Cognitive-Enhancing and Anti-Oxidant Activities of Garlic and Ginger Mixture in Wistar Rats

Abstract

Mental acuity and cognition are intelligent Index that could be threatened by oxidative stress in organisms and the widespread use of ginger and garlic in food is acclaimed to be good anti-oxidant in stressful conditions. The study was designed to examine the relationship between oxidative stress/inflammatory variables and cognition as well as studying comparisons of oxidative stress status and cognition between test groups and controls. A measured quantity (5kg each) of fresh garlic and ginger were purchased, washed, peeled and blended very finely and the pastes were squished to extract the juices (mixture). 20 male rats were randomized into five sets and treated as follows: group 1(control), group 2(low dose mixture), group 3(high dose mixture), group 4(donepezil), group 5(low dose mixture and donepezil), group 6(high dose mixture and donepezil). After two weeks of treatment, the animals were made to undergo Elevated Plus Maze task and Morris Water Maze task while at the end of four weeks, they were sacrificed and 5ml of blood was collected from the rats for oxidative stress maker evaluation. It was observed that the mixture of garlic and ginger in the administered groups improved significantly the performance potential and cognition in both tasks, although the drug donepezil exhibited more activities but the performance was more attenuated when combined with the mixture. The pattern of oxidative stress status decreased significantly with the administration of the mixture indicating strongly, a potent anti-oxidant potential in stress-laden scenarios, the obtained results suggest that the blend of garlic and ginger (GARLGING) (100 and 300 mg/kg) exerts compelling anti-amnesic and intellectual enhancing properties through inflection of the antioxidant action in the hippocampus of the rat model.

Keywords: Mental acuity, Garlic, Ginger, Oxidative stress, Cognition, Donepezil

Introduction

“Garlic, Allium sativum L. is an individual from the Alliaceae family, has been generally perceived as a significant flavor and a well known solution for different infirmities and physiological problems. The name garlic might have begun from the Celtic word 'all' significance impactful. Developed basically all through the world, garlic seems to have begun in focal Asia and afterward spread to China, the Near East, and the Mediterranean area prior to moving west to Central and Southern Europe, Northern Africa (Egypt) and Mexico” (1). The restorative characteristics of garlic were portrayed by Pliny the Elder, Aristophanes, and Galen.

Hippocrates, the Father of Medicine, saw that garlic was astounding for restoring cancers and is a viable diuretic. Aristotle credited garlic as a remedy for rabies, and the Prophet

Mohammad suggested it for treating scorpion stings. In Historia Naturalis by Pliny (2), garlic was suggested for gastro-gastrointestinal problems as well as canine and snake chomps. Wanted restorative consequences of garlic are gotten when bulbs are bitten and gulped or blended in with food and eaten.

“Ginger (Zingiber officinale, Roscoe Zingiberaceae) is perhaps the most broadly consumed spices around the world. From its starting point in Southeast Asia and its spread to Europe, it has a long history of purpose as home grown medication to treat an assortment of diseases, including pain, vomiting, indigestion, and cold-instigated conditions” [4, 5]. Albeit ginger isn't commonly known for its adequacy in diabetes anticipation as well as treatment, current pharmacological examinations support its true capacity for treating both the hyperlipidemic and hyperglycemic parts of diabetes. Nonetheless, there is considerably less data on the instrument of activity of ginger fundamental its consequences for perception. While the synthetic creation of Zingiber officinale is all around researched, it is considerably less clear which of the a large number in ginger are liable for its properties in cognitive activities (6, 7)

Consumers of both garlic and Ginger lay claim on the soothing feelings and cerebral calmness and tranquilization that follow overnight usage of the plants. However there is no direct link between these plants and cognition hence the purpose while this research was carried out.

Materials & Methods

Forty-five healthy and matured male and female rats of 12 weeks old which weighs between 80-200g were used in this study. The rAts were gotten from the Experimental Animal Unit of the department of Human Physiology, University of Port Harcourt, Rivers State. They were housed in traditional wire network confines under standard research facility conditions.

The creatures were permitted free access to water and good care through the time of the trial. The animals feed was gotten from Rumuosi neighborhood market Port Harcourt

Fruit Preparation

A measured quantities (5kg each) of Fresh garlic and ginger were purchased, washed, peeled and blended very finely and the pastes were squished to extract the juices. 2 litters of each were derived and mixed and preserved in a refrigerator to prevent fermentation and for use whenever needed. A standard lab practice convention was seen when all investigations were directed. The suggestions for quality guidelines of biomedical research were noted and executed.

