *Alpinia galanga* was collected from Kanyakumari district, Tamil Nadu, India during the month of August and authenticated by Plant Biotechnologist Dr. Girija Kumari, Reader and Head, Department of Plant Biology, Sree Ayappa College, Chunkankadai,

Acute toxicity studies

The drug EAG fractions were considered as nontoxic, because it did not showed any toxic signs or symptoms and mortality in the oral dose of 2000mg/kg in mice. According to OECD-423 guidelines, the LD_{50} of 2000mg/kg and above is mentioned as unclassified. So further pharmacological screening is carried out.

Effect of EAG fractions on open field

In open field exploration, the studies considered with head dipping, rearing and line crossing depicted the improvement in cognitive function. The standard drug donepezil treated animals

Discussion

Neuroprotective protective study of various fractions of ethanolic extract obtained from *Alpinia galanga* improved the cognition on Aβ induced neurotoxicity in mice. $A\beta_{(25–35)}$ is potential neurotoxic peptide for primary neuronal cortical cells which produces neurofibrillary tangles (Glenner and Wong, 1984, Masters et al., 1985) and the toxicity induced by $A\beta_{(25–35)}$ in rodents resembles to AD which is suitable for the evaluation of Alzheimer's type of dementia. Previous studies suggested that

Conclusion

In conclusion, the evaluation of *Alpinia galanga* fractions indicated the anti-amnesic effect. The evaluation of behavioral parameters promptly indicated the enhancement of hippocampal memory. Furthermore neurotransmitter metabolic enzyme AChE is decreased with increased activity of Na^+/K^+-ATPase indicated the prospective competence of various fractions on membrane integrity and anti-amylodogenic property. It is revealed that the anti-amnesic effect may be mediated through free radical

Acknowledgements

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References (51)

M.S. Akhtar *et al.*

Hypoglycaemic activity of *Alpinia galanga* rhizome and its extracts in rabbits

Fitoterapia (2002)

J.R. Atack *et al.*

Molecular forms of acetylcholinesterase in senile dementia of Alzheimer's type: selective loss of the intermediate (10S) form

Neuroscience Letters (1983)

G.M. Bores *et al.*

Amyloid β-peptides inhibit $Na1^{+}/K^{+}$-ATPase: tissue slices versus primary cultures

Brain Research Bulletin (1998)

D.A. Butterfield *et al.*

Protein oxidation processes in aging brain

Advances in Cell Aging and Gerontology (1997)

H. Carageorgiou *et al.*

Changes in acetylcholinesterase, $Na^{+}K^{+}$ATPase, and $Mg_2{}^{+}$ATPase activities in the frontal cortex and the hippocampus of hyper and hypothyroid adult rats

Metabolism: Clinical and Experimental (2007)

S.B. Dunnett *et al.*

Septal transplants restore maze learning in rats with fornix–fimbria lesions

Brain Research (1982)

G.L. Ellman *et al.*

A new and rapid colorimetric determination of acetylcholinesterase activity

Biochemical Pharmacology (1961)

M. Erecinska *et al.*

Ions and energy in mammalian brain

Progress in Neurobiology (1994)

G.G. Glenner *et al.*

Alzheimer's disease: initial report of the purification and characterization of a novel cerebrovascular amyloid protein

Biochemical and Biophysical Research Communications (1984)

L. Goth

A simple method for determination of serum catalase activity and revision of reference range

Clinica Chimica Acta (1991)

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Chemical compositions and antibacterial activities of essential oils extracted from Alpinia guilinensis against selected foodborne pathogens

2016, Industrial Crops and Products

Citation Excerpt :

…Some species of Genus Alpinia have been reported to possess microbicidal activities and enjoy extensive use in food and even medicine (Sharma and Hashinaga, 2004; Sun et al., 2013; Klancnik et al., 2014). For instance, Alpinia galangal is a popular spice and flavor in Asia and has also found many applications in beverages (Yang et al., 2009; Singh et al., 2011). In addition, the abundant essential oils from Genus Alpinia have been reported to have various bioactivities such as larvicidal and antioxidant properties (Pino et al., 2014b).…

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Ginger improves cognitive function via NGF-induced ERK/CREB activation in the hippocampus of the mouse

2014, Journal of Nutritional Biochemistry

Citation Excerpt :

…Ginger has multiple physiological functions with therapeutic effects on AD-related pathologies, such as memory loss, plaque formation, neurodegeneration and oxidative stress induced by treatment with amyloid-beta peptide [9,47–50]. Furthermore, ginger possesses anti-inflammatory action, neuroprotective effects, acetylcholinesterase inhibition and antioxidant effects in neurological disorders [8,9,18,41,51]. Based on these characteristics, we believe that ginger can be a safe nutraceutical for the treatment of neurodegenerative disorders.…

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2013, Rejuvenation Research

Na⁺-K⁺-ATPase, a potent neuroprotective modulator against Alzheimer disease ↗

2013, Fundamental and Clinical Pharmacology

Alpinia: The gold mine of future therapeutics ↗

2013, 3 Biotech

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