



The Potential Effect of Aqueous Extract of Cloves on Some Physiological and Immunological Parameters in Induced Diabetic Rats

Majeed Hameed Nawar ^{1*} , Salah M.M. Al Chalabi ² , Rasha F. Abdul-Lattif ³ 

^{1*} Department of Plant Protection, Agriculture Engineering Sciences College, University of Baghdad, Baghdad, Iraq. E-mail: majeed.hameed@coagri.uobaghdad.edu.iq

² Biotechnology Research Center, Al-Nahrain University, Iraq. E-mail: salahchalabi63@gmail.com

³ University of Baghdad, College of Education IBN Al-Haitham, Baghdad, Iraq.
E-mail: rasha.f.al.@ihcoedu.uobaghdad.edu.iq

Abstract

The purpose of this study was to investigate the effect of clove aqueous extract on various physiological and immunological markers using a diabetic rat model. Thirty rats participated in the study and were split into three groups: a normal negative-controlled group, a positive control group with diabetes, and a diabetes-induced group that was given a dosage of clove water extract. There is a list of some physiological and immunological parameters which have been measured: blood sugar level, interleukins 1 and 6, TNF, LDH, CRP, SOD, CAT, MDA, total and differential count of white blood cells. According to the research, the animals within the diabetes treatment group that received aqueous extracts from the clove plant had noticeably lower blood sugar levels than the animals in the untreated diabetes treatment group. The results also showed that the group that got induced diabetes but no therapy had significantly higher levels of TNF, lactate dehydrogenase (LDH), or Lac CRP, Superoxide dismutase (SOD), Malondialdehyde (MDA), CAT, and the total number of white blood cells than both the control group as well as the group that receiving diabetic medication. Regarding the aqueous extract of cloves.

Keywords:

Cloves, diabetic, LDH, CRP, SOD, CAT, MDA

Article history:

Received: 19/03/2025, Revised: 02/06/2025, Accepted: 04/07/2025, Available online: 30/08/2025

Introduction

For centuries, natural spices and herbal ingredients have been utilized as food additives (preservatives and flavorings). Medical settings have also been given a chance their apply. Having minimal side effects and minimal interaction with prescriptions, the plants are successfully used as a natural medication for an array of diseases. Hence, natural drugs make anticonvulsant therapy more reasonable and patient-friendly. *Syzygium aromaticum* L. is a plant of the family Myrtaceae. In Hindi, this plant is called laung. This evergreen tree is indigenous to the Indonesian and Malacca islands, which are spread over the ancient world's tropical regions. In Tanzania, it is practiced, Indonesia, Penang, Madagascar, Mauritius and Sri Lanka. The extracted essential oil is a common cooking ingredient among Chinese people. It has also been demonstrated to enhance digestion and prevent microbial development (Giannenas et al., 2021). The discipline of employing herbal medicines to cure illnesses is known as ethnomedicine or phytotherapy, and it has persisted in many civilizations' health care systems despite the availability of effective alternative therapies. In both contemporary and traditional medical systems across the world, plants constitute the primary source of drugs. Plants and their phytoconstituents prevent and treat many illnesses, like epileptic seizures (Famta et al., 2021; İlhami Gülçin et al., 2010). Two of the main phenolic components of clove essential oil are eugenol and eugenyl acetate. However, because eugenol is a primary ingredient of cloves, their inherent analgesic and antibacterial properties make them predominantly utilized in dentistry (Vanin et al., 2022; Grespan et al., 2012). People use it as a home remedy to alleviate dental pain, especially toothaches (Paroul, 2014). The possibility that essential oils could be used as a resistance-modifying agent was highlighted, and they were used as part of a strategy to overcome the problem of antibiotic resistance and exhibit a synergistic effect with antibiotics (Trifan et al., 2002). The medium-sized (812 m) tree *S. aromaticum* L., also called *Eugenia caryophyllata*, is indigenous to the Indonesian island. The common name for this plant, which is a member of the Mirtaceae family, is the clove (6Because of its anticonvulsant, analgesic, anesthetic, anti-Alzheimer, antimicrobial, anticancer, antioxidant, anti-inflammatory, antispasmodic, and neuroprotective properties, *Syzyguim aromaticum* L. has been used as a medicinal plant for thousands of years (Bhatia & Iyer, 2025). The comparison of the previous findings with one of the most efficient antiepileptic drugs against some types of seizures helped to perceive the impact of the aqueous extract of *S. aromaticum* L. on ChE activity, electrolytes, glucose, and total protein. *S. aromaticum* (Cloves) is an evergreen tree, 8.30 feet high, small to medium in size, with fragrant dried flower buds. Clove is a natural culinary flavor with analgesic, antiemetic, toothache, anaesthetic, antibacterial, antiviral, fungicide, fungal static antiseptic, carminative, tonic, antihistamine, astringent and in small quantities, anticarcinogenic properties. Indonesia is one of the tropical and subtropical countries producing cloves, the aromatic flower that belongs to the Myrtaceae family (Ayushi et al., 2020). Eugenol is the main component of clove, accounting for half of its minimum of thirty compounds. Clove, also known as *Eugenia aromaticum*, *Eugenia caryophyllata*, or *S. aromaticum*, is a species of Myrtaceae tree that produces dried flower buds. Clove appears in Chinese medicine, Ayurveda and Western herbalism. Clove is taken to raise the hydrochloric acid in the stomach, improve peristalsis and as a carminative. The dentists also use it, whereby it is applied as a dental emergency anodyne. Cloves are a plant which herbalists consider to have antimicrobial properties. In vitro possible activity of the plant against Gram-positive and Gram-negative species of bacteria has been investigated in the present investigation (Mehta & Singh, 2025). The hallmark of type 2 diabetes (DM), a metabolic disease, is hyperglycemia, or an unwarranted rise in blood glucose levels brought on by abnormalities in insulin synthesis. Type 2 diabetes, also known as T2DM, is caused by decreased insulin action, whereas the first type of diabetes (T1DM) is caused by decreased insulin synthesis. These two forms of diabetes mellitus are the most common varieties. As prevalent as 9.8 %, DM has now become an international concern and is capable of causing several cardiovascular issues and may claim 11.3 % of all deaths worldwide. T2DM is acquired by middle-aged and

