# Enhancement in spatial and recognition memory functions following long term oral administration of ginger extract in rats

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**Abstract**: Ginger (*Zingiber Officinale*) is known over the centuries for its medicinal properties and has been used worldwide as health supplement and for treatment of several diseases. The purpose of this study was to evaluate the effects of whole ginger extract administration on spatial and recognition memory using experimental animal models. The antimicrobial properties of ginger extract against various pathogenic fungal and bacterial species were also examined. Aqueous extract of ginger at a dose of 500 mg/kg was orally administered to test rats and water was orally given to control rats for 6 weeks. Water Maze task (WM) was used to assess spatial memory and recognition memory of rats was evaluated by the Novel Object Recognition (NOR) task. Time spent with novel object was significantly increased in ginger treated rats as compared to control animals in novel object recognition task exhibiting enhanced recognition memory in ginger treated rats. Ginger treated rats exhibited significantly enhanced both short term memory and long term memory as evidenced by decrease in time to reach the hidden platform 1h and 24 h after training as compared to control rats. Short term memory functions of ginger treated rats were more enhanced than long term memory functions. Our findings suggest that ginger consumption may lead to an improvement in spatial and recognition memory. Significant activity of aqueous ginger extract was observed against pathogenic bacteria as well as fungal species. It is therefore suggested in this study that ginger extract can be used in microbial infections and as a memory enhancing drug in various memory disorders.

**Keywords:** Ginger extract, memory functions, antimicrobial activity.

## INTRODUCTION

Role of herbs, spices and their constituents to maintain health and to cure diseases is a hot topic in food related research. With the help of diet various diseases can be treated and good health can be maintained (Tuso *et al.*, 2013). Various herbs and spices have been shown to affect central nervous system, enhance learning, memory and intelligence (Loizzo *et al.*, 2010). Natural products are mostly used in developing countries for medicinal purposes mostly in the treatment of deadly diseases such as cancer, Alzheimer's disease and malaria (Jeong *et al.*, 2012; Meiyanto *et al.*, 2012). Natural products and their traditional uses can play an influential role in potential drug development at low cost by researchers (Tiwari *et al*., 2016).

Ginger, the rhizome of *Zingiber officinalis,* one of the most widely used species of the ginger family, is a common condiment for various foods and beverages. It is cultivated in China, India, Nigeria, Sierra Leone, Jamaica, Haiti and Australia. Extract of ginger has been reported to possess antihyperactivity and anti-inflammation on airway (Mangprayool *et al.*, 2013), relief migraine (Mehdi *et al.*, 2013) and posses antibacterial activity. Previously it has been reported that ginger extract has significant antibacterial activity against *S. pyogenes* (Sebiomo *et al.*, 2011). Ginger extract has been reported to completely inhibit *E. coli* strain which is serious food pathogen involved in diarrhea (Shivani and Sadhana, 2005). It is reported to have antiemetic effect (Palatty *et al.*, 2013) and its consumption has been reported to reverse 3,4-methylenedioxymethamphetamine (MDMA) induced spatial memory impairment (Mehdizadeh *et al.*, 2012). Ginger has been shown to possess free radical scavenging, antioxidant (Krim *et al.*, 2013), inhibition of lipid per oxidation and that these properties might have contributed to its beneficial effects. It has also been reported to possess acetylcholine esterase inhibitor activity (Rungsaeng *et al.*, 2013), due to this activity it might have a role in memory functioning.

One of the most favorable aspects of ginger is that there are no serious or even frequent side effects reported with its use (Boltman-Binkowski, 2016; Dyab *et al*., 2016). Therapeutic role for ginger in vomiting, flatulence and memory problems have been reported before (Ernst and Pittler, 2000). It is now believed that dietary supplements do not have the same health benefits as a diet rich in fruit and vegetables because, taken alone, the individual

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antioxidants may not produced preventive effects. The isolated constituent from food loses its bioactivity and do not behave the same way as the components in whole foods (Liu, 2013; Rodriguez-Casado, 2016). Modern research validates therapeutic effects of ginger, rendering it as a potential medication to maintain health and to treat variety of disorders. Herewith, it is hypothesized that ginger might be applied as a potential natural medicine that could counteract the biochemical abnormalities in various disorders such as depression and cognitive impairment. Therefore the present study was designed to investigate the effect of long term oral ginger extract administration on spatial and recognition memory in rats. Furthermore, antibacterial and antifungal effects of ginger extract were also investigated.

