

RESEARCH ARTICLE DOI: 10.53555/1pszpb02

A REVIEW ON EXPLORING THE MEDICINAL VALUE OF ZINGIBER OFFICINALE AND HYOSCYAMUS NIGER TO PREVENT OR OVERCOME SEASICKNESS

Vatsal Rajput^{1*}, Kuntupalli Sandhya Rani², Dr. Pragnesh Patani³

¹*Student, Khyati College of Pharmacy, Palodia, Ahmedabad.
²Assistant Professor, Khyati College of Pharmacy, Palodia, Ahmedabad
³ Principal and Professor, Khyati College of Pharmacy, Palodia, Ahmedabad

*Corresponding Author: Vatsal D Rajput *Student, Khyati College of Pharmacy, Palodia, Ahmedabad. Email: vatsalrajput50@gmail.com

Abstract: Motion sickness (MS) is a common complication of traveling by sea, air, or land. It is characterized by a variety of symptoms, including headaches, eye strain, difficulty focusing, blurred vision, and headaches. Several studies have identified the role of genetic variations in the pathogenesis of motion sickness. In this article the study is completed focused on the Pharmacognostical and pharmacological aspects of the *Zingiber officinale* and *Hyoscyamus niger*, a medicinal plant with a long history of use.

1. Introduction

Motion sickness (MS) is described as any discomfort or illness that occurs due to motion, such as when traveling by sea, air, or land^{.[1][2]}

Motion sickness occurs when there is a conflict between the sensory signals your brain receives about movement. This typically happens when the inner ear (which helps control balance), eyes, and deeper body parts send different messages about movement. ^[29]

For example, when you're reading in a moving vehicle, your inner ear senses movement, but your eyes do not see it, leading to confusion in the brain.^[29]

Motion sickness (MS) in virtual environments is referred to as Visually Induced Motion Sickness (VIMS). VIMS can be categorized into various types, including:

1.1 Category:

(a) Cybersickness ^[3]

Cybersickness in head mounted display is caused by differences in the user's virtual and physical pose. Current theories, including sensory conflicts, eye-movements, and postural instability, have limitations in fully explaining the mechanisms of motion sickness, suggesting a need for further research to uncover the underlying causes.^[3]

(b) Simulator sickness (SS) experienced in motion simulators.^[4]

Simulator sickness occurs when there's a mismatch between what the eyes see and what the inner ear's balance system feels, causing conflicting signals that can lead to disorientation and discomfort .When most of the visual field moves, the brain usually interprets this as a result of self-motion.^[4]

(c) Game sickness triggered by playing video games ^[5]

A Lots of people feel motion sickness while playing video games. They call it simulator sickness because it was first noticed in people using driving or flying simulators.^[5]

1.2 Symptoms:

There are several key symptoms that can occur during or after experiencing motion sickness (MS), and the severity of MS can be gauged by observing these symptoms. These include eye strain, disorientation, headache, sweating, pallor, dry mouth, stomach discomfort, vertigo (dizzy sensation), ataxia (balance issues), nausea, and vomiting^{.[24] [5]}

Nausea symptoms are linked to gastrointestinal distress and may involve stomach awareness, sweating, excessive salivation, and burping. Eye strain, difficulty focusing, blurred vision, and headaches are associated with oculomotor issues. Disorientation is connected to vestibular disturbances, such as dizziness and vertigo^{[70] [6]}

The symptoms of MS, such as

1. Nausea: The most prominent symptom, often accompanied by a feeling of the urge of vomit.^[5]

2. Dizziness: A sensation of spinning or lightheadness. ^[5]

3. Fatigue: Feeling unusually tired or weak. ^[5]

4. Headache: A dull or throbbing pain in the head. ^[6]

5. Salivation: A sudden increase in saliva production.^[6]

6. Oculomotor disturbances: Oculomotor disturbance refers to issues or abnormalities with the movement of the eyes, typically involving the muscles that control eye movements ^[6]

a. Double Vision (Diplopia): Seeing two images of a single object, often due to misalignment of the eyes. ^[6]

b. Difficulty in Eye Tracking: Trouble following moving objects smoothly, often leading to jerky or incomplete eye movements.^[6].