Drug

Donepezil drug was manufactured by Eisai Medical Research with Approval for use was purchased from a reputable pharmaceutical company in Ibadan, Oyo State and prepared for use.

Table 1. Experimental Design

groups	Treatment	Dosage/Administration
Group 1	Distilled water	1ml/day/4 weeks
Group 2	Garlic/ginger (low dose)	(100+100)mg/kg/4 weeks
Group 3	Garlic/ginger (high dose)	(300+300)mg/kg/4 weeks
Group 4	donepezil drug	50mg/kg/b.w./4 weeks
Group 5	Garlic/ginger+drug (low dose)	(100+100+50)mg/kg/4 weeks
Group 6	Garlic/ginger+drug (high dose)	(300+300+50)mg/kg/4 weeks

Behavioral Assessment and Stress markers quantification

Morris water maze

The Morris water labyrinth comprised of a round pool with a white underside and dark side surface, a white stage, a camera and a PC. The pool was made of round electrifies steel pool (1.2 m width, 0.5 m level) loaded up with water (20-22°C). A white stage (8 cm measurement) was set in one quadrant and lowered 1 cm beneath the outer surface of the

water. A camera arranged over the pool was utilized to capture the mice's swim trace. A PC was used for analysis of the data. Mice were prepared on water labyrinth with four trials for 5 d.

Toward the start of the experiment, mice was permitted to look through stage with four preliminaries tasks. From the day one to the fourth day, the mouse was given four trials, each trial endured 60s or until the mouse arrived at the stage and stayed a couple of moments. On the off chance that a mouse didn't arrive at the stage in 60 s, it implied that its departure dormancy was 60 s, then the mouse was permitted to rest for 30 s between preliminaries. On the fifth day, the stage was eliminated and mice were entrusted with a test trial for 2 min [8].

Elevated Plus Maze (EPM)

Practical Steps in the Use EPM

Behavioral responses withinside the increased plus maze are without difficulty assessed and quantified with the aid of using an observer. Briefly, rodents are positioned withinside the intersection of the 4 hands of the increased plus maze and their conduct is generally recorded for five min. This changed into primarily based totally upon the early research with the aid of using Montgomery (9) that found out that rats proven the maximum sturdy avoidance responses withinside the first five min after placement withinside the increased open alleys. The behaviors which are generally recorded while rodents are withinside the increased plus maze are the time spent and entries made at the open and closed hands. Behavior on this task (i.e., interest withinside the open hands) displays a warfare among the rodent's desire for blanketed areas (e.g., closed hands) and their innate motivation to discover novel environments.

Blood Sample Collection and Analysis

The Animals were sacrificed after the fourth week of administration.

Blood samples were collected via cardiac puncture for liver enzymes evaluation. And this Analysis took place at the Research Laboratory of the department of Biochemistry, University of Port Harcourt.

Measurement of Oxidative Stress Markers

Superoxide dismutase (SOD)

Superoxide dismutase (SOD) are a group of metalloenzymes that are found in all living things. Superoxide dismutase activity was determined according to the method of McCord and Fridovich (10). Momentarily, 0.01 ml of the mind homogenate was blended in with 0.2 ml of 0.1 M EDTA containing 0.0015 % NaCl 0.1 ml of 1.5 mM NBT and phosphate cushion with pH 7.8 to a complete volume of 2.6 ml. On adding 0.05 ml of riboflavin, the absorbance of the arrangement was estimated against refined water at 560 nm. Every one of the cylinders

were enlightened consistently for 15 minutes and absorbance of the blue tone shaped was estimated once more. Percent of hindrance was determined subsequent to contrasting absorbance of test with the absorbance of control (the cylinder containing no catalyst action). The volume of the example expected to rummage 50 % of the created superoxide anion was considered as 1 unit of chemical action and communicated in U/L protein.