## MATERIALS AND METHODS

### *Experimental procedure*

Twelve locally bred albino wistar rats were randomly divided into two groups. The first group (n=6) served as controls and was given tap water orally. The second group (test group, n=6) was orally administered with ginger extract for 6 weeks. Ginger was purchased from local market. It was washed, cut into small pieces and then it was grinded with water in electric blender. It was then filtered and aqueous ginger extract at a dose of 500 mg/kg was given to test rats. Food intake and body weight were monitored weekly for 6 weeks. After the 6 weeks of treatment phase, short term memory and long term memory was assessed with the help of water maze and recognition memory of rats were checked with the help of novel object recognition apparatus. All experiments were approved by the institutional review board (IRB) of Federal Urdu University, Karachi (Reference No: 0025/FUUAST). All treatment and behavioral monitoring were done in a balanced design to avoid order effect. After monitoring the behavioral activities, rats were then decapitated and its plasma and brain samples were collected for further biochemical and neurochemical analysis.

### *Water maze test*

The effects of long term administration of ginger extract on memory functions were examined by determining the performance of rats in a water maze (WM) apparatus. The WM apparatus used in this study consisted of a rectangular tank (90cm x 60cm) that is made up of transparent glass. Tank was filled with room temperature clean tap water; to the depth of 18cm. Powdered milk was added in the water of the tank so that the platform cannot be seen and this wooden platform (16cm x 16cm) was placed 2cm below the surface of water in a fixed location. First the rats were trained for a cut off time of 3 minutes. Short term memory (STM) and long term memory (LTM) of rats were tested 1 h and 24 h respectively after training. STM and LTM were determined by recording the retention latency (RL) which is the time taken by each rat to locate the hidden platform 1h and 24 h after training. The cut off time for each session was 3 minutes.

### *Novel object recognition task*

Cognitive abilities of rats were assessed by using novel object recognition test. The apparatus consists of square box (45x45x45cm$^3$) made of gray painted wood. Familiar objects used in this test were two identical transparent glasses filled with white cement and novel object was a metallic container of same size filled with white cement. This test was performed in three phases; habituation, training and test session. In habituation phase rats were placed in the empty square box for 10 minutes. Training phase was performed 24 hrs after the habituation phase. Rats were trained with two similar objects for 10 minutes. On third day, the test phase was performed during which animal is exposed to one of the known object and one novel object, for 3 minutes. In the test phase the sniffing time for the novel and familiar object was measured.

### *Screening of antibacterial activity*

The antibacterial activity of ginger extract against eleven gram positive and eighteen gram negative bacteria were examined in the present study. All the bacterial isolates were checked for purity and maintained on nutrient agar at 4$^o$C in the refrigerator until required for use. Antibacterial activity of ginger extract against pathogenic bacteria was determined by using agar-well method. In this method, about 100µl of ginger extract was added by sterile syringe into the finely developed wells by borer and allowed to diffuse at room temperature for 2hrs (Murray *et al*., 1995). Moreover, autoclaved Muller Hinton broth (Oxoid, Basingstoke-UK) was used to refresh the bacterial culture to bring them in actively growing log phase culture (Olurinola, 1996). Later wells were punched into Muller Hinton Agar and 10µl of culture were poured into the wells (Perez *et al.*, 1990). All plates were incubated at 28$\pm$2°C for 24-48 hours and after incubation diameter of zone of inhibition was noted by means Vernier caliper for precision. Gentamicin antibiotic was used as a control agent in testing.

