Experimental Study of the Effects of Boswellia Serrata and Ginger (Zingiber officinale) on Alzheimer's Disease Induced in Rats

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Abstract

Alzheimer's disease is now the most common cause of dementia. Increased oxidative stress, accumulation of oxidatively damaged nucleic acids, proteins, and lipids and inflammation induce deficits in cognitive and psychomotor performance and play an important role in development of Alzheimer's disease (AD). AD was induced in rats by giving $AlCl_3$ (17 mg / kg b.wt). Aqueous infusions of ginger (Zingiber officinale) (108 and 216 mg / kg b.wt), Boswellia serrata (45 and 90 mg / kg b.wt), rivastigmine (0.3 mg / kg b.wt) were given orally to study their protective as well as therapeutic effects on $AlCl_3$ induced AD in rats, which were evaluated by using behaviour stress tests as activity cage, rotarod and T-maze as well as by biochemical tests for detection of ACh and ACh E in brain homogenate and histopathologic examination.

Ginger and Boswellia serrata produced protective and therapeutic effects on AD.

Key words: Alzheimer's disease, oxidative, inflammation, cognitive, $AlCl_3$, Ginger, Boswellia serrata, activity cage, rotarod, T-maze, ACh, Ach E.

Contents

Abbreviations

A

Ach: Acetylcholine
AchE: Acetylcholine esterase
AKPA: Acetyl-11-keto-ß-boswellic acid
ADL: Activities of daily living
ATPase: Adenosine triphosphatase
ALA: Alpha lipoic acid
Al: Aluminum
$Alcl_3$: Aluminum chloride
ANOVA :One-way analysis of variance
AD: Alzheimer's disease
APP:Amyloid precursor protein
AICD: Amyloid precursor protein intracellular domain

B

Aβ: Beta-amyloid peptide
BBA: Beta-boswellic acid
BSA :Bovine serum albumin
BDNF :Brain derived neurotorpic factor
BuChE:Butyrylcholinesterase
BHA :Butylated hydroxyanisole
b.wt :Body weight
BSD:Boswellia 45 mg /kg
BLD :Boswellia 90 mg /kg

C

Ca^{2+}:Calcium
ChAT :Choline acetyl transferase
ChE :Cholinesterase
ChEI :Cholinesterase inhibitors
CuZnSOD :Copper zinc Super Oxide Dismutase
CA3:Cornu Ammonis3 area of hippocampus proper
COX :Cyclooxygenase

D

DPPH :1,1-diphenyl-2-picrylhydrazyl
DMBA :7, 12-dimethylbenz anthracene
DNA :Deoxy ribonucleic acid

E

ELISA :Enzyme linked immunosorbent assay
E.S.R :Erythrocyte sedimentation rate
EAA :Excitatory amino acid
ERK :Extracellular signal-regulated kinases 1 and 2

F

FAO :Food and Agriculture Organization of the United Nations
FDA:Food and Drug Administration

G

GABA :Gamma amino butyric acid
GRAS :Generally Recognised as Safe
GBE :Ginkgo biloba extract
GSH-PX :Glutathione peroxidase
gm :Gram
GIT :Gastro intestinal tract
GSD:Ginger 108 mg /kg
GLD:Ginger 216 mg /kg

H

5-HETE :5-hydroxyeicosatetraenoic acid
H_2O_2:Hydrogen peroxide

I

iNOS :Inducible nitric oxide synthetase
IA :Incensole Acetate
IL :Interleukins
i.c.v:Intra-cerebroventricular

J

JNK :c-Jun N-terminal kinase

K

KBA :11-keto boswellic acid
Kg:Kilogram

L

LTB4:Leukotriene B4
LPS :Lipopolysaccarides
LDL: Low density lipoproteins

M

MDA: Malondialdehyde
Mepaco:Arab company for pharmaceutical and medicinal plants
MTP : Microtubule proteins
ml :Milliliter
mg :Milligram
mM: Millimolar
MMSE: Mini mental state examination
MAPKs: Mitogen-activated protein kinases

N

NF-κB: Nuclear factor kappa B
NGF :Nerve growth factor
NFTs :Neurofibrillary tangles
NO :Nitric oxide
NMDA :N-methyl-D-aspartate
NSAID :Non steroidal antiinnflammatory drugs

P

PD: Parkinson's disease
pmol :Picomole
PMN :Polymorpho nuclear leucocytes
PUFA :Polyunsaturated fatty acids
*p*H :Power of hydrogen
PGE2:Prostaglandin E2

R

RNS :Reactive nitrogen species
ROS :Reactive oxygen species
$RO^{\cdot}$: Alkoxyl radical
$ROO^{\cdot}$:Peroxyl radical
rpm :Rotations per minute

S

Nacl: Sodium chloride
s APP :Soluble amyloid precursor protein
S.E :Standard error
$O_2^{\cdot}$:Superoxide anion
SOD :Super oxide dismutase

T

TPA :12-O-tetradecanoylphorbol-13-Acetate
TBARS: Thiobarbituric acid reactive substance
TRPV3:Transient receptor potential vanilloid3
Tris-HCl: 2-Amino-2-hydroxymethyl-1,3-propanediol hydrochloride
TNF-α :Tumour necrosis factor

V

V717F :Valine at residue 717 substituted by phenylalanine
VLDL :Very low density lipoproteins

W

WBCs: White blood cells
Wks:weeks
WHO :World Health Oraganisation

1.1) Introduction

1.1.1) Alzheimer's disease

Alzheimer's disease (AD), which represents one of the most economically costly diseases to society is a neurodegenerative disorder characterized by progressive degeneration of hippocampal and cortical neurons that leads to impairment of memory and cognitive ability**.** Impairment of short-term memory is usually the first clinical feature, whereas retrieval of distant memories is preserved relatively well into the course of the disease. When the condition progresses, additional cognitive abilities are impaired, as the ability to calculate, and use common objects and tools. The pathological hallmarks of AD are senile plaques, which are spherical accumulations of the protein β-amyloid accompanied by degenerating neuronal processes, and neurofibrillary tangles, composed of paired helical filaments and other proteins. This corresponds to the clinical features of marked impairment of memory and abstract reasoning, with preservation of vision and movement **(Ryoichi & Masuo, 2009).**

The selective deficiency of acetylcholine in AD, has given rise to the "cholinergic hypothesis," which proposes that a deficiency of acetylcholine is critical in the genesis of the symptoms of AD **(Terry & Buccafusco, 2003).** Therefore a major approach to the treatment of AD has involved attempts to augment the cholinergic function of the brain. This involves the use of inhibitors of acetyl cholinesterase as tacrine, donepezil, rivastigmine, and galantamine **(Lon et al, 2008).**
Also other hypotheses state that inflammation plays a key role in the pathogenesis of AD**.** In addition excessive reactive oxygen species (ROS) levels are implicated in the aetiology of AD **(Zhu et al, 2006).**