older people and is caused by poor eating habits and lifestyles, whereas T1DM tends to attack children or adolescents. Complications of diabetes could occur according to the severity and duration of diabetes that is not well-treated or managed. Nephropathy, neuropathy, retinopathy, and cardiovascular disease are some of the side effects of diabetes mellitus, particularly when it co-occurs with other illnesses (Bungau et al., 2023). Hyperglycemia is one of the symptoms of diabetes mellitus, which can be brought on by either a relative (type 2 DM) or absolute (type 1 diabetes) insulin deficiency. Over 180 million people worldwide suffer from the common illness. By rearranging structural proteins, hyperglycemia damages cells and promotes non-enzymatic glycosylation of proteins, producing advanced glycosylation end products. Rats can develop diabetes and hyperglycemia when streptozotocin (STZ) is administered. It is produced by *Streptomyces achromogenes* and is used to cause type 1 and type 2 diabetes. Although greater doses may be used, 40–60 mg/kg of total body weight is the typical dose. STZ, being a nitric oxide donor and DNA-damaging agent, is most effective when used intraperitoneally and in a dose equivalent to or greater than that. When it enters the cell, it modifies the DNA of pancreatic beta cells, making them fragment (Rajan & Chawla, 2024). There are numerous plants that have been tried over the past few years under numerous clinical circumstances. Some of them are prescribed to overcome diabetes mellitus. Clove is also applied in the field of dentistry as a local anaesthetic and topical antiseptic. Also, it is applied to heal gastrointestinal problems. Clove has been demonstrated to have antiplatelet, insecticidal, insulin mimetic, antioxidant, anti-inflammatory and antihypertensive effects (Apparecido et al., 2009). Clove can be extracted into oil (Ullah et al., 2023). Cloves are frequently used in traditional medicine and have been the subject of several studies; yet, little is known about how they affect the immune system, particularly the lymphocytes. Eugenol, the main substance in cloves, is what gives the spice its strong, unique scent (Gosavi et al., 2020). 15 per cent of the dried clove buds and 7090 per cent of the essential oil are formed of eugenol. Cloves contain alcohols, phenols, sesquiterpene esters, tannin (1013%), and volatile oil (1421%). These components are responsible for the reactions that cloves cause in different environments (Dibazar et al., 2014). By strengthening insulin resistance, glucose tolerance, and the activity of cells that make insulin, the chemical nigericin found in cloves serves as a natural blood sugar regulator. Eugenol, a component of clove compounds, enhances liver function and lowers cirrhosis, inflammation, chronic fatty liver disorder, and oxidative stress—a state in which a system of oxidative and anti-oxidant forces is out of balance. The benefits of cloves for cancer prevention (Hassanen, 2010). Numerous studies show that chemicals in cloves, particularly eugenol, have anti-cancer effects. The extract of clove has been shown to help halt tumor development and encourage cancer cell death; therefore, it helps prevent cancer. Because of their antibacterial qualities, cloves can help inhibit the growth of germs. One study suggests that clove essential oil may be able to eliminate three prevalent bacterial species, including *E. coli*, which is the cause of food poisoning. The body is shielded from external threats, including bacteria, fungus, viruses, poisons, and compounds made by germs, by its immune system, which is strengthened by antioxidants (Tungare et al., 2024). Consuming cloves aids in controlling body temperature and promoting metabolic activity. In addition to lowering the body's percentage of triglycerides, one of the blood fats, and dangerous cholesterol, cloves can also cleanse the blood since they contain antioxidants. Before going to bed, cloves might help clear up stomach issues.

The study of employing herbal medicines to cure illnesses is known as ethnomedicine or phytotherapy, and it is still a part of many civilizations' healthcare systems despite the availability of effective alternative therapies (Traditional Formulations and Uses, 2025; Kumari et al., 2025).

Materials and Methods Materials

Sample collection and preparation of clove extract

We bought the fruits and stem of the clove (*S. aromaticum*) from the local supermarket. The stem and fruits of the clove were cleaned and then oven-dried at fifty degrees Celsius for 24. The material was mechanically ground into a powder after drying and then sieved through a 250 µm mesh screen before being kept at the ambient temperature until it was needed. 250 millilitres of water that was distilled were used to soak 50 grams of clove powder for 48 hours. The water was removed using an electric oven that was set to 40°C.

Diabetes induction

Rats of male gender who had fasted overnight were given a subcutaneous injection of the STZ, fifty milligrams per kilogram of body weight, mixed in a pH 4.5 citrate buffer solution to induce diabetes. By monitoring fasting glucose levels from blood extracted from the treatment rats' tail vein, the beginning of diabetes was confirmed just 72 hours after the injection. Acu-Chek OneTouch glucometers were used to check the levels of blood glucose. The blood glucose levels of diabetic rats are higher than 250 mg/d (Chalabi et al., 2019).

Experimental design

The purpose of the study was to ascertain if aqueous clove extract improved certain physiological and immunological markers in diabetic albino rats. 30 male albino rats, ages 5–6 months, weighing 175–185 g, were used in this investigation. They were split into three groups.

The first group was given only food and drink as a control. The second group is the untreated diabetes group. For 25 days, each one of the animals within the third group—the diabetic group—was given oral doses of 250 mg/kg of clove aqueous extract (Yasuda et al., 2017). The animals were anaesthetized with 10% ketamine at the end of the trial, and blood was extracted from their hearts. A centrifuge was used to separate the blood for ten minutes at 3000 rpm. To complete the biochemical tests, which included measuring the serum's glucose level, the enzyme catalase SOD, IL-6, which IL-1, LDH, CRP, malondialdehyde (MDH), TNF- α , & total of and differentiating white blood cells, the serum was stored in the refrigerator at -20 degrees.

Tests of Biochemistry

IL-1; Human Interleukin 6 (IL-1) ELISA Kit\CUSABIO\USA

IL-6; Human Interleukin 6 (IL-6) ELISA Kit\CUSABIO\USA

CRP; BioSource/USA

LDH; BioLife Sciences

TNF- α ; Human TNF- α (Tumor Necrosis Factor Alpha) ELISA Kit\USA

4-Malondialdehyde My BioSource/USA

Catalase; Human Catalase (CAT) ELISA Kit My BioSource/USA

6-SOD; Bio System S, A. Costa Brava, Barcelona\Spain

Results

On the first day, the two groups that received 50 mg/kg of STZ had substantially higher glucose levels than the control group (90 ± 3.32 , 395 ± 6.58 , 385 ± 5.73) mg/dl, respectively. The group that received the aqueous extract of cloves, however, showed a substantial decrease in glucose levels on the tenth day (390 ± 4.45) mg/dl compared to those in the group that developed diabetes without therapy. On the 25th day, the blood glucose levels of the clove-using group were significantly lower (176 ± 2.79) than those of the diabetes-non-treating group (387 ± 7.52 mg/dl) shown in Table 1.

Table 1. Effect of aqueous extract of cloves on the glucose level in the diabetic rats

Mean $\pm$ SE			
Groups	First day Glucose mg\dl	10 th day Glucose mg\dl	25 th day Glucose mg\dl
control	90 ± 3.32 b	92 ± 3.60 c	99 ± 1.56 c
Positive control (diabetic)	395 ± 6.58 a	390 ± 4.45 a	387 ± 7.52 a
diabetic $\pm$ extract of Cloves250- mg\kg	385 ± 5.73 a	262 ± 5.90 b	176 ± 2.79 b
LSD	25.32**.	20.67**.	23.98**.
P-value	0.0001	0.0001	0.0001
There is a significant difference between the means with different letters in a single column ($P < 0.01$).			