### *Screening of antifungal activity*

The test organisms for this study were members of the 5 saprophytic fungi *Penicillium* sp, *Aspergilus flavus*, *Aspergillus niger*, *Fusarium* sp, *Rhizopus, Helminthosporum* and *Neurospora*, 5 dermatophytic *Microsporum canis*, *Microsporum gypseum, Trichophyton rubrum, Trichophyton mentagrophytes, Trichophyton tonsurans* and 6 yeast including *Candida albicans*, *Candida albicans* ATCC 0383, *Saccharomyces cerevisiae, Candida galbrata, Candida tropicalis, Candida kruzei.* All the fungal isolates were checked for purity and maintained on Sabourd Dextrose agar (SDA) (Oxoid, Basingstoke-UK) at 4$^o$C in the refrigerator until required for use. Antifungal activity of ginger extract

against human, environmental and phyto-pathogenic fungi was determined by using agar-well method. Autoclaved distilled water was used for the preparation of fungal spore suspension and transferred aseptically into each SDA plates (Wuthi-udomlert and Vallisuta, 2011). All plates were incubated at 28±2°C for 24-48 hours and after incubation diameter of zone of inhibition was measured by Vernier caliper. Gresiofulvin antifungal agent was used as a control.

## STATISTICAL ANALYSIS

Results are presented as Means ± S.D. Data were analyzed by student's *t* test; p value<0.05 were considered significant.

## RESULTS

### *Effect of oral administration of ginger extract on recognition memory*

Effect of oral administration of ginger extract at doses of 500 mg/kg on recognition memory in rats was monitored in novel object recognition task (fig. 1). Data analyzed by student's *t*-test revealed a significant treatment effect of ginger administration on recognition memory. Time spent with novel object was significantly increased (p<0.01) in ginger treated rats as compared to the control rats.

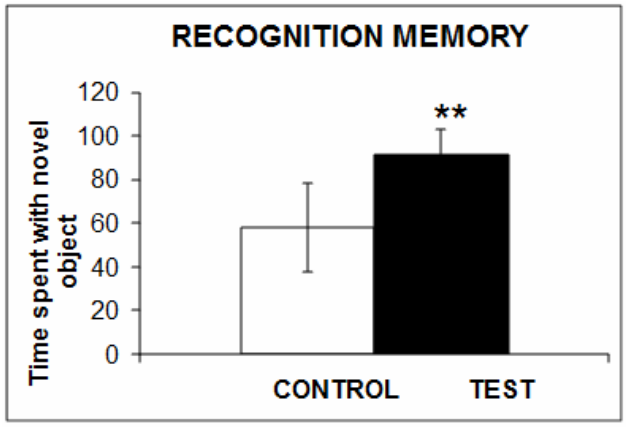


**Fig. 1**: Effect of ginger administration for 6 weeks on recognition memory of rats in novel object recognition task. Values are mean ± SD (n=6). Significant differences by Student's t-test; **p<0.01vs control rats.

### *Effect of oral administration of ginger extract on short term and long term memory*

Effect of oral administration of ginger extract at doses of 500 mg/kg on short term memory and long term memory was monitored in water maze apparatus (fig. 2). Data analyzed by student's *t*-test revealed a significant treatment effect of ginger administration on short term memory (p<0.01) and on long term memory (p<0.05). The results indicate that ginger treated rats exhibited significantly enhanced memory as compared to control rats.

### *Antibacterial and antifungal activities of ginger extract*

As far as antibacterial results are concerned, maximum zone of inhibition was achieved in case of gram positive organism in *Streptococus fecalis* (20±3mm) and against gram negative *Shigella dysteriae* (17±0mm) (table 1). While in case of fungi, found good activity against all the species of Candida with a maximum zone of inhibition against *Candida albicans* ATCC 0383 but no activity against dermatophytes. Similarly moderate level of activity against two *Aspergillus niger* (10±2mm) was also obtained (table 2).