c. Nystagmus: Involuntary, rapid, and repetitive eye movements, which can be horizontal, vertical, or rotational.^[6]

d. Strabismus: Misalignment of the eyes, where one eye may turn inward, outward, upward, or downward.^[6]

e. Ptosis: Drooping of the upper eyelid, which can partially cover the eye and impair vision.^[6]

f. Convergence Insufficiency: Difficulty in focusing both eyes on a near object, leading to eye strain and headaches.^[6]

g. Oscillopsia: The sensation that the visual environment is moving or bouncing, often due to abnormal eye movements.^[6]

[1.3]: Occurrence

A study was conducted to assess motion sickness among ferry passengers. Researchers collected data from 20,029 passengers across 114 voyages on 9 different vessels, including 6 ships, 2 hovercraft, and 1 jetfoil. They gathered information on symptoms of illness, vomiting, use of anti-seasickness tablets, alcohol consumption, travel frequency, age, and gender.^[31]

Results showed that 7% of passengers experienced vomiting, 21% felt "slightly unwell," 4% felt "quite ill," and another 4% felt "absolutely dreadful." Female passengers reported higher rates of vomiting and illness compared to males, and the occurrence of sickness slightly decreased with age. Vomiting was linked to the use of anti-seasickness tablets and alcohol consumption, with some interactions between these factors. The study also includes anecdotal evidence from passengers and examines the impact of environmental variables.^[31]

[1.4]: Pathogenesis

The traditional sensory conflict theory suggests that motion sickness in virtual reality (VR) systems occurs when there's a discrepancy between what the eyes see and what the inner ears (balance system) feel, leading to a clash between visual and vestibular senses.^[3]

Recent research highlights the importance of otoliths in the pathogenesis of motion sickness, suggesting that new theories may offer additional explanations beyond the traditional sensory conflict theory. One notable advancement is the discovery of a link between genetic variations in the alpha2-adrenergic receptor and heightened autonomic responses to stress and motion sickness.^[49]

[2]: Detailed Plant Studies: [2.1] Zingiber officinale: [8]



FIGURE 1: ZINGIBER OFFICINALE

[2.1.1] Taxonomical classification: [8]

Kingdom	Plantae
Division	Magnoliophyta
Class	Liliopsida – Monocotyledons
Order	Zingiberales
Family	Zingiberaceae
Genus	Zingiber
Species	Zingiber officinale roscoe

[2.1.2] Vernacular Names:[8]

- Sanskrit: Adarka (Fresh), Sunthi (Dried)
- Hindi: Adrak (Fresh), Sonth (Dried)
- English: Ginger
- Gujarati : Adhu(Fresh), Sunth, Shuntya (Dried)

[2.1.3] Geographical Distribution:

Ginger is a tropical plant that thrives in hot and humid climates. It is cultivated in various countries, including China, Nepal, the US, India, Bangladesh, Taiwan, Jamaica, Nigeria, and Indonesia. India is the largest producer of *Zingiber officinale*. In Indonesia, Z. officinale is an important export commodity, with a cultivation area of 6,053 hectares and an annual demand of 12,106 tonnes of rhizomes for ginger seed production.^[52]

[2.1.4] Botanical Description:

Ginger (*Zingiber officinale*), a member of the Zingiberaceae family, is a flowering plant whose rhizomes (ginger roots) are widely used both as a spice and in traditional medicine. This herbaceous perennial has narrow-bladed leaves and develops annual pseudostems that are around one meter tall. Plants in the Zingiberaceae family possess rhizomes, either tuberous or non-tuberous, that emit a distinctive aroma and have various medicinal properties. Traditionally, the knobby, thick underground stem (rhizome) of ginger is commonly utilized in herbal medicine.^[50]

Rhizomes are rich in a variety of biologically active compounds^[32]. The primary pungent compound in ginger is gingerol ^[33] along with other gingerol analogues such as shogaols ^[34]. Additional constituents include ginger proteases, capsaicin, and various sesquiterpenes like zingiberol and zingiberenol^{.[27]}.