According to the results in Table 2, the diabetes group's level of interleukin 1 was significantly higher (4.05 ± 0.34) pg/ml than that of control group (2.43 ± 0.23) and the diabetic group that received 250 mg/kg of Clove extract (2.65 ± 0.87) pg/ml. Additionally, the diabetic group's interleukin 6 levels (5.63 ± 1.70) pg/ml were substantially greater than those of the ones in the control the group (2.89 ± 0.65) and the diabetic group that received 250 milligrams per kilogram of extract of cloves (3.43 ± 0.47 pg/ml).

Table 2. Effect of aqueous clove extract on the levels of IL-1 and IL-6 in induced diabetic rats

Mean $\pm$ SE		
groups	IL-1 pg\ml	IL-6 pg\ml
Control	2.43 ± 0.23 b	2.89 ± 0.65 b
Positive control (diabetic)	4.05 ± 0.34 a	5.63 ± 1.70 a
diabetic $\pm$ Extract of Cloves250- mg\kg	2.65 ± 0.87 b	3.43 ± 0.47 b
LSD	** 1.162	** 0.545
P-value	0.0001	0.0001
The means of distinct letters in a single column are substantially different from one another ($P < 0.01$ **).		

The results statistically showed in the Table 3 that the diabetes group (12.15 ± 1.58) had a significantly higher level of CRP than both the control group (2.76 ± 0.32) mg/ml and the group with diabetes that received aqueous extract of clove (6.37 ± 1.43) mg/ml. The LDH enzyme activity, however, was significantly higher in the diabetic group (218.07 ± 13.99) IU\l than in the control group (154.54 ± 7.32) IU\l, and the group with diabetes treated with the based on water clove extract had a lower level of LDH (175.43 ± 3.79) IU\l than the diabetic group. When it came to the tumor necrosis factor-related factor, or TNF- α , the data showed that the group with diabetes who received treatment with the water-soluble extract of cloves had a considerably higher concentration of the peptide (815.82 ± 20.53) pg/ml compared to the control group's (555.82 ± 13.62) (538.58 ± 16.43) pg/ml).

Table 3. Effect of aqueous clove extract on the levels of CRP, LDH, and TNF in induced diabetic rats

Mean $\pm$ SE			
Groups	CRP mg/ml	LDH IU/l	TNF- α pg/ml
Control	2.76 $\pm$ 0.32b	154.54 $\pm$ 7.32 c	555.82 $\pm$ 13.62b
Positive control (diabetic)	12.1 $\pm$ 1.58 a	218.07 $\pm$ 13.99 a	815.82 $\pm$ 20.53 a
Diabetic $\pm$ extract of Cloves250- mg/kg	6.37 $\pm$ 1.43 a	175.43 $\pm$ 3.79 b	538.58 $\pm$ 16.43 b
LSD	** 2.432	16.32**	20.21**
P-value	0.0001	0.0006	0.0001
Means with different letters in the same column are significantly different from one another (P<0.01**).			

The WBC count (8.65 $\pm$ 1.60) is significantly higher in the diabetes group than in the control group (6.40 $\pm$ 1.22) cells X10³. Additionally, cell X10³ (5.34 $\pm$ 1.97) in the diabetes group received the aqueous extract of cloves. But the results revealed that the proportions of WBC (56.34 $\pm$ 2.79) and neutrophils were significantly lower in the diabetes group that received dissolved in water extract of clove (50.21 $\pm$ 3.55) and compared to the control group (51.21 $\pm$ 1.08). Compared to the control group (42.84 $\pm$ 1.28%) and the diabetic group treated with cloves (38.32 $\pm$ 4.21%), the proportion of lymphocyte white blood cells was significantly reduced in the diabetic group (30.08 $\pm$ 3.72) %. However, the percentage of white blood cells that were eosinophilic, basophilic, and monocytes did not significantly differ across the groups, according to the data shown in Table 4.

Table 4. Effect of aqueous clove extract on the total count and differential percentage of white blood cells

Mean $\pm$ SE						
Groups	WBC:CellX10 ³	Neutrophil %	Lymphocyte %	Monocyte %	Basophil %	Eosinophil %
Control	6.40 $\pm$ 1.22 b	51.21 $\pm$ 3.53a	42.84 $\pm$ 1.28a	5.86 $\pm$ 0.96	00. $\pm$ 0.001	1.06 $\pm$ 0.07
Positive control (diabetic)	8.65 $\pm$ 1.60 a	56.34 $\pm$ 2.79 a	30.08 $\pm$ 3.72 b	7.42 $\pm$ 0.77	0.93 $\pm$ 0.04	2.65 $\pm$ 0.37
diabetic $\pm$ extract of Cloves250 - mg/kg	5.34 $\pm$ 1.97 b	50.21 $\pm$ 3.55a	38.32 $\pm$ 4.21a	7.33 $\pm$ 15.28	09. $\pm$ 2.231.	2.29 $\pm$ 0.74
LSD	**1.668	** 3.157	4.42*	NS 2.43	.NS 0.52	1.621NS
P-value	0.0001	0.0001	0.0466	0.388	0.451	0.251
Means with distinct letters in a single column are substantially different from one another.) ** P<0.01.(						

The Results

The diabetes group's level of MDA (4.42 $\pm$ 0.53) nmol/ml was substantially greater than that of the control group (1.60 $\pm$ 0.30) nmol/ml as well as the group with diabetes that took clove aqueous extract (2.06 $\pm$ 0.63) nmol/ml, as shown in Table 5. The CAT enzyme level was significantly higher in the diabetic group (6.32 $\pm$ 1.89) IU/l than in both the control group and diabetic treatment with the clove dissolved in water extract (3.28 $\pm$ 0.62, 4.52 $\pm$ 0.94) IU/l, according to the results. The findings concluded that the diabetic group had a significantly higher level of the enzyme superoxide dismutase (3.62 $\pm$ 0.84) than both the control group (2.69 $\pm$ 0.23) IU/l & the diabetic group that received the clove extract (2.59 $\pm$ 0.57) IU/l.