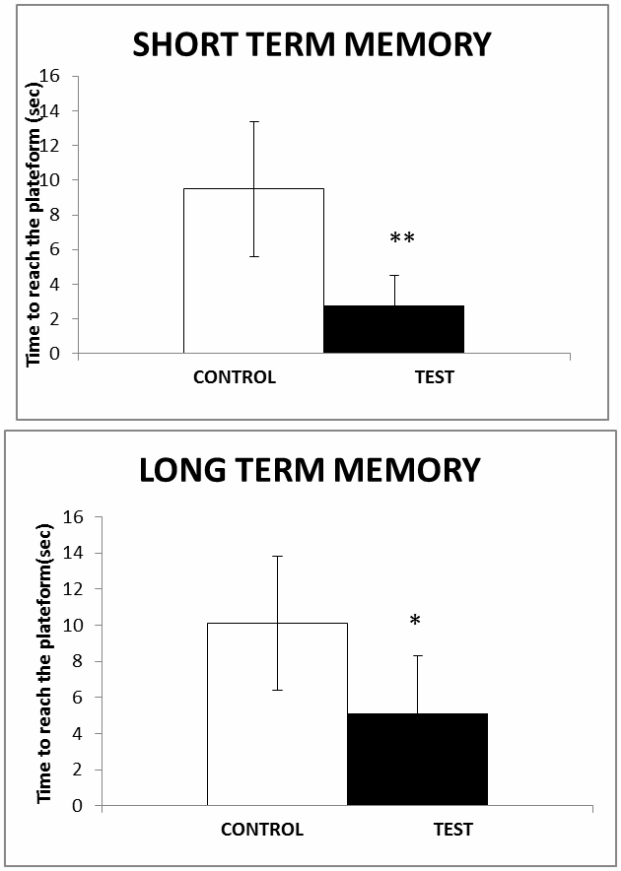


**Fig. 2**: Effect of ginger administration for 6 weeks on short term and long term memory of rats in water maze test. Values are mean ± SD (n=6). Significant differences by Student's t-test; *p<0.05, **p<0.01vs control rats.

## DISCUSSION

The main finding of this experiment is that the memory functions of ginger treated rats were significantly enhanced as compared to control rats. The improved recognition memory retention was seen in novel object recognition task where ginger treated rats spent significantly more time with novel object as compared to control rats. Results of spatial memory functions in water maze also emphasized enhanced memory function in ginger treated rats as they took less time to reach the hidden platform after 1h and 24 h after training session.

**Table 1**: Antibacterial profile of Ginger extract against pathogenic bacteria

| Gram positive bacteria | Zone of inhibition in mm (mean± S.D) | Gram negative bacteria | Zone of inhibition in mm (mean± S.D) |
|---|---|---|---|
| *Bacillus cereus* | 16±2 | *Enterobacter aerogenes* | - |
| *Bacillus subtilis* | 14±2 | *Escherichia coli ATCC 8739* | - |
| *Bacillus thruingiensis* | 12±1 | *Escherichia coli* | - |
| *Corynebacterium diptheriae* | - | *E. coli multi drug resistance* | - |
| *Corynebacterium hofmanii* | - | *Klebsiella pneumoniae* | - |
| *Corynebacterium xerosis* | - | *Salmonella typhi* | - |
| *Staphylococcus epidermidis* | 18±1 | *Salmonella paratyphi A* | - |
| *Streptococcus saprophyticus* | 16±3 | *Salmonella paratyphi B* | - |
| *M. smegmatis* | - | *Shigella dysenteriae* | 17±0 |
| *Streptococcus fecalis* | 20±3 | *Serratia marcesens* | - |
| *Streptococcus pyogenes* | 16±0 | *Acinetobacter baumanii* | 12±2 |
| | | *Campylobacter jejuni* | - |
| | | *Campylobacter coli* | - |
| | | *Helicobacter pylori* | - |
| | | *Hemophilus influenzae* | - |
| | | *Vibrio cholerae* | - |
| | | *Aeromonas hydrophila* | - |
| | | *Pseudomonas aeruginosa* | 15±1 |