Malondialdehyde (MDA)

The degree of lipid peroxidation was estimated as malondialdehyde (MDA) as indicated by the strategy for Ohkawa et al. (11). Absorbance of the unmistakable supernatant was estimated at 532 nm against the butamol: pyridine blend. The MDA level was determined and is communicated in μmol/L

Catalase (CAT)

CAT is a common and very important antioxidant enzyme which catalyses hydrogen peroxide to water and oxygen. Catalase breaks down two hydrogen peroxide molecules into one molecule of oxygen and two molecules of water in a two-step reaction. Deisseroth (12). Catalase activity was evaluated according to sadauskiene et al (13). The obtained result was expressed in U/ml.

Glutathione peroxidase (GPx):

Glutathione peroxidase activity was determined according to the method of Hafeman et al. (14). The absorbance of the yellow colored complex was measured at 412 nm after incubation for 10 minutes at 37 o C against distilled water.

Statistical Analysis

Data from the study were analyzed with the aid of SPSS version 20 and results were presented as Mean ± SEM. Post Hoc test was done using LSD. Level of significance was set at $P \leq 0.05$.

Results

Table 2. Assessment of stress markers in lipid peroxidation levels on exposure to a mixture of Garlic and ginger administration in the brain homogenates of rats

groups	Treatment	Superoxide dismutase (u/ml±sem)	Malonhydehyde (µg/ml±sem)	PROTEIN (g/L±sem)	Glutathione oxidase (µg/ml±sem)	CATALASE (u/g±sem)
Group 1	Distilled water	364.56±49.89	54.54±1.66	10.30±1.49	28.05±4.52	36.20±6.59
Group 2	Garlic/ginger (low dose)	260.52±16.41	67.78±3.68	10.10±1.03	19.43±2.15	18.80±7.83
Group 3	Garlic/ginger (high dose)	262.64±38.67	49.27±10.27	9.65±0.64	25.43±8.17	42.80±12.32
Group 4	donepezil drug	395.36±37.89	65.62±5.74	12.98±1.34	21.89±2.00	42.00±13.92
Group 5	Garlic/ginger+drug (low dose)	455.93±59.15	49.75±10.68	7.80±1.61	22.30±3.58	52.00±14.63
Group 6	Garlic/ginger+drug (high dose)	743.04±225.05	62.86±5.14	7.15±1.61	44.49±10.79	70.00±13.04

"Values are presented in mean ± sem. n= 5. $P \leq 0.05$ *means values are statistically significant when compared to the control'

Key: Garlic and ginger low dose, (100mg/kg) , Garlic and ginger high dose, (300mg/kg), Donepezil drug (50mg/kg b.w.).

TABLE 3. Pattern of time spent on the open arm of EPM at different trials on exposure to various doses of mixture of garlic and ginger and Donepezil drug of test groups.

GROUPS	ELEVATED PLUS MAZE OPEN ARM (s±sem)			
	TASK 1 (O Minute)	TASK 2 (After 30 Minutes)	TASK 3 (AFTER 60 MINUTES)	% RELATIVE CHANGE IN PERFORMANCE
control	13.60±4.56	10.20±7.57	10.60±4.96	-22.06
Garlic/ginger low dose	10.40±4.22	22.60±8.41	15.40±2.94	48.08
Garlic/ginger high dose	12.00±11.92	38.20±4.02	45.00±19.59	275
donepezil drug	15.00±8.09	39.40±7.20	41.40±16.01	176
Garlic/ginger+drug low	25.00±10.75	39.20±6.18	52.00±16.87	108
Garlic/ginger+drug high	40.00±3.35	48.80±1.63	58.00±8.24	45

Values are presented in mean ± sem. n= 5. P ≤ 0.05 *means values are statistically significant when compared to the control

Key: Garlic and ginger low dose, (100mg/kg) , Garlic and ginger high dose, (300mg/kg), Donepezil drug (50mg/kg b.w.).