Table 5. Effect of aqueous cloves extract on the MDA, CAT and SOD

Mean $\pm$ SE			
Groups	MDA nmol\ml	CAT IU\l	SOD IU\l
Control	1.60 $\pm$ 0.30 b	3.28 $\pm$ 0.62 c	2.69 $\pm$ 0.23 a
diabetic	4.42 $\pm$.0.53 a	6.32 $\pm$ 1.89 a	3.62 $\pm$ 0.84 a
diabetic $\pm$ extract of Cloves250- mg\kg	2.06 $\pm$ 0.63 b	4.52 $\pm$ 0.94 b	2.59 $\pm$ 0.57 a
LSD	** 0.845	* 1.871	** 0.989
P-value	0.0001	0.045	0.0018
means with different letters within one column differ significantly from each other *P<0.01.**			

Discussion

Clove extract was shown to have a positive impact on reducing the glucose levels of rats given diabetes, which is consistent with the results of earlier research. According to previous research, clove improves glycemic control by raising blood insulin levels while lowering glucose levels (Abtahi-Eivari et al., 2021), which is consistent with research by Kuroda et al. showing that *S. aromaticum* has hypoglycemic effects (Kuroda et al., 2012). The genes encoding "phosphoenolpyruvate carboxyl kinase" as well as "glucose 6-phosphatase," which are known for having an enzyme role in gluconeogenesis, may be suppressed by *S. aromaticum*, according to another study. By reducing intestine alpha-glucosidase activity of enzymes and, hence, glucose absorption, *S. aromaticum* reduces the demand for insulin and shows effects akin to the actions of insulin (Prasad et al., 2005). Adefegha et al. claim that the low blood sugar levels of clove may be caused by a reduction in intestinal alpha-glucosidase activity, which is involved in the digestion of glucose (Adefegha et al., 2014). Higher levels of blood glucose in diabetic rats may be caused by elevated amounts of this enzyme (Chan et al., 2018). Eugenol may inhibit the body's glucagon-induced synthesis of glucose and decrease the activity of glycogen phosphorylase (Sanae et al., 2014). Diabetic patients often have abnormalities of the lipoproteins and are susceptible to hyperlipidemia, which is defined by reduced HDL cholesterol and increased cholesterol, TG, and LDL cholesterol (Yasuda et al., 2017; Grespan et al., 2012).

Moreover, mice given eugenol were shown to have a significant reduction in TNF- α . Furthermore, additional studies suggest that components of cloves may affect immunological responses. For instance, an examination of the components of cloves, including isoeugenol and its analogues (eugenics and allylbenzene), revealed dose-dependent reduction of nitric oxide production and the expression of nitric oxide synthase in rat macrophages stimulated by lipopolysaccharide. Clove may inhibit IL-1 β and IL-6 production, per another study. Following the macrophages' LPS challenge, the essential oil's eugenol has also demonstrated a decrease in TNF- α production by Kupffer cells. Research on macrophages and other cells revealed that the components of cloves have identical anti-inflammatory and modulatory effects. Cloves can thereby improve the growth, functionality, and humoral responses of B cells while suppressing T cells and their activities .

They found that by boosting humoral immunity and lowering cellular immunity, clove oil can alter the immunological response (Dibazar et al., 2014). There were some enhancements in humoral and cellular responses, according to another study. Contradictory results indicated that clove essential oil improved both humoral and cellular immune responses and raised total white blood cell counts in mice with cyclophosphamide immunity. Since the mice's immune systems were impaired, improving T cell responses required function restoration. Cloves thereby control T cell proliferation and activity; moreover, they can reestablish cellular immunity, which might result in advantageous uses. Our research showed humoral immunological responses and B cell proliferation with clove components, which is consistent with other

publications that showed improved antibody production and B cell recovery. We examined the inflammatory profile in the treated cells after assessing the lymphocyte expansion responses (Gülçin et al., 2010). Numerous biological properties of clove oil have been documented, including fungicidal, antioxidant, analgesic, antibacterial, anti-inflammatory, and antineoplastic properties.

Clove extract positively impacted antioxidants in this research, which helped to keep blood sugar levels low by lowering SOD, CAT, and MDA levels. Clove oil was also employed to enhance the antioxidant system, which comprises CTA, GSH, and GST, as well as blood and biochemical markers in another study (Elgharib et al., 2025). In a prior research, a drop in MDA levels was noted in both diabetic and healthy mice, indicating that clove supplementation decreased oxidative stress. Because supplementing with cloves changes the blood's antioxidant activity of enzymes, which in turn leads the red blood cell enzyme in mice to change and become less active, the study also discovered a drop in the number of both SOD and CAT. This effect was caused by a decrease in both MDA levels and SOD activity (Shukri et al., 2010).

Clove, or *S. aromaticum*, is farmed all over the world and grows natively in Indonesia (Apparecido et al., 2009). In addition to being a well-known food taste, it is also a common traditional medicine in Australia and numerous Asian nations for treating respiratory, dental, and headache conditions, as well as sore throats (Domaracky et al., 2007). Cloves have anti-inflammatory, cytotoxic, and anaesthetic qualities in addition to their antiviral, antifungal, and antibacterial ones (Chaieb et al., 2007). Clove components have been shown to reduce lipid peroxidation and confer antioxidant properties (Ko et al., 1995).

β -cariophyllene, tanene, thymol, eugenol (50–87%), and eugenyl acetate have been identified as the main components of clove. The methods of action of these components are yet unknown, although it has been demonstrated that they affect several immune responses and many of the previously listed effects (Choi et al., 2007). Processing cloves yields additional water-soluble substances besides eugenol, some of which may have significant toxicologic roles. Aside from its anti-inflammatory properties already mentioned, certain physiological consequences of clove exposure have been recorded (and discussed above). However, research into the effects of clove or significant compounds (like eugenol) on specific immune system elements or processes has only recently begun. We conducted a number of investigations in the hopes of shedding some light on the immunotoxicity and immunomodulatory effects of compounds linked to cloves, as many of those studies have frequently produced contradictory findings (Bachiega et al., 2012). According to certain earlier research, clove oil preparations' apparent antioxidant properties may be due to the phenolic components in clove (Parthipan et al., 2022). According to one study, flavonoids extracted from clove buds and clove extracts in ethanol and dichloro-methane were potent inhibitors of free radicals, in contrast to commercialized antioxidants like BHT. The high concentration of phenolic components, such as a compound called thymol, in addition to eugenol acetate, in clove extract may be the cause of its antioxidant qualities, per that study (Nassar et al., 2007). An important part of the healthcare system is still the traditional medical system's use of herbal remedies. In recent decades, medicinal plants have gained more acceptability due to the perception that natural plants are more effective and have fewer negative effects compared to their synthetic counterparts (Abushouk et al., 2017). Conventional medications currently provide the majority of basic medical care for over 80% of people globally (Ekor, 2014). Due to their pharmacological properties, which include bactericidal, virucidal, and fungicide effects, several herbal plants are utilized in food preservation and embalming. In addition, they have sedative, analgesic, spasmolytic, antibacterial, anti-inflammatory, and local anaesthetic properties. Glycosides and saponins are two examples of the phytoconstituents found in many plant species that have been shown to have pharmacological qualities. It has become widely known that herbal remedies play a significant role in the development of novel pharmaceutical chemicals that have been utilized to treat a variety of serious disorders. These phytochemicals are believed to have been discovered and