**Table 2**: Antifungal profile of Ginger extract against pathogenic fungi

| Yeasts | Zone of inhibition in mm (mean± S.D) | Dermatophytes | Zone of inhibition in mm (mean± S.D) | Saprophytes | Zone of inhibition in mm (mean± S.D) |
|---|---|---|---|---|---|
| *Candida albicans* | 17±2 | *Microsporum canis* | - | *Aspergillus flavus* | 8±1 |
| *Candida albicans ATCC 0383* | 19±1 | *Microsporum gypseum* | - | *Aspergillus niger* | 10±2 |
| *Saccharomyces cerevisiae* | - | *Trichophyton rubrum* | - | *Fusarium species* | - |
| *Candida galbrata* | 18±1 | *Trichophyton mentagrophytes* | - | *Penicillium sp* | - |
| *Candida tropicalis* | 9±2 | *Trichophyton tonsurans* | - | *Rhizopus* | - |
| *Candida kruzei* | 10±1 | | | *Helminthosporum* | - |
| | | | | *Neurospora* | - |

Short term memory functions of ginger treated rats were more enhanced than long term memory functions. The antimicrobial properties of ginger extract were also observed in this study against pathogenic fungal and bacterial species.

The occurrence of age related neurodegenerative disorders in the population consuming ginger is lower than in countries where it is not used regularly in their diet (Kannappan *et al.*, 2012). Use of herbs and spices has been reported to have a role in cultural heritage and its use links to healthy life (Tapsel *et al.*, 2006). Oxidative processes in the body are closely related to several metabolic diseases and age-related degenerative disorders, the use of herbs and spices as a source of antioxidants to oppose oxidation need further attention. It was reported that Z. officinale is a source of antioxidants that rids the body of free radicals (Chohan *et al.*, 2008). Therefore it is suggested in this study that its administration might be able to protect against brain damage and memory impairments in various memory disorders.

Memory function in rats was examined by two methods, NOR task and WM. The present study showed that long term oral ginger extract administration for 6 weeks increased memory retention in rats. The results are in agreement with the previously reported studies. Previously it has been reported that administration of ginger reverses behavioral dysfunction and prevent Alzheimer's disease-like symptoms in rat models (Zeng *et*

*al.*, 2013). It was also reported that ginger can also improve memory impairment following cerebral ischemia (Jittiwat and Wattanathorn, 2012). Previous study showed that cognitive functions of rats receiving ginger extract were enhanced (Wattanathorn, 2010). In the present study, oral administration of ginger extract for 6 weeks significantly enhanced STM, LTM and recognition memory in rats in WM and NOR task.

Memory formation is the complex process and many neurotransmitters and neuronal pathways are involved in this complex process. Acetyl choline is considered as one of the neurotransmitter involved in regulation of cognitive functions (Ray *et al.*, 2012). A decrease in the levels of this neurotransmitter is believed to be involved in the occurrence of amnesia in impaired cognitive diseases. Ginger extract has been reported to possess acetylcholine esterase inhibitor activity (Rungsaeng *et al.*, 2013), antagonize muscarinic autoreceptors and increase cholinergic activity (Ghayur *et al.*, 2008) that may increase acetylcholine levels in the brain of ginger treated rats. In the present work enhancement of spatial and recognition memory following ginger administration for 6 weeks may be associated with an increase in the level of acetylcholine.

It was reported earlier that ginger extract possessed remarkable activity against *E. coli* (Chandarana *et al.*, 2005). Some studies indicated that the inhibition of bacterial growth was dose dependent and organic ginger extracts possessed more characteristic antibacterial properties and could be used for the treatment of bacterial infections *(*Malu *et al.*, 2009). It was also reported ethanolic extract of ginger powder showed inhibitory activities against *Candida albicans* species (Supreetha *et al.*, 2011). In the present study aqueous ginger extract has been reported to possess antimicrobial properties against pathogenic fungal and bacterial species. It is suggested in the present study that extract of ginger can be used for the treatment of microbial infections.

## CONCLUSION

The existing memory enhancing agents ineffective against certain stimuli are expensive and possess side effects. The present results suggest potential health benefits of ginger extract and strengthen the suggestions that ginger administration enhances cognitive brain functions and may be considered as safe herbal medicine in various disorders.

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## REFERENCES

Boltman-Binkowski H (2016). A systematic review: Are herbal and homeopathic remedies used during pregnancy safe? *Curationis*., **39**(1): 1514.

Chandarana H, Baluja B and Chanda S (2005). Comparison of antibacterial activities of selected species of zingiberaceae family and some synthetic compounds. *Turk. J. Biol.*, **29**: 83-97.