Ginger root also contains essential oils, phenols, oleoresins, proteolytic enzymes, as well as vitamins and minerals. Among the essential oils, important constituents include zingiberene, zingiberol, camphene, cineole, bisabolene, phellandrene, citral, borneol, citronellol, geraniol, linalool, limonene, and camphene.^[27]

[2.1.5] Phytochemical profile:

Ginger contains over 50 active constituents, each displaying various physiological effects. Among these, 6-gingerol is recognized as a key pharmacologically active compound, particularly effective against colon cancer cells^[51]

Chemical constituent	Bioactive compound
Essential oil	Cineole, phellandrene, citral, borneol, citronellol,
	geraniol, linalool, limonene, zingiberene, zingiberole,
	camphene, and bisabolene
Phenol	gingerol and zingerone
Oleoresin	gingerol and shogaol
Proteolytic enzymes	Zingibain, zingipain,



FIGURE 2 GINGEROL

FIGURE 3 GINGERONE



FIGURE 3 BISABOLENE

Some of the major chemical constituents 8-12 and their structures are:^[50]

• Volatile oils (1 to 2%): bisabolene, gingerol, citral, citronellal, geranial, linalool, limonene, camphene, borneol, cineole, phelandrene, zingiberene.^[50]

- **Bisabolene:** It is a sesquiterpene.^[50].
- Zingiberene (6%): sesquiterpene hydrocarbon. Phenols: gingerol, zingerone.^[50].

• **Gingerol:** A yellow, pungent oil that breaks down into Gingerone (a ketone) and aliphatic aldehyde. Oleo-resin: comprising shogaol and zingiberole^[50]

- **Shogaol:** It is formed by loss of water from Gingerol. ^[50]
- Zingiberole: sesquiterpene alcohol. ^[50]
- Lipids (1 to 2%): free fatty acids, lecithins, phosphatidic acid, triglycerides.^[50]
- Vitamins: A, B3(niacin), B6(riboflavin), C.^[50]
- Minerals: calcium, magnesium, phosphorus, potassium. Proteins (2 to 3%) Starch (50%).^[50]

[2.1.6] Pharmacological profile: Numerous pharmacological studies have been conducted on the plant using different experimental models. Some of these key pharmacological activities are highlighted below:

a) **Anti-Microbial**: Ginger exhibits direct antimicrobial properties and can be used to treat bacterial infections. Gingerol and related compounds have been studied for their antimicrobial effects. Specifically, [6]-gingerol and [12]-gingerol, isolated from ginger rhizome, have demonstrated antibacterial activity against periodontal bacteria. Ginger extract also shows antibiotic effects against three major mastitis-causing bacteria in a concentration-dependent manner.^[43]

b) **Anticoagulant Effects:** Ginger has been found to inhibit platelet aggregation and reduce platelet thromboxane production in vitro ^{[35,36,37].} Compounds like (8)-gingerol, (8)-shogaol, (8)-paradol, and gingerol analogs (1 and 5) have displayed antiplatelet activity.^[48]

c) Anti- Emetic: While the exact mechanism by which ginger reduces nausea and vomiting is unclear, its antiemetic effects are believed to be due to gingerols, shogaols, and galanolactone—a diterpenoid found in ginger. ^[39,40,41] There is evidence that ginger rhizome (root) increases stomach acid production. If so, it may interfere with antacids, sucralfate (Carafate), H2 antagonists, or proton pump inhibitors ^[39,40,41]

d) **Anti-Oxidant:** Ginger is known for its antioxidant properties, with (6)-gingerol identified as a key antioxidant component in the plant. ^{[42].}

e) **Hypolipidemic:** The significant increase in serum and tissue cholesterol, serum triglycerides, lipoproteins, and phospholipids following 10 weeks of cholesterol feeding was notably reduced by ethanolic ginger extract. These results were compared to Gemfibrozil, a standard hypolipidemic drug^{.[47]}

f) **Gastrointestinal Effects**: Ginger rhizome (root) is believed to increase stomach acid production, which could potentially interfere with medications like antacids, sucralfate (Carafate), H2 antagonists, or proton pump inhibitors ^{[44] [45]}