are regarded as a remarkable lead compound in the search for new and powerful drugs (Beshbishy et al., 2019). The dried flower bud known as clove (*S. aromaticum*) is indigenous to the Maluku islands of Indonesia and is a member of the Myrtaceae family. It has lately grown in a number of places throughout the globe. The leaves and buds of the clove tree are its commercial components, and within four years afterward planting, flowering buds begin to appear. Harvesting can be carried out manually or with the help of a naturally occurring phytohormone during the pre-flowering stage (Cortés-Rojas et al., 2014). It's crucial to note that they are employed in the perfume business in addition to several medicinal applications. Because of its antibacterial and antioxidant properties, clove is considered one of the spices which may be used in place of artificial preservatives in a range of meals, especially when cooking meat. Studies have demonstrated that several aromatic herbs, including mint, thyme, garlic cloves, oregano, and cinnamon, among others, have antifungal, antiviral, antibacterial, and anticarcinogenic properties. However, due to its potent antibacterial and antioxidant qualities, clove has garnered a lot of attention among other spices (Shan et al., 2005). Clove is thought to help prevent a number of degenerative illnesses since it contains a lot of chemical components that have antioxidant properties (Astuti et al., 2019). Burns and wounds, as well as infections and toothaches, have traditionally been treated using clove essential oil (CEO). It is also often used in soaps, fragrances, and as a cleaner in histology, and it has been employed in a range of industrial situations (Sarrami et al., 2002). As a warming and invigorating herb, cloves are employed in traditional Chinese and Indian medicine (Batiha et al., 2019). Cloves have been used for several thousand years to cure stomach, intestinal, and liver problems as well as gas, nausea, and vomiting. Additionally, they have been used as a nerve stimulant. In tropical Asia, Many ailments, including cholera, TB, malaria, and scabies, have been treated with cloves. Clove has also been used for a long time in America to fight against food-borne illnesses brought on by viruses, worms, candida, and other microbes and protozoan diseases (Bhowmik et al., 2012). For several thousand years, people have used clove to heal stomach, intestinal, and liver problems as well as gas, nausea, and vomiting. They have also been used as a nerve stimulator. Many diseases, such as cholera, TB, malaria, and scabies, have been treated with cloves throughout tropical Asia. Historically, clove was additionally utilized in America to prevent food-borne illnesses, such as worms, viruses, candida, and other bacteria and protozoan disorders (Neveu et al., 2010). According to pharmacology, the main source of phenolic compounds, including hydroxybenzoic acids, flavonoids, hydroxyphenyl propene, hydroxycinnamic acids, and derivatives of gallic acid, including hydrolyzable tannins, is clove. Cloves also contain eugenol (C₁₀H₁₂O₂), the main bioactive compound that is present in significant concentrations in the fresh plant (Jirovetz et al., 2006). The flavonoids quercetin and kaempferol are found in cloves together with phenolic acids, which include ferulic, caffeic, salicylic, and ellagic acids. Up to 18% of essential oil, composed of eugenol, acetic and β -cariofileno, is present in clove flower buds (Gülçin, 2011). provided information on eugenol's antioxidant effectiveness in vitro and looked into the relationship between structure and activity (Shaghayegh Pishkhan Dibazar et al, 2014). By fixing the phenoxil radical and donating the hydrogen atom, they showed that eugenol produces stable compounds that neither cause nor exacerbate oxidation. Additionally, if both the eugenol molecule and a ring of aromatic chemicals create a happy chain carbon link, resonance can stabilize phenoxil radicals. A study using gas chromatography-mass spectroscopy (GC-MS) revealed that the chief executive officer was composed of eugenol, eugenyl acetate, β -caryophyllene, calacorene, α -humulene, 2-heptanone, humulenol, & calamine. Hydro-distillation was used to separate it, and 36 components (Chaieb et al., 2007) appeared. The antioxidant activity of caraway seeds and clove was shown to be similar to that of the artificial food preservative called butylated hydroxytoluene (BHT) by a variety of in vitro techniques, including ferric thiocyanate, β -carotene-linoleate, 1, 1-diphenyl-2-picrylhydrazyl, the hydroxyl (DPPH) radical, and hydroxyl radical (Bamdad et al., 2006). Additionally, the DPPH radical scavenging of clove oil was compared by Gülçin et al. to that of other synthetic antioxidant agents, such as alpha-tocopherol, BHT, butylated hydroxyanisole, which is & Trolox (Gülçin et al., 2012) demonstrated that using BHT reduced the activity of

antioxidants of clove oil, followed by Trolox, butylated hydroxyanisole, clove oil, and alpha-tocopherol. In vitro methods such as DPPH, ferric reducing antioxidant power, oxygen radical absorbing capacity, -2-deoxyguanosine, 2, 1'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acids) (ABTS), and the oxidase xanthine were used to evaluate the antioxidant activity of the aqueous *S. aromaticum* extract. They found that the metal-chelating ability, strong hydrogen-donating capacity, and scavenge of oxygen peroxide, free radicals, and superoxide may all contribute to the water-based substances *S. aromaticum* extract's significant antioxidant efficacy (Gülçin et al., 2003). Clove extracts and antioxidants like the CEO can help alleviate memory impairments brought on by oxidative stress (Mehta et al., 2010). According to Halder et al. (Halder et al., 2011), in the mice's brains, the CEO therapy decreased the oxidative stress markers glutathione and malondialdehyde. They came to the conclusion that because clove oil lowers oxidative stress, it can help repair memory and learning deficits brought on by both short-term and long-term scopolamine therapy. By opening calcium and chloride channels found in ganglionic cells, clove and eugenol were additionally demonstrated they have analgesic effects against joint and tooth pain (Shields et al., 2004). However, another study by Daniel et al. (Daniel et al., 2009) suggests that clove's analgesic qualities may be connected to its agonistic capsaicin activity (Vriens et al., 2008; Verma et al., 2018). used the acetic acid-stimulated abdomen wriggle technique to demonstrate the efficacy of a compound as an in vivo analgesic. Interestingly, the CEO has been shown to exhibit anti-carcinogenic and cytotoxic effects on the human tumor cell lines Hep G2 and PC-3 (Ogunwande et al., 2005). It has also been shown that eugenol and dehydrodieugenol encourage the killing of human cancer cells. Additionally, cinnamon aldehyde's antimutagenic efficacy has been investigated against the human-derived hepatic tumor cell lines due to its decreased occurrence of micronuclei caused by different heterocyclic amines (Lin et al., 2013). It has been demonstrated that natural products are the most efficient in changing the activity in proteins associated with cancer (Russo et al., 2013; Kouidhi et al., 2010; Kumar et al., 2014) have shown that leukaemia, pulmonary, breast, and colorectal cancer cells can be treated with CEO and a chemical named. Clove inhibits lipopolysaccharide (LPS) activity and the nuclear transcriptional factor- κ B (NF- κ B) pathway, which results in anti-inflammatory and immunomodulatory effects.

Furthermore, when used in conjunction with CCl₄ treatment, eugenol was demonstrated to protect against CCl₄-induced hepatotoxicity (El-Hadary & Hassanien, 2016). Clove treatment tends to enhance lipid concentrations in the liver, serum, and kidney system, as well as ALT, urea, and AST, compared with healthy levels in rats with elevated lipid levels (Shyamala et al., 2003). The presence of insulin-stimulating chemicals in *S. aromaticum* preparations may be the cause of their antidiabetic actions (Kuroda et al., 2012).