Chohan M, Forster-Wilkins G and Opara EI (2008). Determination of the antioxidant capacity of culinary herbs subjected to various cooking and storage processes using the ABTS (*+) radical cation assay. *Plant Foods Hum Nutr.*, **63**(2): 47-52.

Dyab AK, Yones DA, Ibraheim ZZ and Hassan TM (2016). Anti-giardial therapeutic potential of dichloromethane extracts of *Zingiber officinale* and Curcuma longa in vitro and in vivo. *Parasitol Res.*, **115**(7): 2637-45.

Ernst E and Pittler MH (2000). Efficay of ginger for nausea and vomiting: a systematic review of randomized clinical trials. *Br. J. Anaesth.*, **84**(3): 367-71.

Ghayur MN, Gilani AH, Ahmed T, Khalid A, Nawaz SA, Agbedahunsi JM, Choudhary MI and Houghton PJ (2008). Muscarinic, Ca antagonist and specific butyrylcholinesterase inhibitory activity of dried ginger extract might explain its use in dementia. *J. Pharm. Pharmacol.*, **60**(10): 1375-83.

Haniadka R, Saldanha E, Sunita V, Palatty PL, Fayad R and Baliga MS (2013). A review of the gastro protective effects of ginger (Zingiber Officinale Roscoe). *Food Funct*. [ahead to print].

Jeong HR, Jo YN, Jeong JH, Jin DE, Song BG, Choi SJ, Shin DH and Heo HJ (2012). Antiamnesic effects of ethyl acetate fraction from chestnut (Castanea crenata var. dulcis) inner skin on Aβ(25-35)-induced cognitive deficits in mice. *J. Med. Food.*, **15**(12): 1051-6.

Jittiwat J and Wattanathorn J (2012). Ginger pharmacopuncture improves cognitive impairment and oxidative stress following cerebral ischemia. *J. Acupunct. Meridian Stud.*, **5**(6): 295-300.

Kannapan R, Gupta SC, Kim JH, Reuter S and Aggarwal BB (2011). Neuroprotection by spice-derived nutraceuticals: You are what you eat! *Mol. Neurobiol.*, **4**(2): 142-59.

Krim M, Messaadia A, Maidi I, Aouacheri O and Saka S (2013). Protective effect of ginger against toxicity induced by chromate in rats. *Ann. Biol. Clin.*, **71**(2): 165-173.

Liu RH (2013). Dietary bioactive compounds and their health implications. *J. Food Sci.,* **78**(1): 18-25.

Loizzo MR, Tundis R, Conforti F, Menichini F, Bonesi M, Nadjafi F, Frega NG and Menichini F (2010). *Salvia leriifolia* Benth (Lamiaceae) extract demonstrates in vitro antioxidant properties and

cholinesterase inhibitory activity. *Nutr. Res.*, **30**(12): 823-30.

Malu SP, Obochi GO, Tawo EN and Nyong BE (2009). Antibacterial Activity and Medicinal Properties Of Ginger (*Zingiber Officinale*). *Global Journal of Pure and Applied Sciences*, **15**: 3-4.

Mangprayool T, Kupittayanant S and Chudapongse (2013). Participation of citral in the bronchodilatory effect of ginger oil and possible mechanism of action. *Fetoterapia.* [ahead to print]

Mansuang Wuthi-udomlert and Omboon Vallisuta (2011). *In vitro* effectiveness of *Acacia concinna* extract against dermatomycotic pathogens. *Pharmacognosy Journal*, **3**(19): 69-74.

Mehdi M, Farhad G, Alireza ME and Mehran Y (2013). Comparison between the efficacy of ginger and Sumatriptan in the ablative treatment of the common migraine. *Phytother.* [ahead to print].

Mehdizadeh M, Dabaghian F, Nejhadi A, Fallah-Huseini H, Choopani S, Shekarriz N, Molavi N, Basirat A, Mohammadzadeh Kazorgah F, Samzadeh-Kermani A and Soleimani Asl S (2012). Zingiber Officinale alters 3,4-methylenedioxymethamphetamine induced neurotoxicity in rat brain. *Cell J.*, **14**(3): 177-84.