^{g)} **Antimutagenic activity**: Ginger root extract and its main polyphenolic component have shown antimutagenic effects by inhibiting the transcription factor NF- κ B^[46] in several cell types. Additionally, ginger essential oil inhibited mutagenicity induced by direct-acting mutagens in a dose-dependent manner.^[46]



FIGURE 5: HYOSCYAMUS NIGER

[2.2] *Hyoscyamus niger*: [2.2.1] Taxonomical Classification:^[22]

Kingdom	Plantae
Division	Tracheophyta
Subdivision	Spermatophytina
Class	Magnoliopsida
Family	Solanaceae
Genus	Hyoscyamus
Species	Hyoscyamus albus, H. Niger

[2.2.2] Vernacular Names:[22]

- Sanskrit: Parasika Yavni
- Hindi: Khurasani Ajawayan
- English: Henbane
- Gujarati: Ajwain

[2.2.3] Geographical Distribution: This plant is also found in Europe, Sabaria, Egypt, and Iran. The white flower variety is considered the most effective for medicinal use. Extracts from the seeds, leaves, and roots of henbane are reportedly used by some witches for rituals involving running or flying through fire, as well as by thieves to enhance their activities. ^[22]

To prepare samples, the leaves, flowering tops, stems with fruits, and roots were dried at 103°C until they reached a constant weight, after which they were analyzed.^[22].

[2.2.4] Botanical Description: *Hyoscyamus niger* (Black henbane) is a medicinal plant with a long history of use. It can grow up to 36 inches tall and features sticky, hairy leaves. The plant exists in two forms: annual and biennial.^[24,25]

Stem: The stem is thick, simple, and can reach up to 0.5 meters in height. It is dark in color, erect, leafy, and densely covered with long glandular hairs. Mature stems are branched and can grow 1 to 3 feet tall. The leaves are hairy, dark-colored, and have an irregular border. The fruits resemble pomegranates, filled with seeds similar to poppy seeds.^[24]

Leaves: The upper leaves (cotyledons) are lance-shaped to oblong with a few hairs on the lower (basal) margins. The leaf margins are slightly wavy, with prominent veins that are depressed on the upper surface. The plant also emits a distinct odor.^[25]

Flower: The flowers of Black henbane typically bloom from June to September. The annual form flowers in July or August, while the biennial form flowers in May and June.^[26] The flowers are brownish-yellow with a purple center and veins, arranged in long racemes that grow from the axils of the upper leaves. ^[26]

A Review On Exploring The Medicinal Value Of Zingiber Officinale And Hyoscyamus Niger To Prevent Or Overcome Seasickness



Figure 6 : *Hyoscyamus niger* (Black henbane)

[2.2.5] Phytochemical profile: H. niger seeds have been reported to contain a variety of compounds, including: Alkaloids: Hyoscyamine, hyoscine, scopolamine, atropine, and others.^[53,54,55] Volatile oils, Glycosides, Mucilage, Albumin ,Steroidal glycosides: Atroposide A, atroposide C, atroposide E, and petuniaside L Phenolics: Vanillic acid, vanillin, pinoresinol, and N-trans-feruloyl tyramine Phytosterols: Daucosterol and β -sitosterol.^[56,32]

Chemical constituent	Bioactive compound
Alkaloid	This includes Hyoscyamine, Hyoscine,
	Scopolamine, Atropine
Phytosterol	This includes Daucosterol and Betasitosterol
Steroidal Glycoside	Atroposide A, Atroposide C, Atroposide E,
	and Petunia side L
Phenolics	Vanillic acid, Vanillin, Pinoresinol, and N
	trans-feruloyl tyramine