Conclusion

The findings show that in diabetic rats, clove aqueous extract significantly affects blood sugar regulation. Apart from being a great antioxidant, it also significantly improves some immunological markers and lowers the level of inflammation in diabetic rats given clove aqueous extract.

Author Contributions

All Authors contributed equally.

Conflict of Interest

The authors declared that no conflict of interest.

References

- Abtahi-Eivari, S. H., Shokoohi, M., Ghorbani, M., Halimi, M., Hajizadeh, H., Poulak, T., ... & Ghoreishi, Z. (2021). Effects of Hydroalcoholic Extracts of Cloves (*Syzygium aromaticum*) on the Serum Biomarkers, Antioxidant Status, and Histopathological Changes of Kidneys in Diabetic Rats. *Crescent Journal of Medical & Biological Sciences*, 8(4).
- Abushouk, A. I., Ismail, A., Salem, A. M. A., Afifi, A. M., & Abdel-Daim, M. M. (2017). Cardioprotective mechanisms of phytochemicals against doxorubicin-induced cardiotoxicity. *Biomedicine & Pharmacotherapy*, 90, 935-946. <https://doi.org/10.1016/j.biopha.2017.04.033>
- Adefegha, S. A., Oboh, G., Adefegha, O. M., Boligon, A. A., & Athayde, M. L. (2014). Antihyperglycemic, hypolipidemic, hepatoprotective and antioxidative effects of dietary clove (*Syzygium aromaticum*) bud powder in a high-fat diet/streptozotocin-induced diabetes rat model. *Journal of the Science of Food and Agriculture*, 94(13), 2726-2737. <https://doi.org/10.1002/jsfa.6617>
- Al-Chalabi, S. M., Abdul-Latif, R. F., Al-Mahdawi, F. A., & Abud, H. N. (2019). Effect of fenugreek (*Trigonella foenum graecum*) seed aqueous extract on blood glucose, lipid profile and some hormonal assay in streptozotocin-induced diabetic male albino rats. *International Journal of Drug Delivery Technology*, 9(3), 19-25.
- Astuti, R. I., Listyowati, S., & Wahyuni, W. T. (2019, July). Life span extension of model yeast *Saccharomyces cerevisiae* upon ethanol derived-clover bud extract treatment. In *IOP Conference Series: Earth and Environmental Science* (Vol. 299, No. 1, p. 012059). IOP Publishing. . <https://doi.org/10.1088/1755-1315/299/1/012059>
- Ayushi, K. U., Danish, S. M., & Mohammad, P. U. (2020). A review on biological and therapeutic uses of *Syzygium aromaticum* Linn.(Clove): Based on phyto-chemistry and pharmacological evidences. *International Journal of Botany Studies*, 5(4), 33-39.
- Bachiega, T. F., de Sousa, J. P. B., Bastos, J. K., & Sforcin, J. M. (2012). Clove and eugenol in noncytotoxic concentrations exert immunomodulatory/anti-inflammatory action on cytokine production by murine macrophages. *Journal of Pharmacy and Pharmacology*, 64(4), 610-616. <https://doi.org/10.1111/j.2042-7158.2011.01440.x>
- Bamdad, F., Kadivar, M., & Keramat, J. (2006). Evaluation of phenolic content and antioxidant activity of Iranian caraway in comparison with clove and BHT using model systems and vegetable oil. *International journal of food science & technology*, 41, 20-27. <https://doi.org/10.1111/j.1365-2621.2006.01238.x>
- Batiha, G. E. S., Beshbishy, A. M., Tayebwa, D. S., Shaheen, H. M., Yokoyama, N., & Igarashi, I. (2019). Inhibitory effects of *Syzygium aromaticum* and *Camellia sinensis* methanolic extracts on the growth of *Babesia* and *Theileria* parasites. *Ticks and tick-borne diseases*, 10(5), 949-958. <https://doi.org/10.1016/j.ttbdis.2019.04.016>

- Beshbishy, A. M., Batiha, G. E. S., Adeyemi, O. S., Yokoyama, N., & Igarashi, I. (2019). Inhibitory effects of methanolic *Olea europaea* and acetic *Acacia laeta* on growth of *Babesia* and *Theileria*. *Asian Pacific Journal of Tropical Medicine*, 12(9), 425-434. <https://doi.org/10.4103/1995-7645.267586>
- Bhatia, M., & Ramesh Iyer, R. (2025). Immunological Responses to Viral Infections. In *Medxplore: Frontiers in Medical Science* (pp. 52-70). Periodic Series in Multidisciplinary Studies.
- Bhowmik, D., Kumar, K. S., Yadav, A., Srivastava, S., Paswan, S., & Dutta, A. S. (2012). Recent trends in Indian traditional herbs *Syzygium aromaticum* and its health benefits. *Journal of Pharmacognosy and Phytochemistry*, 1(1), 13-22.
- Bungau, S. G., Vesa, C. M., Bustea, C., Purza, A. L., Tit, D. M., Brisc, M. C., & Radu, A. F. (2023). Antioxidant and hypoglycemic potential of essential oils in diabetes mellitus and its complications. *International Journal of Molecular Sciences*, 24(22), 16501. <https://doi.org/10.3390/ijms242216501>
- Chaieb, K., Hajlaoui, H., Zmantar, T., Kahla-Nakbi, A. B., Rouabhia, M., Mahdouani, K., & Bakhrouf, A. (2007). The chemical composition and biological activity of clove essential oil, *Eugenia caryophyllata* (*Syzygium aromaticum* L. Myrtaceae): a short review. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives*, 21(6), 501-506. <https://doi.org/10.1002/ptr.2124>
- Chan, C. W., Yu, C. L., Lin, J. C., Hsieh, Y. C., Lin, C. C., Hung, C. Y., ... & Wu, T. J. (2018). Glitazones and alpha-glucosidase inhibitors as the second-line oral anti-diabetic agents added to metformin reduce cardiovascular risk in type 2 diabetes patients: a nationwide cohort observational study. *Cardiovascular diabetology*, 17(1), 20. <https://doi.org/10.1186/s12933-018-0663-6>
- Choi, C. Y., Park, K. R., Lee, J. H., Jeon, Y. J., Liu, K. H., Oh, S., ... & Yea, S. S. (2007). Ioeugenol suppression of inducible nitric oxide synthase expression is mediated by down-regulation of NF- κ B, ERK1/2, and p38 kinase. *European journal of pharmacology*, 576(1-3), 151-159. <https://doi.org/10.1016/j.ejphar.2007.07.034>
- Cortés-Rojas, D. F., de Souza, C. R. F., & Oliveira, W. P. (2014). Clove (*Syzygium aromaticum*): a precious spice. *Asian Pacific journal of tropical biomedicine*, 4(2), 90-96. [https://doi.org/10.1016/S2221-1691\(14\)60215-X](https://doi.org/10.1016/S2221-1691(14)60215-X)
- Daniel, A. N., Sartoretto, S. M., Schmidt, G., Caparroz-Assef, S. M., Bersani-Amado, C. A., & Cuman, R. K. N. (2009). Anti-inflammatory and antinociceptive activities A of eugenol essential oil in experimental animal models. *Revista Brasileira de Farmacognosia*, 19, 212-217. <https://doi.org/10.1590/S0102-695X2009000200006>
- Dibazar, S. P., Fateh, S., & Daneshmandi, S. (2014). Clove (*Syzygium aromaticum*) ingredients affect lymphocyte subtypes expansion and cytokine profile responses: An in vitro evaluation. *journal of food and drug analysis*, 22(4), 448-454. <https://doi.org/10.1016/j.jfda.2014.04.005>