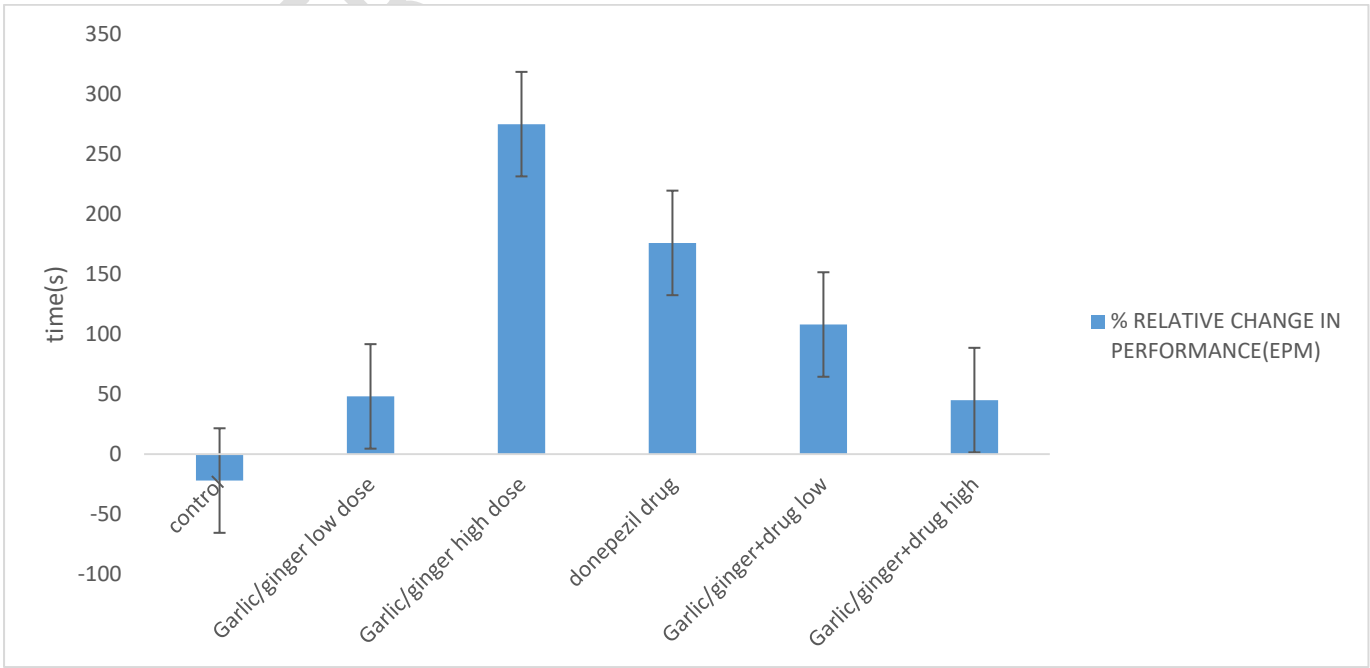

Fig. 1. Relative change in performance during Morris Water Maze (MWM) at 1st trial on exposure to various doses of mixture of garlic and ginger and Donepezil drug of test groups.

TABLE 4. Pattern of time spent during Morris Water Maze (MWM) at different trials on exposure to various doses of mixture of garlic and ginger and Donepezil drug of test groups

GROUPS	MORRIS WATER MAZE TEST (s±sem)			
	TASK 1 (O Minute)	TASK 2 (After 30 Minutes)	TASK 3 (AFTER 60 MINUTES)	% RELATIVE CHANGE IN PERFORMANCE
control	15.60±3.76	21.40±1.72	32.40±2.84	105
Garlic/ginger low dose	10.40±4.98	10.80±2.71	9.40±1.36	-9.62
Garlic/ginger high dose	12.80±12.57	12.60±3.44	5.20±9.50	-59.4
donepezil drug	10.00±4.57	9.80±2.59	8.40±1.91	-16
Garlic/ginger+drug low	12.00±2.00	6.20±2.63	8.40±3.12	-30
Garlic/ginger+drug high	11.00±2.88	6.00±1.64	9.20±3.48	-16.4

Values are presented in mean ± sem. n= 5. $P \leq 0.05$ *means values are statistically significant when compared to the control

Key: Garlic and ginger low dose, (100mg/kg) , Garlic and ginger high dose, (300mg/kg), Donepezil drug (50mg/kg b.w.).