Meiyanto E, Hermawan A and Anindyajati (2012). Natural products for cancer-targeted therapy: Citrus flavonoids as potent chemopreventive agents. *Asian Pac. J. Cancer Prev.*, **13**(2): 427-36.

Morris RGM (1981). Spatial localization does not require the presence of local cues. *Learning and Motivation*, **12**: 239-260.

Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken HR (1995). Manual of Clinical Microbiology, 6th Ed. ASM Press, Washington DC; 15-18.

Olurinola PF (1996). A laboratory manual of pharmaceutical Microbiology, Idu, Abuja, Nigeria. pp.69 -105.

Palatty PL, Haniadka R, Valder B, Arora R and Baliga MS (2013). Ginger in the prevention of nausea and vomiting: A review. *Crit. Rev. Food Sci. Nutr.*, **53**(7): 659-69.

Perez C, Paul M and Bazerque P (1990). An antibiotic assay by the agar well diffusion method. *Acta. Biol. Med. Exp*., **15**: 113-115.

Plech A, Klimkiewicz T, Jakrzewska H (2000). Neurotoxic effect of copper salts in rats. *Pol. J. Environ Stud*, **9**: 301-4.

Ray B, Bailey JA, Simon JR and Lahiri DK (2012). High-affinity choline uptake (HACU) and choline acetyltransferase (ChAT) activity in neuronal cultures for mechanistic and drug discovery studies. *Curr. Protoc. Neurosci.*, Chapter 7: Unit 7.23.

Rodriguez-Casado A (2016). The Health Potential of Fruits and Vegetables Phytochemicals: Notable Examples. *Crit. Rev. Food Sci. Nutr.*, **56**(7):1097-107.

Rungsaeng P, Sangvanich P and Karnchanatat A (2013). Zingipain, a ginger protease with acetylcholinesterase inhibitory activity. *Appl. Biochem. Biotechnol*., **170**(4): 934-950.

Sebiomo A, Awofodu AD, Awosanya AO, Awotona FE and Ajayi AJ (2011). Comparative studies of antibacterial effect of some antibiotics and ginger (*Zingiber officinale*) on two pathogenic bacteria. *Journal of Microbiology and Antimicrobials*, **3**(1): 18-22.

Shivani G and Sadhana RA (2005). Comparison of the Antimicrobial Activity of Garlic, Ginger, Carrot, and Turmeric Pastes against Escherichia coli O157: H7 in Laboratory Buffer and Ground Beef. *Foodborne Pathogens and Disease,* **2**(4): 330-340

Supreetha S, Sharadadevi Mannur, Sequeira Peter Simon, Jithesh Jain, Shreyas Tikare and Amit Mahuli (2011). Antifungal activity of ginger extract on *Candida albicans*: An *In vitro* study. *Journal of Dental Sciences and Research*, **2**(2): 1-5.

Tapsell LC, Hemphill I, Cobiac L, Patch CS, Sullivan DR, Fenech M, Roodenrys S, Keogh JB, Clifton PM, Williams PG, Fazio VA and Inge KE (2006). Health benefits of herb and spices: The past, the present and the future. *Med. J. Aust.*, **185**(4): 4-24.

Tiwari P, Ahmad K and Baig MH (2016). Gymnema sylvestre for diabetes: From traditional herb to future s therapeutic. *Curr. Pharm. Des*., [Epub ahead of print].

Tuso PJ, Ismail MH, Ha BP and Bartolotto C (2013). Nutritional update for physicians: Plant based diets. *Perm J.*, **17**(2): 61-6.

Wattanathorn J, Jittiwat J, Tongun T, Muchimapura S and Ingkaninan K (2011). Zingiber Officinale mitigates brain damage and improves memory impairement in focal cerebral ischemic rat. *Evid. Based Complement Alternat. Med.*, 2011: 429505.

Zeng GF, Zhang ZY, Lu L, Xiao DQ, Zong SH and He JM (2013). Protective effect of ginger root extract on Alzheimer disease induced behavioral dysfunction in rats. *Rejuvenation Res.*, **16**(2): 124-133.