- Domaracký, M., Rehak, P., Juhás, Š., & Koppel, J. (2007). Effects of selected plant essential oils on the growth and development of mouse preimplantation embryos in vivo. *Physiological research*, 56(1). <https://doi.org/10.33549/physiolres.930929>
- Ekor, M. (2014). The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in pharmacology*, 4, 177. <https://doi.org/10.3389/fphar.2013.00177>
- Elgharib, I. M., Abdelhamid, F. M., Elshopakey, G. E., Sembawa, H., Albukhari, T. A., Filimban, W. A., ... & Risha, E. F. (2025). Therapeutic Potential of Clove Oil in Mitigating Cadmium-Induced Hepatorenal Toxicity Through Antioxidant, Anti-Inflammatory, and Antiapoptotic Mechanisms. *Pharmaceuticals*, 18(1), 94. <https://doi.org/10.3390/ph18010094>
- El-Hadary, A. E., & Ramadan Hassanien, M. F. (2016). Hepatoprotective effect of cold-pressed Syzygium aromaticum oil against carbon tetrachloride (CCl₄)-induced hepatotoxicity in rats. *Pharmaceutical biology*, 54(8), 1364-1372. <https://doi.org/10.3109/13880209.2015.1078381>
- Giannenas, I., Sidiropoulou, E., Bonos, E., Christaki, E., & Florou-Paneri, P. (2020). The history of herbs, medicinal and aromatic plants, and their extracts: Past, current situation and future perspectives. In *Feed additives* (pp. 1-18). Academic Press. <https://doi.org/10.1016/B978-0-12-814700-9.00001-7>
- Gosavi, N. S., Koli, S. S., Jire, D. S., & Shaikh, A. Z. (2020). Clove (Syzygium Aromaticum): A Miraculous Spice. *AJPTR*, 8(5), 1-17.
- Grespan, R., Paludo, M., de Paula Lemos, H., Barbosa, C. P., Bersani-Amado, C. A., de Oliveira Dalalio, M. M., & Cuman, R. K. N. (2012). Anti-arthritic effect of eugenol on collagen-induced arthritis experimental model. *Biological and Pharmaceutical Bulletin*, 35(10), 1818-1820. <https://doi.org/10.1248/bpb.b12-00128>
- Gülçin, İ., Elmastaş, M., & Aboul-Enein, H. Y. (2012). Antioxidant activity of clove oil—A powerful antioxidant source. *Arabian Journal of chemistry*, 5(4), 489-499. <https://doi.org/10.1016/j.arabjc.2010.09.016>
- Gülçin, İ., Şat, İ. G., Beydemir, Ş., Elmastaş, M., & Küfrevioğlu, Ö. İ. (2004). Comparison of antioxidant activity of clove (*Eugenia caryophyllata* Thunb) buds and lavender (*Lavandula stoechas* L.). *Food chemistry*, 87(3), 393-400. <https://doi.org/10.1016/j.foodchem.2003.12.008>
- Halder, S., Mehta, A. K., Kar, R., Mustafa, M., Mediratta, P. K., & Sharma, K. K. (2011). Clove oil reverses learning and memory deficits in scopolamine-treated mice. *Planta Medica*, 77(08), 830-834.
- Hassanen, N. H. (2010). Protective Effect of cinnamon, clove and ginger spicces or their essential oils on oxidative stress of streptozotocin-induced diabetic rats. *Arab Universities Journal of Agricultural Sciences*, 18(1), 137-154. <https://dx.doi.org/10.21608/ajs.2010.15019>
- Jirovetz, L., Buchbauer, G., Stoilova, I., Stoyanova, A., Krastanov, A., & Schmidt, E. (2006). Chemical composition and antioxidant properties of clove leaf essential oil. *Journal of agricultural and food chemistry*, 54(17), 6303-6307. <https://doi.org/10.1021/jf060608c>

- Kaur, J., Famta, P., Famta, M., Mehta, M., Satija, S., Sharma, N., ... & Khurana, N. (2021). Potential anti-epileptic phytoconstituents: An updated review. *Journal of ethnopharmacology*, 268, 113565. <https://doi.org/10.1016/j.jep.2020.113565>
- Ko, F. N., Liao, C. H., Kuo, Y. H., & Lin, Y. L. (1995). Antioxidant properties of demethyldiisoeugenol. *Biochimica et Biophysica Acta (BBA)-Lipids and Lipid Metabolism*, 1258(2), 145-152. [https://doi.org/10.1016/0005-2760\(95\)00111-O](https://doi.org/10.1016/0005-2760(95)00111-O)
- Kouidhi, B., Zmantar, T., & Bakhrouf, A. (2010). Anticariogenic and cytotoxic activity of clove essential oil (*Eugenia caryophyllata*) against a large number of oral pathogens. *Annals of microbiology*, 60(4), 599-604. <https://doi.org/10.1007/s13213-010-0092-6>
- Kumar, P. S., Febriyanti, R. M., Sofyan, F. F., Luftimas, D. E., & Abdulah, R. (2014). Anticancer potential of *Syzygium aromaticum* L. in MCF-7 human breast cancer cell lines. *Pharmacognosy research*, 6(4), 350. <https://doi.org/10.4103/0974-8490.138291>
- Kumari, S., Singh, P. A., Sindhwani, R., Hazra, S., Bajwa, N., & Suri, A. (2025). Traditional Formulations and Uses. In *Compendium of Clove* (pp. 223-241). CRC Press.
- Kuroda, M., Mimaki, Y., Ohtomo, T., Yamada, J., Nishiyama, T., Mae, T., ... & Kawada, T. (2012). Hypoglycemic effects of clove (*Syzygium aromaticum* flower buds) on genetically diabetic KK-Ay mice and identification of the active ingredients. *Journal of natural medicines*, 66(2), 394-399. <https://doi.org/10.1007/s11418-011-0593-z>
- Lin, L. T., Wu, S. J., & Lin, C. C. (2013). The anticancer properties and apoptosis-inducing mechanisms of Cinnamaldehyde and the herbal prescription Huang-Lian-Jie-Du-Tang (黃連解毒湯 Huáng Lián Jiě Dú Tang) in human hepatoma cells. *Journal of traditional and complementary medicine*, 3(4), 227-233. <https://doi.org/10.4103/2225-4110.119732>
- Mehta, A., & Singh, R. K. (2025). Targeting Tumor Microenvironment in Metastatic Cancer. In *Medxplore: Frontiers in Medical Science* (pp. 1-18). Periodic Series in Multidisciplinary Studies.
- Mehta, K. D., Garg, G. R., Mehta, A. K., Arora, T., Sharma, A. K., Khanna, N., ... & Sharma, K. K. (2010). Reversal of propoxur-induced impairment of memory and oxidative stress by 4'-chlorodiazepam in rats. *Naunyn-Schmiedeberg's archives of pharmacology*, 381(1), 1-10. <https://doi.org/10.1007/s00210-009-0475-z>
- Nassar, M. I., Gaara, A. H., El-Ghorab, A. H., Farrag, A., Shen, H., Huq, E., & Mabry, T. J. (2007). Chemical constituents of clove (*Syzygium aromaticum*, Fam. Myrtaceae) and their antioxidant activity. *Revista Latinoamericana de Química*, 35(3), 47.
- Neveu, V., Perez-Jiménez, J., Vos, F., Crespy, V., du Chaffaut, L., Mennen, L., ... & Scalbert, A. (2010). Phenol-Explorer: an online comprehensive database on polyphenol contents in foods. *Database*, 2010. <https://doi.org/10.1093/database/bap024>