Figure 7: Hyoscyamine, Scopolamine

[2.2.6] Pharmacological profile: Numerous pharmacological studies have been conducted on the plant using various experimental models, revealing its diverse pharmacological activities:

a. Antibacterial activity: The alkaloidal extract demonstrated antibacterial effects against Pseudomonas stutzeri, Staphylococcus aureus, Escherichia coli, and Klebsiella pneumonia. ^[10]

b. **Anticancer activity:**The alkaloidal extract exhibited anticancer properties by reducing the spontaneous frequency of chromosomal aberrations, enhancing the mitotic index, and performing micronuclei assays in mice bone marrow cells. Additionally, grossamide and cannabisins D and G, compounds isolated from H. niger seeds, showed moderate cytotoxic effects on cultured LNCaP human prostate cancer cells.^[11]

c. Antispasmodic activity: The crude extract exhibited antidiarrheal and antisecretory properties against castor oil-induced diarrhea and fluid accumulation in the intestines of mice. ^[12]

d. **Antidiarrheal activity**: The crude extract exhibited antidiarrheal and antisecretory properties against castor oil-induced diarrhea and fluid accumulation in the intestines of mice. ^[12]

e. **Antihypertensive**: The crude extract of *H. niger* lowered blood pressure in rats and guinea pigs through a dose-dependent calcium-antagonist mechanism and also demonstrated a cardiodepressant effect on the rate and strength of spontaneous atrial contractions.^[13]

f. Anti-inflammatory activity: The methanolic extract of *H. niger* seeds exhibited antiinflammatory effects in carrageenin-induced paw edema and cotton pellet granuloma methods.^[14]

g. **Cardioprotective activity**: Oral administration of crude *H. niger* powder protected rats from cardiac damage caused by lipid peroxidation and activated antioxidant enzymes. It also prevented cardiac necrosis, as evidenced by inhibitory effects on CK-Mb and TGL. ^[15]

[3] Conclusion:

Motion sickness is caused by a conflict between sensory signals received by the brain about movement. This can occur in various types, such as Cybersickness, Simulator sickness, and Game sickness. Symptoms of motion sickness include nausea, dizziness, fatigue, headache, salivation, and oculomotor disturbances. Motion sickness can be assessed by observing these symptoms. Studies have shown that different factors such as gender, age, and use of anti-seasickness tablets can affect the occurrence of motion sickness. Additionally, research has identified the role of genetic variations in the pathogenesis of motion sickness.

On the other hand, detailed studies on plants like *Zingiber officinale* and *Hyoscyamus niger* have revealed their taxonomical classification, vernacular names, geographical distribution, botanical descriptions, chemical constituents, and pharmacological profiles. Ginger is known for its anti-microbial, anti-inflammatory, anti-emetic, and antioxidant properties, while Henbane has been found to have antibacterial, anticancer, antispasmodic, antidiarrheal, antihypertensive, anti-inflammatory, and cardioprotective activities. These plants offer a range of health benefits due to their bioactive compounds.

In conclusion, the future of Henbane (*Hyoscyamus niger*) looks promising with various dosage forms and delivery methods in development. These innovations have the potential to:

Enhance therapeutic effects, Improve patient outcomes, Expand treatment options, Create new market opportunities

However, it's crucial to address: Safety concerns, Efficacy, Regulatory considerations Responsible development and use of Henbane products will ensure that their potential benefits are realized while minimizing risks.

Reference:

- 1. Irwin JA. THE PATHOLOGY OF SEA-SICKNESS. The Lancet. 1881 Nov 26;118(3039):907-9.
- 2. Lawther A, Griffin MJ. A survey of the occurrence of motion sickness amongst passengers at sea. Aviation, space, and environmental medicine. 1988 May 1;59(5):399-406.
- 3. McCauley ME, Sharkey TJ. Cybersickness: Perception of self-motion in virtual environments. Presence: Teleoperators & Virtual Environments. 1992 Aug 1;1(3):311-8.
- Brooks JO, Goodenough RR, Crisler MC, Klein ND, Alley RL, Koon BL, Logan Jr WC, Ogle JH, Tyrrell RA, Wills RF. Simulator sickness during driving simulation studies. Accident analysis & prevention. 2010 May 1;42(3):788-96.
- 5. Davis S, Nesbitt K, Nalivaiko E. A systematic review of cybersickness. In Proceedings of the 2014 conference on interactive entertainment 2014 Dec 2 (pp. 1-9).
- 6. LaViola Jr JJ. A discussion of cybersickness in virtual environments. ACM Sigchi Bulletin. 2000 Jan 1;32(1):47-56.
- 7. Kennedy RS, Lane NE, Berbaum KS, Lilienthal MG. Simulator sickness questionnaire: An enhanced method for quantifying simulator sickness. The international journal of aviation psychology. 1993 Jul 1;3(3):203-20.
- 8. Rhode J, Fogoros S, Zick S, Wahl H, Griffith KA, Huang J, Liu JR. Ginger inhibits cell growth and modulates angiogenic factors in ovarian cancer cells. BMC complementary and Alternative Medicine. 2007 Dec;7:1-9.

- 9. Poeloengan M. The effect of red ginger (*Zingiber officinale Roscoe*) extract on the growth of mastitis causing bacterial isolates. African Journal of Microbiology Research. 2011 Feb 18;5(4):382-9.
- Kadi K, Yahia A, Hamli S, Auidane L, Khabthane H, Ali WK. In vitro antibacterial activity and phytochemical analysis of White henbane treated by phytohormones. Pakistan Journal of Biological Sciences: PJBS. 2013 Oct 1;16(19):984-90.
- 11. Ma CY, Liu WK, Che CT. Lignanamides and nonalkaloidal components of *Hyoscyamus n iger* seeds. Journal of natural products. 2002 Feb 22;65(2):206-9.
- 12. Gilani AH, Khan AU, Raoof M, Ghayur MN, Siddiqui BS, Vohra W, Begum S. Gastrointestinal, selective airways and urinary bladder relaxant effects of *Hyoscyamus niger* are mediated through dual blockade of muscarinic receptors and Ca2+ channels. Fundamental & Clinical Pharmacology. 2008 Feb;22(1):87-99.
- 13. Khan AU, Gilani AH. Cardiovascular inhibitory effects of *Hyoscyamus niger*. Methods and findings in experimental and clinical pharmacology. 2008 May 1;30(4):295-300.
- 14. Begum S, Saxena B, Goyal M, Ranjan R, Joshi VB, Rao CV, Krishnamurthy S, Sahai M. Study of anti-inflammatory, analgesic and antipyretic activities of seeds of *Hyoscyamus niger* and isolation of a new coumarinolignan. Fitoterapia. 2010 Apr 1;81(3):178-84.
- 15. Vallabi DE, Elango V. Preliminary studies on cardio protective effect of *Hyoscyamus niger Linn* in male albino rats. J Chem Pharm Res. 2016 Aug 10;8(7):860-4.
- 16. Paulsen BS. Highlights through the history of plant medicine. Bioactive compounds in plantsbenefits and risks for man and animals. 2010;50.
- 17 Dey KL, Bahadur R, Mair W. Indigenous Drugs of India. New Delhi: Pama Primalane, The Chronia Botanica; 1973. p. 160.
- 18. Li R, Reed DW, Liu E, Nowak J, Pelcher LE, Page JE, Covello PS. Functional genomic analysis of alkaloid biosynthesis in *Hyoscyamus niger* reveals a cytochrome P450 involved in littorine rearrangement. Chemistry & Biology. 2006 May 1;13(5):513-20.
- 19. Bernhoft AJ. A brief review on bioactive compounds in plants. Bioactive compounds in plantsbenefits and risks for man and animals. 2010;50:11-7.
- 20. Sajeli B, Sahai M, Suessmuth R, Asai T, Hara N, Fujimoto Y. Hyosgerin, a new optically active coumarinolignan, from the seeds of *Hyoscyamus niger*. Chemical and pharmaceutical bulletin. 2006;54(4):538-41.
- 21. Ma CY, Liu WK, Che CT. The flowering hormones. Ber Dtsch Bot Ges 2002;57:29-48.
- 22. Azhar M. Phytopharmacology of an important unani drug Bazr-Ul-Banj (*Hyoscyamus Niger Linn.*)-Review. Asian Journal of Pharmaceutical and Clinical Research. 2020 Sep;13(9):28-32.
- 23. Vella K. Investigation of the alkaloidal content of local hyoscyamus albus l.
- 24. Daneshvar S, Mirhossaini ME, Balali-Mood M. Hyoscyamus poisoning in Mashhad. Toxicon. 1992;30:501.
- 25 Graham and Johnson, 2010
- 26 Grieve M. A Modern Herbal. 1913.http://botanical.com/botanical/mgmh/h/henban23.html.
- 27 Saeed S, Tariq P. PHARMACOLOGICAL ACTIVITIES OF GINGER (*ZINGIBER OFFICINALE*): A REVIW.
- 28 Shupak A, Gordon CR. Motion sickness: advances in pathogenesis, prediction, prevention, and treatment. Aviation, space, and environmental medicine. 2006 Dec 1;77(12):1213-23.
- 29) Koohestani A, Nahavandi D, Asadi H, Kebria PM, Khosravi A, Alizadehsani R, Nahavandi S. A knowledge discovery in motion sickness: a comprehensive literature review. IEEE access. 2019 Jun 14 ;7:85755-70
- 30)Walker AD, Muth ER, Switzer FS, Hoover A. Head movements and simulator sickness generated by a virtual environment. Aviation, space, and environmental medicine. 2010 Oct 1;81(10):929-34.