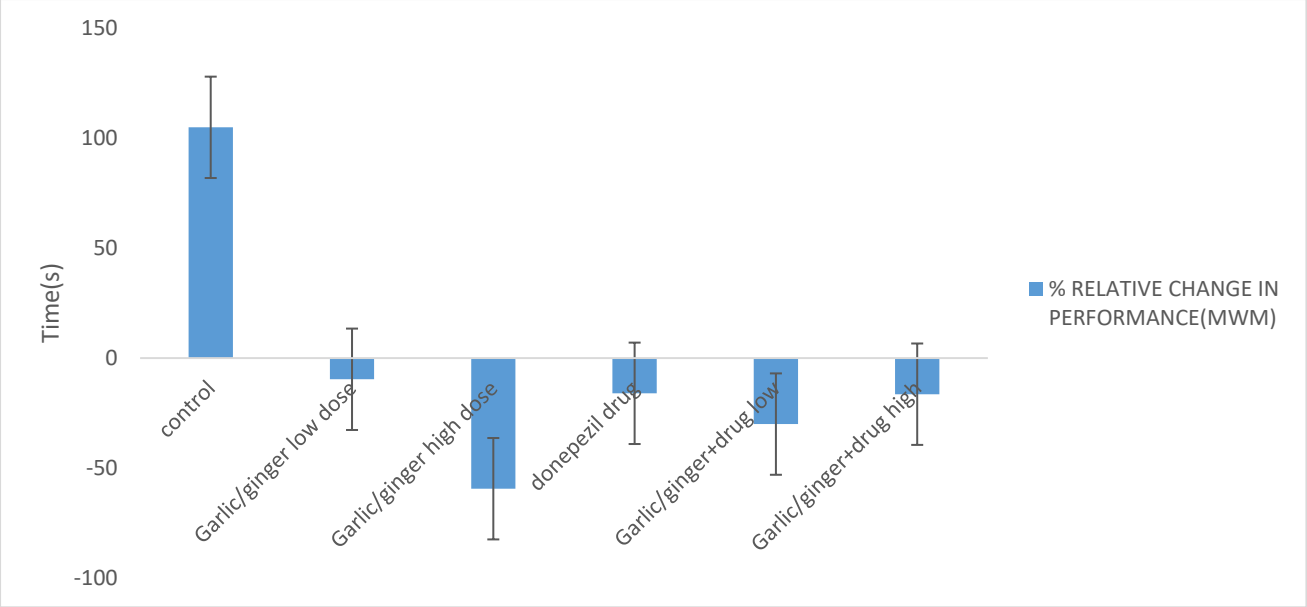

Fig. 2 Relative change in performance during Morris Water Maze (MWM) at 1st trial on exposure to various doses of mixture of garlic and ginger and Donepezil drug of test groups

Discussions

The results of present work revealed that chronic treatment with a mixture of garlic and ginger blend (GARLGING) prevents cognitive deficits in rats. Indeed, the in vitro assays showed a clear antioxidant effect.

Morris Water Maze (MWM) challenge is used to check spatial reference memory and is extensively concept to have relevance for human hippocampal-established reminiscence (15-19). Although now no longer as typically used, reversal learning withinside the MWM is extra tough than the same old task, and consequently may be used to come across diffused memory deficits (15). Further, due to its extra complicated nature, reversal learning can be regarded as a challenge of executive function (20, 21) MWM challenge is used to check

spatial reference reminiscence and is extensively concept to have relevance for human hippocampal-established reminiscence (16, 17).

Although now no longer as usually used, reversal studying withinside the MWM is extra tough than the same old challenge, and consequently may be used to detect diffused memory deficits (17). Further, due to its extra complicated nature, reversal studying can be regarded as a challenge of govt function (20, 21)

“It was evidently shown and demonstrated in the results that animals in the test groups swim more slowly throughout the experiments in all trials of the Morris Water Maze (MWM), when compared to controls especially at higher dose, with no difference from each other, no differences were observed between groups in relation to ambulatory activity in the open field and in the latency to enter in the dark compartment of the inhibitory avoidance apparatus during the training the opposite was the case when the drug Donepezil was introduced”.

Probing further, the beneficial effect of GARLGING on the MWM and inhibitory avoidance paradigms are unlikely to be a result of differences in motor abilities. Indeed, because no significant difference was found in grooming time and in explorative tendency in open field, in addition to in the share of entries and time spent withinside the open palms of the improved plus maze, changes withinside the motivational and/or emotional country of the animal, that could have affected overall performance in each inhibitory avoidance and water maze learning, cannot be overlooked.

Trullas & Skolnick [22] considered elevated plus-maze performance on the source of levels of open arm consideration. Thus, test group 6 (high dose GARLGING PLUS DRUG group) and control group exhibiting low levels of open arm activity were classified as ``high reactive", while those showing high levels of activity in the open arms (e.g., groups 2-5) were labeled ``low reactive." “However, while time spent in the open arms was indeed relatively

high, levels of exploratory behaviors and general locomotors activity in the rats were also substantially higher than those observed in laboratory/Swiss mice or those previously observed" (23).