- Ogunwande, I. A., Olawore, N. O., Ekundayo, O., Walker, T. M., Schmidt, J. M., & Setzer, W. N. (2005). Studies on the essential oils composition, antibacterial and cytotoxicity of *Eugenia uniflora* L. *International journal of Aromatherapy*, 15(3), 147-152. <https://doi.org/10.1016/j.ijat.2005.07.004>
- Parthipan, S., Gokul, S., Eswaran, C., Jaya Surya, S., Nithyakalyan, S., & Suganaya, S. (2022). Security for Medical Image Using RSA. *International Academic Journal of Innovative Research*, 9(1), 20–27.
- Prasad, R. C., Herzog, B., Boone, B., Sims, L., & Waltner-Law, M. (2005). An extract of *Syzygium aromaticum* represses genes encoding hepatic gluconeogenic enzymes. *Journal of ethnopharmacology*, 96(1-2), 295-301. <https://doi.org/10.1016/j.jep.2004.09.024>
- Rajan, V., & Chawla, R. (2024). Anthropometric Variations and Adaptations across Diverse Ecological Zones. *Progression journal of Human Demography and Anthropology*, 1-4.
- Russo, A., Formisano, C., Rigano, D., Senatore, F., Delfine, S., Cardile, V., ... & Bruno, M. (2013). Chemical composition and anticancer activity of essential oils of Mediterranean sage (*Salvia officinalis* L.) grown in different environmental conditions. *Food and Chemical Toxicology*, 55, 42-47. <https://doi.org/10.1016/j.fct.2012.12.036>
- Sanae, F., Kamiyama, O., Ikeda-Obatake, K., Higashi, Y., Asano, N., Adachi, I., & Kato, A. (2014). Effects of eugenol-reduced clove extract on glycogen phosphorylase b and the development of diabetes in db/db mice. *Food & function*, 5(2), 214-219.
- Sarrami, N., Pemberton, M. N., Thornhill, M. H., & Theaker, E. D. (2002). Adverse reactions associated with the use of eugenol in dentistry. *British dental journal*, 193(5), 257-259. <https://doi.org/10.1038/sj.bdj.4801539>
- Shan, B., Cai, Y. Z., Sun, M., & Corke, H. (2005). Antioxidant capacity of 26 spice extracts and characterization of their phenolic constituents. *Journal of agricultural and food chemistry*, 53(20), 7749-7759. <https://doi.org/10.1021/jf051513y>
- Shields, K. M., McQueen, C. E., & Bryant, P. J. (2004). National survey of dietary supplement resources at drug information centers. *Journal of the American Pharmacists Association*, 44(1), 36-40. <https://doi.org/10.1331/154434504322713219>
- Shukri, R., Mohamed, S., & Mustapha, N. M. (2010). Cloves protect the heart, liver and lens of diabetic rats. *Food chemistry*, 122(4), 1116-1121. <https://doi.org/10.1016/j.foodchem.2010.03.094>
- Shyamala, M. P., Venukumar, M. R., & Latha, M. S. (2003). Antioxidant potential of the *Syzygium aromaticum* (Gaertn.) Linn.(cloves) in rats fed with high fat diet. *Indian Journal of pharmacology*, 35(2), 99-103.
- Trifan, A., Luca, S. V., Greige-Gerges, H., Miron, A., Gille, E., & Aprotosoiaie, A. C. (2020). Recent advances in tackling microbial multidrug resistance with essential oils: Combinatorial and nano-based strategies. *Critical Reviews in Microbiology*, 46(3), 338-357. <https://doi.org/10.1080/1040841X.2020.1782339>

- Tungare, K., Bhorl, M., Patil, S. A., Iyer, P., Jagtap, N., Kadam, A., & Vijayakuma, S. (2024). Clove Buds (*Syzygium aromaticum*). In *Medicinal Spice and Condiment Crops* (pp. 200-224). CRC Press.
- Ullah, M. A., Hassan, A., & Hamza, A. (2023). Role of clove in human medical history. *SAR Journal of Anatomy and Physiology*, 4(2), 10-19. <https://doi.org/10.36346/sarjap.2023.v04i02.001>
- Vanin, A. B., Orlando, T., Piazza, S. P., Puton, B. M., Cansian, R. L., Oliveira, D., & Paroul, N. (2014). Antimicrobial and antioxidant activities of clove essential oil and eugenyl acetate produced by enzymatic esterification. *Applied biochemistry and biotechnology*, 174(4), 1286-1298. <https://doi.org/10.1007/s12010-014-1113-x>
- Vennekens, R., Vriens, J., & Nilius, B. (2008). Herbal compounds and toxins modulating TRP channels. *Current neuropharmacology*, 6(1), 79-96. <https://doi.org/10.2174/157015908783769644>
- Verma, S. K., Garg, D. A. K., Singh, D. M., Panwar, D. N., Meena, D. M., & Singh, D. C. (2018). Evaluation of analgesic activity of *Syzygium aromaticum* w. sr to painful tooth. *World J Pharm Res*, 7(5), 827-834. <https://doi.org/10.20959/wjpr20185-11212>
- Yasuda, H., Fujiwara, A., Komiya, S., & Haze, T. (2017). Effects of rosuvastatin add-on treatment on hyperlipidemia in type 2 diabetic patients with chronic kidney disease receiving ethyl icosapentate. *Atherosclerosis*, 263, e241-e242.