- 31)Lawther A, Griffin MJ. A survey of the occurrence of motion sickness amongst passengers at sea. Aviation, space, and environmental medicine. 1988 May 1;59(5):399-406.
- 32) Ma CY, Liu WK, Che CT. The flowering hormones. Ber Dtsch Bot Ges 2002;57:29-48.
- 33)Mishra BB, Gautam S, Sharma A. Shelf-Life Extension of Fresh Ginger (*Zingiber officinale*) by Gamma Irradiation. Journal of food science. 2004 Dec;69(9):M274-9.
- 34)Shadmani A, Azhar I, Mazhar FA, Hassan MM, Ahmed SW, Ahmad I, Usmanghani K, Shamim S. Kinetic studies on *Zingiber officinale*. Pakistan journal of pharmaceutical sciences. 2004 Jan 1;17(1):47-54.
- 35)Wang CC, Chen LG, Lee LT, Yang LL. Effects of 6-gingerol, an antioxidant from ginger, on inducing apoptosis in human leukemic HL-60 cells. In vivo (Athens, Greece). 2003 Nov 1;17(6):641-5.
- 36)Mahady GB, Pendland SL, Yun GS, Lu ZZ, Stoia A. Ginger (*Zingiber officinale Roscoe*) and the gingerols inhibit the growth of Cag A+ strains of Helicobacter pylori. Anticancer research. 2003 Sep ;23:3699.
- 37)Nurtjahja-Tjendraputra E, Ammit AJ, Roufogalis BD, Tran VH, Duke CC. Effective anti-platelet and COX-1 enzyme inhibitors from pungent constituents of ginger. Thrombosis research. 2003 Jan 1;111(4-5):259-65.
- 38)GUH JH, KO FN, JONG TT, TENG CM. Antiplatelet effect of gingerol isolated from *Zingiber* officinale. Journal of Pharmacy and Pharmacology. 1995 Apr;47(4):329-32.
- 39)Bhattarai S, Duke CC. The stability of gingerol and shogaol in aqueous solutions. Journal of pharmaceutical sciences. 2001 Oct 1;90(10):1658-64.
- 40)Yamahara J, Rong HQ, Iwamoto M, Kobayashi G, Matsuda H, Fujimura H. Active components of ginger exhibiting anti-serotonergic action. Phytotherapy Research. 1989;3(2):70-1
- 41)HUANG Q, IWAMOTO M, AOKI S, TANAKA N, TAJIMA K, YAMAHARA J, TAKAISHI Y, YOSHIDA M, TOMIMATSU T, TAMAI Y. Anti-5-hydroxytryptamine3 effect of galanolactone, diterpenoid isolated from ginger. Chemical and pharmaceutical bulletin. 1991 Feb 25;39(2):397-9.
- 42)Fuhrman B, Rosenblat M, Hayek T, Coleman R, Aviram M. Ginger extract consumption reduces plasma cholesterol, inhibits LDL oxidation and attenuates development of atherosclerosis in atherosclerotic, apolipoprotein E-deficient mice. The Journal of nutrition. 2000 May 1;130(5):1124-31.
- 43)Park M, Bae J, Lee DS. Antibacterial activity of [10]-gingerol and [12]-gingerol isolated from ginger rhizome against periodontal bacteria. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives. 2008 Nov;22(11):1446-9.
- 44)Al-Yahya MA, Rafatullah S, Mossa JS, Ageel AM, Parmar NS, Tariq M. Gastroprotective activity of ginger *zingiber officinale rosc.*, in albino rats. Am J Chin Med. 1989 Jan 1;17(1-2):51-6.
- 45)Thomson M, Al-Qattan KK, Al-Sawan SM, Alnaqeeb MA, Khan I, Ali M. The use of ginger (*Zingiber officinale Rosc.*) as a potential anti-inflammatory and antithrombotic agent. Prostaglandins, leukotrienes and essential fatty acids. 2002 Dec 1;67(6):475-8.
- 46)Mahady GB, Pendland SL, Yun GS, Lu ZZ, Stoia A. Ginger (Zingiber officinale Roscoe) and the gingerols inhibit the growth of Cag A+ strains of Helicobacter pylori. Anticancer research. 2003 Sep;23:3699
- 47)Bhandari U, Sharma JN, Zafar R. The protective action of ethanolic ginger (*Zingiber officinale*) extract in cholesterol fed rabbits. Journal of Ethnopharmacology. 1998 Jun 1;61(2):167-71.
- 48)Nurtjahja-Tjendraputra E, Ammit AJ, Roufogalis BD, Tran VH, Duke CC. Effective anti-platelet and COX-1 enzyme inhibitors from pungent constituents of ginger. Thrombosis research. 2003 Jan 1;111(4-5):259-65.
- 49) B. J Yates,^{1*} A.D. Miller2 and J. B. Lucot3, "Department of otolaryngology and Neuroscience", "Physiological basis and pharmacology of motion sickness" 28 April 1998.