As such, instead of showing low responsiveness to the plus-maze, the activities of the test groups including the Donepezil drug group, (group 4), would be more accurately described as one of high reactivity.

"From trial 1 through trial 6, there was a consistent and repetitive similar behavior and responses recorded from the test groups (both at low and high doses), and donepezil drug group. This interpretation is supported. Thus, the checked animals made more than a few of ``leap attempts" from the open side, a conduct that turned to be very pronounced and which concerned the animal status on hind-paws on the rims of the open arms and making moves as though to jump, however failing to do so. A very comparable conduct has currently been stated in laboratory rats exposed to an unstable plus-maze apparatus [23, 24] and interpreted as proof of an excessive anxiety (panic-like) state".

In addition, check group animals definitely explored the top ledges of the closed fingers, i.e., animals jumped onto the pinnacle of the closed arm partitions and ambulated alongside the very slim ledges. Although time spent at the top ledges accounted for a exceedingly small share of the check session, it turned into although very putting and seemed to similarly display the get away motivation of those animals.

Also noticeable was freezing in the plus-maze, a response that was noticeably higher in groups treated with the mixture and the drug at both higher and lower doses. Consonant with this observation, Blanchard et al. [25] found that "similar treatment with certain pro-oxidant substances show more movement inhibition than do normal rats in response to potential threat".

One of the important mechanism in the development and progression amnesia is oxidative stress and any substance that will inhibit or ameliorate oxidative stress would be highly beneficial to the organisms. In the present study, GARLING mixture at both high and low doses increased SOD, GPX, and GSH and decreased the MDA and protein carbonyl levels in the rat hippocampal homogenates opposite to what was obtained in the control group that was not treated.

“It is widely recognized that oxidative stress continually ends in oxidative damage of bio-macromolecules, together with lipoprotein in the cellular membranes. Elevated MDA is regarded as a particular indicator of lipid peroxidation in the course of oxidative impairment” [25]. “In addition, oxidative injury can also wreck the anti-oxidant protection system, such SOD, GSH-PX and CAT. In fact, it was formerly discovered that oxidative brain harm caused by oxidative strain contributed to the critical impairment of learning and reminiscence deficits in the course of ageing in rats” [26]

“It was observed that the mixture worked in opposite fashion to what was observed by Parks et al., that scopolamine administration induced a neurochemical alteration in the brain along with changes in oxidative status of the brain” [28]. Thus, scopolamine created an imbalance between antioxidant and oxidant defense systems which may be responsible for observed impairment of memory in rats.

“Furthermore, many studies have reported that the scopolamine-induced amnesic rats show similar patterns of memory impairments and oxidative damage with amnestic mild cognitive impairment (MCI) patients” [29].

The evidence from the study suggested that the GARLGING mixture could possess potent cognitive effects that may be mediated by improving the brain oxidative status [30]. Consequently, the mixture treatment restored the antioxidants status as evidenced by an

increase of SOD, GPX, and GSH while the levels of MDA (lipid peroxidation) and protein carbonyl significantly decrease which supports its antioxidant property.

From previous works, “several natural products with antioxidant proprieties have been reverting the cognitive impairment in aged rats” (31-35). “Reactive oxygen species (ROS) can be highly damaging to cells due to the oxidation of essential cellular constituents such as lipids, proteins and DNA. The brain is particularly susceptible to oxidation by ROS because of its dependency on aerobic metabolism, large contents of polyunsaturated lipid in the mitochondrial and plasma membranes of brain cells and its low antioxidant defenses, such the antioxidant enzyme catalase” (36). The ROS-production mediated protein oxidation can be measured by tyrosine nitration (37), as well as, lipid peroxidation as indicated by malondialdehyde (38).

Conclusions

In summary, the obtained results suggest that the blend of garlic and ginger (GARLGING) (100 and 300 mg/kg) exerts potent anti-amnesic and cognitive enhancing effects through modulation of the antioxidant activity in the hippocampus of the rat model. Therefore, the aqueous extract may possibly be used as a promising natural product for the prevention of memory disorders and Amnesia and ultimately Alzheimer’s disease.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the

advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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