- 50) Sharma Y. Ginger (*Zingiber officinale*)-an elixir of life a review. The Pharma Innovation. 2017 Nov 1;6(11, Part A):22.
- 51) Brown AC, Shah C, Liu J, Pham JT, Zhang JG, Jadus MR. Ginger's (Zingiber officinale Roscoe) inhibition of rat colonic adenocarcinoma cells proliferation and angiogenesis in vitro. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives. 2009 May;23(5):640-5.
- 52) Syafitri DM, Levita J, Mutakin M, Diantini A. A review: Is ginger (Zingiber officinale var. Roscoe) potential for future phytomedicine. Indonesian Journal of Applied Sciences. 2018 Apr 30;8(1):8-13.
- 53)Paulsen BS. Highlights through the history of plant medicine. Bioactive compounds in plantsbenefits and risks for man and animals. 2010;50.
- 54)Li R, Reed DW, Liu E, Nowak J, Pelcher LE, Page JE, Covello PS. Functional genomic analysis of alkaloid biosynthesis in Hyoscyamus niger reveals a cytochrome P450 involved in littorine rearrangement. Chemistry & Biology. 2006 May 1;13(5):513-20.
- 55)Bernhoft AJ. A brief review on bioactive compounds in plants. Bioactive compounds in plantsbenefits and risks for man and animals. 2010;50:11-7.
- 56)Begum Sajeli BS, Mahendra Sahai MS, Suessmuth R, Asai T, Hara N, Fujimoto Y. Hyosgerin, a new optically active coumarinolignan, from the seeds of Hyoscyamus niger.